

# Advances in Medicinal and Aromatic Plants

Production, Processing,  
and Pharmaceuticals



Amritesh C. Shukla | Sunita Facknath  
Debashis Mandal | Bernadette Montanari  
Editors

 **CRC Press**  
Taylor & Francis Group  
APPLE ACADEMIC PRESS

# Advances in Medicinal and Aromatic Plants

Production, Processing,  
and Pharmaceuticals

VOLUME 1



Amritesh C. Shukla | Sunita Facknath  
Debashis Mandal | Bernadette Montanari  
Editors

 **CRC Press**  
Taylor & Francis Group  
APPLE ACADEMIC PRESS

**ADVANCES IN MEDICINAL AND  
AROMATIC PLANTS**

**Volume 1**

**Production, Processing, and Pharmaceutics**

Advances in Medicinal and Aromatic Plants: Production, Processing, and Pharmaceutics,  
2-volume set

Hardback ISBN: 978-1-77491-488-5

Paperback ISBN: 978-1-77491-489-2

Ebook ISBN: 978-1-03268-690-5

**Volume 1:**

Hardback ISBN: 978-1-77491-790-9

Paperback ISBN: 978-1-77491-791-6

**Volume 2:**

Hardback ISBN: 978-1-77491-792-3

Paperback ISBN: 978-1-77491-793-0

# **ADVANCES IN MEDICINAL AND AROMATIC PLANTS**

**Volume 1**

**Production, Processing, and Pharmaceutics**

*Edited by*

**Amritesh C. Shukla, PhD**

**Sunita Facknath, PhD**

**Debashis Mandal, PhD**

**Bernadette Montanari, PhD**

**AAP** | APPLE  
ACADEMIC  
PRESS

First edition published 2025

**Apple Academic Press Inc.**  
1265 Goldenrod Circle, NE,  
Palm Bay, FL 32905 USA  
760 Laurentian Drive, Unit 19,  
Burlington, ON L7N 0A4, CANADA

**CRC Press**  
2385 NW Executive Center Drive,  
Suite 320, Boca Raton FL 33431  
4 Park Square, Milton Park,  
Abingdon, Oxon, OX14 4RN UK

© 2025 by Apple Academic Press, Inc.

*Apple Academic Press exclusively co-publishes with CRC Press, an imprint of Taylor & Francis Group, LLC*

Reasonable efforts have been made to publish reliable data and information, but the authors, editors, and publisher cannot assume responsibility for the validity of all materials or the consequences of their use. The authors, editors, and publishers have attempted to trace the copyright holders of all material reproduced in this publication and apologize to copyright holders if permission to publish in this form has not been obtained. If any copyright material has not been acknowledged, please write and let us know so we may rectify in any future reprint.

Except as permitted under U.S. Copyright Law, no part of this book may be reprinted, reproduced, transmitted, or utilized in any form by any electronic, mechanical, or other means, now known or hereafter invented, including photocopying, microfilming, and recording, or in any information storage or retrieval system, without written permission from the publishers.

For permission to photocopy or use material electronically from this work, access [www.copyright.com](http://www.copyright.com) or contact the Copyright Clearance Center, Inc. (CCC), 222 Rosewood Drive, Danvers, MA 01923, 978-750-8400. For works that are not available on CCC please contact [mpkbookspermissions@tandf.co.uk](mailto:mpkbookspermissions@tandf.co.uk)

Trademark notice: Product or corporate names may be trademarks or registered trademarks and are used only for identification and explanation without intent to infringe.

---

### Library and Archives Canada Cataloguing in Publication

Title: Advances in medicinal and aromatic plants : production, processing, and pharmaceuticals / edited by Amrithesh C. Shukla, PhD, Sunita Facknath, PhD, Debashis Mandal, PhD, Bernadette Montanari, PhD.

Names: Shukla, Amrithesh C., editor. | Facknath, Sunita, editor. | Mandal, Debashis, editor. | Montanari, Bernadette, editor.

Description: First edition. | Includes bibliographical references and indexes.

Identifiers: C anadiana ( print ) 2 0230593216 | C anadiana ( ebook ) 2 0230593275 | I SBN 9 781774914885 ( set ) | ISBN 9781774917909 (v. 1 ; hardcover) | ISBN 9781774917916 (v. 1 ; softcover) | ISBN 9781032686905 (ebook)

Subjects: LCSH: Medicinal plants. | LCSH: Aromatic plants. | LCSH: Materia medica, Vegetable. | LCSH: Botany, Medical. | LCSH: Pharmacognosy.

Classification: LCC QK99.A1 A38 2024 | DDC 581.6/34—dc23

### Library of Congress Cataloging-in-Publication Data

Names: Shukla, Amrithesh C., editor. | Facknath, Sunita, editor. | Mandal, Debashis, editor. | Montanari, Bernadette, editor.

Title: Advances in medicinal and aromatic plants. Volume 1, Production, processing, and pharmaceuticals / edited by Amrithesh C. Shukla, Sunita Facknath, Debashis Mandal, Bernadette Montanari

Description: First edition | Palm Bay, FL : Apple Academic Press, 2025 | Includes bibliographical references and index | Summary: "This new two-volume book categorically provides detailed information on highly demanded and medicinally important plants and their natural habits and habitats, taxonomy, cultivation practices, essential oils, active ingredients, biomolecules, modes of action, drug development, and value additions for marketing purpose. Examples of such plants include *Achillea* spp. (yarrow), *Acorus calamus* (sweet flag), *Ocimum* spp. (basil), *Dioscorea* spp., *Eucalyptus* spp., *Commiphora* spp. (guggul), *Kaempferia galanga* (aromatic ginger), and *Lavandula* spp. (lavender). Many others are included in the volume as well. With contributions from international experts, these two volumes present chapters that detail the history of these major medicinal and aromatic plants and also report on systematic botany, advanced production and propagation technologies, plant nutrition, moisture management, intercultivation, plant protection, postharvest technology, processing-value addition, and marketing trade. Further, the book presents promising low-cost and ecofriendly plant products and biomolecules, which are free from side-effects for use as pharmaceuticals and herbal drugs. The most ancient form of medical therapies involving herbs has been neglected for a few decades back and has regained enormous popularity because of the effectiveness and fewer hazardous properties of many medicinal and aromatic plants. Nature has all sorts of protective medicinal compounds within its huge bioresources, which are still being identified for beneficial health purposes. Herbs containing aromatic properties because of their essential oils also have medicinal uses apart from being used as dependable sources of natural fragrance for cosmetics, perfumery, and food industries competing with synthetic aroma chemicals. These volumes will be an excellent and comprehensive compendium for academicians and professionals working in plant resources. The compilation will also be valuable for students, researchers, medical practitioners, farmers, entrepreneurs, traders, industrialists, and NGOs who are involved in research and development and production and pharmaceuticals of medicinally important plants"-- Provided by publisher

Identifiers: LCCN 2023055751 (print) | LCCN 2023055752 (ebook) | ISBN 9781774917909 (hardcover) | ISBN 9781774917916 (paperback) | ISBN 9781032686905 (ebook)

Subjects: LCSH: Medicinal plants. | Materia medica, Vegetable. | Botany, Medical. | Pharmacognosy.

Classification: LCC QK99.A1 A38 2024 (print) | LCC QK99.A1 (ebook) | DDC 581.6/34--dc23/eng/20231219

LC record available at <https://lccn.loc.gov/2023055751>

LC ebook record available at <https://lccn.loc.gov/2023055752>

---

ISBN: 978-1-77491-790-9 (hbk)

ISBN: 978-1-77491-791-6 (pbk)

## About the Editors

---



**Amritesh C. Shukla, PhD**

*Professor, Department of Botany,  
University of Lucknow, Lucknow, India*

Amritesh C. Shukla, PhD, is currently working as a Professor in the Department of Botany at the University of Lucknow, India. Dr. Shukla did his DPhil and DSc in Botany at the University of Allahabad, India. He served as a Reader/Professor and Head of the Department of Horticulture, Aromatic and Medicinal Plants at Mizoram University, Aizawl, India (2007–16). He has been working on medicinal and aromatic plants, cultivation, conservation, bioprospection, natural products, drug development, and patenting since 1995. He has standardized various scientific methods, such as MSGIT, MDKT MS-97, NCCLS (2002–03), and successfully handled six major research projects and is currently supervising one European Union project (No. 8944160). He has developed commercial herbal formulations and has US, UK, Japanese, and Indian patents. In addition to this, he has supervised 21 master's theses and 10 PhD dissertations. He has published over 115 research papers/articles in nationally and internationally reputed journals as well as 10 books (authored four and edited six), published by AAP-CRC Press (2019), Springer (2020), etc.

Dr. Shukla works as an editor, associate editor, and editorial board member of many internationally reputed journals, such as the *American Journal of Food Technology*, *Journal of Pharmacology and Toxicology*, *Research Journal of Medicinal Plants*, and as reviewer for *Scientific Reports*, *International Journal of Dermatology*, *European Journal of Medicinal Plants*, *African Journal of Agricultural Research*, *International Journal of Agricultural Chemistry*, and *Journal of Herbs, Spices, and Medicinal Plants*.

Prof. Shukla has vast overseas experience in R&D for medicinal and aromatic plants in India and several countries in Asia and the Pacific regions. He has been an invited speaker at the Indo-Brazilian Symposium (2020); and delivered lecture and chaired session at the ISHS-IV Asia Symposium on Quality Management in Postharvest Systems, Jeonju, Korea (2017).

He is a member of the International Society for Horticultural Science, Belgium (2016). He was an invited scientist at the International Conferences on Controlled Atmosphere and Fumigation in Stored Products (CAF), Gold Coast, Australia (2004); CAF, Fresno, USA (2000); 7th International Working Conference on Stored-Product Protection, Beijing, China (1998); and 4th European Foundation for Plant Pathology, Berlin, Germany. He has also been a Visiting Professor at the University of Mauritius (2014) and at the University of British Columbia, Canada (2013–14), as well as a member of an expert panel for promotion to Professor in the Department of Botany and Microbiology, College of Science, King Saud University, Saudi Arabia (2018), and in the Research Degrees and Scholarships Committee, Murdoch University, Perth, Australia (2019–21).

For his outstanding scientific contribution, Prof. Shukla has been honored with a Y.S. Murty Memorial Gold Medal; Prof. R.C. Pant Memorial Award; NESA-Scientist of the Year Award; ISC-Member of the Sectional Committee, Plant Sciences Section of the 101st Indian Science Congress; and IPS Medal-98. He has been the executive councilor of the Indian Botanical Society; chairman of the International Symposium on Sustainable Horticulture (ISSH-2016); member of the State-Level Steering Committee for the National Mission on Medicinal Plants, Government of Mizoram; program coordinator of the Indian Academy of Sciences, Bangalore; program coordinator – CSIR-CIMAP Training; convener at the ASSOCHAM Conference; course director of RAMAPS; and convener – NCNRM, India. In addition, he is a fellow of the Ethnobotanical Society, the Society of Life Sciences, the Indian Botanical Society, the International Young Scientist Association, and the Linnean Society of London (2021).



**Sunita Facknath, PhD**

*Professor, Faculty of Agriculture,  
University of Mauritius, Mauritius*

Sunita Facknath, PhD, is a Professor engaged in teaching and research in agricultural technology for the past 25 years at the University of Mauritius. She has published more than 100 research papers and articles in reputed journals and conference proceedings. In addition, she dealt with 20 research projects externally funded by important internally renowned institutes/agencies, such



as the World Bank, European Union, International Atomic Energy Agency, ACU, African Union, Development Finance International, Climate and Development Knowledge Network (CDKN), etc. Further, she is a consultant agriculturist for many public-private sectors and NGOs based in Mauritius (FAO, EUCDP, UNDP, UNEP-Mauritius, FANRPAN, Mauritius Research Council, Government of Mauritius; SGS Co Ltd., DDS, MACOSS, etc.). She has guided 15 MPhil and PhD students and also has profound administrative experience at the University of Mauritius and also at multiple national and international bodies like the African Network of Research on Bruchids, Mauritius Council for Social Services (MACOSS), African Regional Program in Insect Science (ARPIS) Academic Board, Fishermen Investment Trust, Ministry of Fisheries and Rodrigues, National Biosecurity Technical Advisory Committee, Mauritius Standards Bureau Committee, National Marine Biotechnology Advisory Council, National Ocean Knowledge Cluster Advisory Council, UoM Senate, etc.



**Debashis Mandal, PhD**

*Assistant Professor, Department of Horticulture,  
Aromatic and Medicinal Plants,  
Mizoram University, Aizawl, Mizoram, India*

Debashis Mandal, PhD, is an Assistant Professor in the Department of Horticulture, Aromatic and Medicinal Plants at Mizoram University, Aizawl, Mizoram, India. He is a young academician and research fellow who has been working in sustainable hill farming for the past 11 years. He did his PhD at BCKV, India, and was a post-doctoral project scientist at IIT, Kharagpur, India. He previously worked as an Assistant Professor at Sikkim University, India, and has published 48 research papers and book chapters in reputed journals and books. He has also published nine books from Apple Academic Press, American Academic Press, and Lambert Academic Publishing. He is also working as a member of the Working Group Lychee and Other Sapindaceae Crops, ISHS, Belgium, and is also a member in the ISHS section on tropical and subtropical fruits, organic horticulture, and the commission on quality and postharvest horticulture. Currently, he is working as an Editor-in-Lead (Horticulture) for the *International Journal of Bio-Resources and Stress Management (IJBSM)* and editorial board member of *Bulletin Agrotechnology, Research on Crops, Crop Research, Journal of*

*Postharvest Technology*, *Senhri Journal of Multidisciplinary Studies*, etc. Dr. Mandal is also an editorial advisor in Horticulture Science for Cambridge Scholar Publishing, United Kingdom, and a regular reviewer of journals that include *Fruits*, *HortScience*, *Acta Physiologica Plantarum*, *African Journal of Agricultural Research*, *Journal of Food Quality*, etc. Further, he is a consultant horticulturist in the Department of Horticulture and Agriculture (Research and Extension), Government of Mizoram, India, and Himadri Specialty Chemicals Ltd., and is also handling externally funded research projects. He was a convener for the International Symposium on Sustainable Horticulture, 2016, India, and a co-convener for the International Conference of Bio-Resource and Stress Management, 2017, Jaipur, India. In addition, he was a session moderator and keynote speaker at the ISHS Symposium on Litchi, India, in 2016, on postharvest technology in Vietnam, 2014, and at South Korea, 2017, and AFSA Conference in 2018, Cambodia. He is the recipient of the Best Editor Award (2017) by IJBSM, the Young Achiever Award (2019) by SADHNA, the Best Researcher Award (2020) by Scifax, and the Young Scientist Award (2020) by the Society of Tropical Agriculture. He has visited countries like Thailand, China, Nepal, Bhutan, Vietnam, South Korea, South Africa, and Cambodia for professional meetings, seminars, and symposia. His thrust areas of research are organic horticulture, pomology, postharvest technology, plant nutrition, and micro-irrigation.



**Bernadette Montanari, PhD**

*Interdisciplinary Institute of Social Studies,  
University Sidi Mohamed Ben Abdellah,  
Fez, Morocco*

Bernadette Montanari, PhD, is a proactive Research Scholar with degrees (PhD Ethnobiology and MSc Ethnobotany) from the School of Anthropology and Conservation, University of Kent, UK. Her work is at the intersection of medicinal plants, natural resources and natural products as well as in the development for women and community enterprises, women's traditional ecological knowledge, social policies, and social justice. She has consistent research activities through multiple interdisciplinary research projects on the social-economic impact of international and national policies on community development. Her latest two Marie-Curie Fellowships of the European Union reflect her engagement. The first related to policies for the recognition of women's traditional knowledge in natural product

development in the Green Morocco Plan, Morocco; the latter on the factors that determined the attribution of Access to Benefit Sharing (ABS) of the Nagoya Protocol for mint farmers in India and for women working in argan oil cooperatives in Morocco. She has published several significant research papers and book chapters in reputed international journals and books. She is currently a research member of the Interdisciplinary Institute of Social Studies at the University Sidi Mohamed Ben Abdallah, Fes, Morocco, where she is pursuing her work on community development. She is an affiliated member of the Centre for Biocultural Diversity, University of Kent, UK, and a collaborating researcher at the Centre for Research in Anthropology at the University Institute of Lisbon, Portugal. Moreover, she is a member of several organizations: Société Française d'ethno-pharmacologie, France; Conservatoire des Plantes à Parfum, Médicinales et Aromatiques (CNPMAI), France; IUCN Sustainable Use and Livelihoods Specialist Group (SULi); Species Survival Commission (SSC) and Commission on Environmental, Economic, and Social Policy (CEESP); IPACC, North Africa. Previously she held professional affiliations with the Laboratoire Population, Environnement & Développement (LPED), University Aix-Marseille, France; Women and Global Perspectives Program (WGPP), University of Illinois, USA, among others.



# Taylor & Francis

Taylor & Francis Group

<http://taylorandfrancis.com>

# Contents

---

<i>Contributors</i> .....	<i>xiii</i>
<i>Abbreviations</i> .....	<i>xv</i>
<i>Preface</i> .....	<i>xix</i>
<b>1. <i>Achillea</i> (Yarrow): Diversity, Trade Potential, and Ethnomedicinal Uses .....</b>	<b>1</b>
Mustafa Eray Bozyel, Elif Merdamert-Bozyel, Kerem Canli, and Amritesh C. Shukla	
<b>2. <i>Acorus calamus</i> L. (Sweet Flag): Bioactive Compounds, Medicinal Properties, and Biological Activity .....</b>	<b>21</b>
Sabyasachi Banerjee, Karan Kumar Das, Goutam Pal, and Sankhadip Bose	
<b>3. <i>Ocimum</i> spp. (Basil): An Incredible Plant .....</b>	<b>89</b>
Moumita Malakar and Debashis Mandal	
<b>4. <i>Dioscorea</i> spp.: Medicinal Plant with Pharmaceutical Uses .....</b>	<b>165</b>
Raza Waris, Priyanka Agnihotri, Debashis Mandal, and Amritesh C. Shukla	
<b>5. <i>Eucalyptus</i> spp.: A Wonder Tree .....</b>	<b>185</b>
Moumita Malakar	
<b>6. <i>Commiphora</i> spp. (Guggul): A Wonder Ayurvedic Drug.....</b>	<b>261</b>
Jai Malik and Subash C. Mandal	
<b>7. <i>Kaempferia galanga</i> L. (Aromatic Ginger): A High Potential Zingiberaceae Species .....</b>	<b>283</b>
Lilly Zeitler	
<b>8. <i>Lavandula</i> spp. (Lavender): A Herb More Than Just a Relaxing Scent.....</b>	<b>315</b>
Moumita Malakar	
<b><i>Index</i>.....</b>	<b>389</b>



# Taylor & Francis

Taylor & Francis Group

<http://taylorandfrancis.com>

# Contributors

---

## **Priyanka Agnihotri**

Plant Diversity, Systematics and Herbarium Division, CSIR–National Botanical Research Institute, Lucknow, Uttar Pradesh, India

## **Sabyasachi Banerjee**

Department of Phytochemistry, Gupta College of Technological Sciences, Ashram More, Asansol, West Bengal, India

## **Sankhadip Bose**

School of Pharmacy, The Neotia University, Sarisa, Diamond Harbour Road, West Bengal, India

## **Elif Merdamert-Bozyel**

Health Institutes of Türkiye (TUSEB), Istanbul, Türkiye

## **Mustafa Eray Bozyel**

Department of Biology, Faculty of Science, Dokuz Eylül University, Izmir, Türkiye

## **Kerem Canli**

Department of Biology, Faculty of Science, Dokuz Eylül University, Izmir, Türkiye;  
Fauna and Flora Research and Application Center, Dokuz Eylül University, Izmir, Türkiye

## **Karan Kumar Das**

Bharat Technology, Jadurberia, Uluberia, Howrah, West Bengal, India

## **Moumita Malakar**

Assistant Professor, Department of Horticulture, Central University of Tamil Nadu, Neelakudy, Thiruvavur, Tamil Nadu, India

## **Jai Malik**

University Institute of Pharmaceutical Sciences, Centre of Advanced Study, Panjab University, Chandigarh, India

## **Debashis Mandal**

Department of Horticulture, Aromatic and Medicinal Plants, Mizoram University, Aizawl, Mizoram, India

## **Subash C. Mandal**

Department of Pharmaceutical Technology, Jadavpur University, Kolkata, West Bengal, India

## **Goutam Pal**

Institute of Pharmacy, Kalyani, West Bengal, India

## **Amritesh C. Shukla**

Department of Botany, Faculty of Science, University of Lucknow, Lucknow, Uttar Pradesh, India

## **Raza Waris**

Department of Botany, University of Lucknow, Lucknow, Uttar Pradesh, India; Plant Diversity, Systematics and Herbarium Division, CSIR–National Botanical Research Institute, Lucknow, Uttar Pradesh, India

## **Lilly Zeitler**

Sustainable International Agriculture Student, Georg-August University of Göttingen and University of Kassel, Germany



# Taylor & Francis

Taylor & Francis Group

<http://taylorandfrancis.com>



# Abbreviations

---

AA	arachidonic acid
AFM	atomic force microscopy
BGC	blue gum chalcid
BMI	body mass index
BOP	bleeding on probing
BP	blood pressure
BSA	bulked segregant analysis
BSEP	bile salt export pump
C4H	cinnamate 4-hydroxylase
CAL	clinical attachment level
Camp	cyclic adenosine monophosphate
CCoAOMT	caffeoyl coenzyme A O-methyltransferase
CDK	cyclin-dependent kinase
CDRI	Central Drug Research Institute
CIMAP	Central Institute of Medicinal and Aromatic Plants
CITES	convention on international trade in endangered species
CLX	chlorhexidine
CNS	central nervous system
COMT1	caffeate/5-hydroxyconiferaldehyde O-methyltransferase 1
COX-2	cyclooxygenase-2
CPM	continuous passive motion
CRP	c-reactive protein
CSF	cerebrospinal FLUID
DAP	days after planting
DMAPP	dimethylallyl pyrophosphate
DTH	delayed-type hypersensitivity
EAC	Ehrlich ascites carcinoma
ECHA	European Chemical Agency
ECS	endocannabinoid system
EEG	electroencephalography
EO	essential oil
EST	expressed sequence tag
FU	5-fluorouracil
FXR	farnesoid X receptor
GGPPS	geranylgeranyl pyrophosphate synthase, precursor of diterpenes
GI	gingival index
GK	glucokinase

GPPS	geranyl pyrophosphate synthase
GRAS	generally recognized as safe
GSTP1	glutathione S-transferase-pi
HA	hemagglutination
HCC	hepatocellular carcinoma
HCV	hepatitis C virus
HDLP	high-density lipoproteins
HK	hexokinase
IC	inhibitory concentration
ICBN	international code of botanical nomenclature
IPP	isopentenyl pyrophosphate
IPRs	intellectual property rights
IRAP	Institute of Roses and Aromatic Plants
IUCN	International Union for Conservation of Nature
JA	jasmonic acid
JNK	c-Jun NH <sub>2</sub> -terminal kinase
LPS	lipopolysaccharides
MAPK	mitogen-activated protein kinases
MAS	marker-assisted selection
MDMs	monocyte-derived macrophages
MGMT	methylguanine-DNA methyl transferase
MI	myocardial infraction
MIC	minimum inhibitory concentration
MMP-9	matrix metalloproteinase 9
MRSA	methicillin-resistant Staphylococcus aureus
MTT	methyl thiazol tetrazolium
NFE2	nuclear factor erythroid 2
NGF	nerve growth factor
NI	North India
NO	nitric oxide
NPK	nitrogen, phosphorus, potassium
NSAIDS	non-steroidal anti-inflammatory drug
OMC	organic matter content
PAL	phenylalanine ammonia-lyase
PC	prostate cancer
PCA	principal component analysis
PCR	polymerase chain reaction
PD	probing depth
PFK	phosphofructokinase
PGE2	prostaglandin E2
PGIMS	Post Graduate Institute Memory Scale
PI	plaque index
PKA	protein kinase A

PLA	plaque accumulation
POH	perillyl alcohol
PPAR	peroxisome proliferator-activated receptor
PSQI	Pittsburgh sleep quality index
PVPFR	plant variety protection and farmers right
QTL	quantitative trait locus
RANKL	receptor activator of NF- $\kappa$ B ligand
RBC	red blood cells
RH	relative humidity
RIFA	red imported fire ant
ROS	reactive oxygen species
SBP	systolic blood pressure
SCAR	sequenced characterized amplified region
SEM	scanning electron microscope
SFE	supercritical fluid extraction
SRAP	sequence-related amplified polymorphism
SRBCs	sheep red blood cells
SSCP	single-strand conformation polymorphism
SSR	simple sequence repeat
SWE	Subcritical-water extraction
TALGA	The Australian Lavender Growers Association
TCI	total calories intake
TKR	total knee replacement
TLRs	toll-like receptors
UP	Uttar Pradesh
UPGMA	unweighted pair group method with arithmetic mean
VAS	visual analog scale
VCAM-1	vascular cell adhesive molecules
VRE	vancomycin-resistant <i>Enterococcus faecalis</i>
VSMC	vascular smooth muscle cells
WBC	white blood cell
WHO	World Health Organization
WTO	World Trade Organization



# Taylor & Francis

Taylor & Francis Group

<http://taylorandfrancis.com>

# Preface

---

We are witnessing massive development in science and technology today, which has contributed to positive changes in the way of living. In tune with that, medical science has also become more technology-driven and sophisticated. Robotics nano-sciences are the latest in this regard. However, the most ancient form of medical therapy involving herbs, which was neglected a few decades back, is now gaining enormous popularity because of its effectiveness and reduced side-effects. Nature, from where we developed, has all sorts of protective medicinal compounds within its huge bioresources, which are either being identified or yet to be identified for our health and remedies.

Herbs containing aroma, because of the essential oil, also have medicinal uses apart from being used as dependable sources of natural fragrance for cosmetics, perfumery, and food industries competing with synthetic aroma chemicals.

Although a large number of books, monographs, scientific articles, and papers dealing with reports of therapeutic properties are available for certain identified plants and listed biomolecules, and are used for the management of specific or multiple ailments, however, they are scattered. Therefore, the exclusively compiled volumes of this book, are an effort to categorically provide detailed information on natural habit and habitat, taxonomy, detailed cultivation practices, processing of essential oil, active ingredients, biomolecules, mode of action, drug development, value additions as well as traditional and industrial uses for marketing purposes.

The current volume of this book, *Advances in Medicinal and Aromatic Plants: Production, Processing, and Pharmaceutics* (Vol. 1), is uniquely written, focusing on some highly demanding medicinally important plants such as *Achillea* spp. (yarrow), *Acorus calamus* (sweet flag), *Ocimum* spp. (basil), *Dioscorea* spp., *Eucalyptus* spp., *Commiphora* spp. (guggul), *Kaempferia galanga* (aromatic ginger) and *Lavandula* spp. (lavender).

This book contains precisely referenced chapters, emphasizing not only the plant history, taxonomy-botany, and production technologies involving advanced propagation, nutrition, moisture management, inter-cultivation, and plant protection but also the postharvest technology, processing-value addition, and marketing-trade. The book attempts to present emerging low-cost and environmentally friendly phytoconstituents/plant biomolecules

and herbal drugs that are free from side effects studied in the overlapping disciplines of medicinal chemistry, biochemistry, microbiology, and pharmacology.

—*Editors*

## CHAPTER 1

---

# *Achillea* (Yarrow): Diversity, Trade Potential, and Ethnomedicinal Uses

MUSTAFA ERAY BOZYEL,<sup>1</sup> ELIF MERDAMERT-BOZYEL,<sup>2</sup>  
KEREM CANLI,<sup>1,3</sup> and AMRITESH C. SHUKLA<sup>4</sup>

<sup>1</sup>*Department of Biology, Faculty of Science, Dokuz Eylül University, Izmir, Türkiye*

<sup>2</sup>*Health Institutes of Türkiye (TUSEB), Istanbul, Türkiye*

<sup>3</sup>*Fauna and Flora Research and Application Center, Dokuz Eylül University, Izmir, Türkiye*

<sup>4</sup>*Department of Botany, Faculty of Science, University of Lucknow, Lucknow, Uttar Pradesh, India*

---

### ABSTRACT

*Achillea* L. is one of the important medicinal plants, belongs to the family Asteraceae, and is distributed worldwide. Since long back, various *Achillea* species have been used for the treatment of various ailments, including wound healing, bleeding, headache, flatulence, dyspepsia, body pains, inflammation, and spasmodic diseases. Further, phytochemical studies of *Achillea* spp. have also reported several bioactive constituents, viz., terpenoids (monoterpenes, diterpenes, triterpenes, and sesquiterpenes), flavonoids, sterols, phenolic acids, and coumarins; which have strong efficacy. Besides this, the plant has already been mentioned in the traditional system of medicine. Keeping these views in mind, the present chapter reviews the diversity, market potential, and ethnomedicinal uses of *the Achillea* genus, which have been explored based on systematic validation, including *in-vitro* and *in-vivo* investigations.

## 1.1 INTRODUCTION

Since human existence on earth, man has been surrounded by ample plants that serve several purposes, including food, shed, and shelter, as well as a source of oxygen to sustain their life. The significance of plants in support of well-being is progressively perceived to the degree that the line between food and medication proved unable, in some cases, to be separated. For instance, *Allium sativum* (garlic) is a world-renowned medicinal plant species, but at the same time, it has been used for flavor in the food industry and is also one of the best natural antibiotics known in traditional medicine (Simonetti, 1990). Plants play an important and unique role in disease prevention and management.

It has been deductively shown that eating certain vegetables with cell reinforcement properties, particularly those that have a place with the Brassicaceae bunch like cabbage (*Brassica oleracea* L.) or certain Liliaceae, for example, garlic or onion, has the ability to oppose the improvement of some degenerative sicknesses like malignant growth or different illnesses of the circulatory framework (Rupp, 2011). Lycopene, a flavonoid that is available in tomatoes, has an extraordinary ability to forestall or defer the headway of diseases (Khan et al., 2008). Similarly, *Malus domestica* Borkh (apples) and *Cucumis melo* (watermelon), as they are rich in antioxidant composition, guard the digestive system against colorectal cancer (Guaâdaoui et al., 2015). Besides this, *Citrus sinensis* (oranges), *Citrus limonum* (lemon), and other species of citrus, which are rich sources of vitamin C and pectin, have shown protecting ability on the digestive system against various diseases, including cancer (Mazed et al., 2009).

Further, medicinal plants and plant parts have been used for the treatment of various ailments. In developed nations like the United States, a critical number of Americans utilize medicinal plants to fight against specific sicknesses.

Several years back, about 25% of the medicines contained plant-inferred bioactive constituents, and the quantity of visits to suppliers of customary medication surpassed the number of visits to all primary care doctors (WHO, 1999a; Kong et al., 2003). In Pakistan, it is assessed that about 52% of the populace picked complementary and alternative medication to deal with their diseases (Shaikh et al., 2009). In Japan, around 60–70% of allopathic specialists suggested customary medications for their patients. Despite this, in China, conventional medication represents about 40% of all medical



services therapies (WHO, 1999b, 2002). This review focuses on the research on *Achillea* species diversity, trade potential, and ethnomedicinal uses.

## 1.2 THE ASTERACEAE FAMILY

Asteraceae or Compositae is an enormous and far-reaching group of blooming plants within excess of 23,600 at present acknowledged species, spread across 1,620 genera and 13 subfamilies (Tamokou et al., 2017). The larger part of the individuals from the Asteraceae family are yearly or perpetual species, however remarkable number are likewise plants, bushes, and trees. The family has overall conveyance, from the polar areas to the jungles, colonizing a wide assortment of natural surroundings. It is almost entirely expected in the parched and semiarid locales of subtropical and lower temperate latitudes (Barkley et al., 2006).

The Asteraceae family includes a diverse gathering of plant spp. which are important for human food, oil creation, ornamentals, insect poisons, therapeutic uses, and trade applications (Dempewolf et al., 2008). Asteraceae is of a financially significant family, giving items like cooking oils, sunflower seeds, espresso substitutes, natural teas, lettuce, artichokes, and improving specialists. Other than this, a few genera are of green significance, like *Echinacea* (coneflowers), pot marigold (*Calendula officinalis*), different daisies, fleabane, chrysanthemums, dahlias, zinnias, and heleniums. Asteraceae are significant in-home-grown medications, including *Grindelia*, yarrow, and numerous others (Anonymous, 2019a). Various species are considered obtrusive, including, most remarkably in North America, dandelion (*Taraxacum officinale*), which was initially presented by European pioneers who utilized the young leaves as a serving of mixed green salad (Anonymous, 2019b).

## 1.3 PHARMACOLOGY AND PHYTOCHEMISTRY OF ASTERACEAE

Asteraceae species have been used medicinally to treat a variety of illnesses and symptoms, including inflammation, colds, flu, and pulmonary and respiratory diseases. Further, ethnobotanical records suggested that various plant/plant parts have been used for the treatments of pulmonary illnesses, viz., asthma, bronchitis, colds, coughs, chest constrictions, pneumonia, and sinus attacks (Moerman, 2003). The rationale behind bioactivity research of plant secondary metabolites is often based on these ethnobotanical reports. For instance, *Echinacea* species are often used in traditional medicine to

treat colds, coughs, and flu (Barrett, 2003). Further, the anti-inflammatory properties of *Echinacea* extracts on 5-lipoxygenase (5-LOX) were reported to have a considerable inhibitory effect (Merali et al., 2003). Research determining the anti-inflammatory properties of the genus recorded noteworthy inhibitory effects of *Echinacea* extracts on 5-lipoxygenase (5-LOX) activity (Merali et al., 2003).

This enzyme is liable for leukotriene amalgamation, bringing about bronchoconstriction and mucous creation in different pneumonic conditions. At the point when hindered, these physiological side effects would diminish. By looking at the aspiratory applications inside Asteraceae, this chapter further examines the customary utilization of North American species as pneumonic and respiratory medicines (Kachura, 2018). Within this family, the Anthemideae tribe comprises 110 genera scattered transcendentally all around the Mediterranean, Southern Africa, and Central Asia; however, there is also the profusion of North American species. Over half of the species are classified into five genera, including *Artemisia*, the largest of the group, as well as *Achillea* (Watson et al., 2000). Several *Artemisia* species are widespread across North America, though many are located in the western United States and Canada.

*Achillea* and *Artemisia* are two genera commonly utilized for treating pneumonic diseases and their side effects, like respiratory contaminations, colds, hacks, stiffness, and asthma, dependent on North American ethnobotanical reports. A few *Artemisia* spp. have been tried for bioactivity and contain phytochemicals liable for these therapeutic properties. The three main classes of components within Anthemideae are flavonoids, polyacetylenes, and sesquiterpene lactones (Greger, 1977). Luteolin, a flavonoid found in *Artemisia afra*, contributes to the bronchodilatory effects of this species. Using an isolated perfused lung system to test the effects of *A. afra* and the traditional method of steam inhalation, extracts were found to decrease tidal volume and lung resistance, both involved in the bronchodilatory process (Mjiqiza et al., 2013). Further, *Artemisia* has been broadly used to take care of pulmonary symptoms, however, extracts of yarrow have not yet been tested in respiratory models. Here, it is important to assess different plant parts and organs for discrepancy in bioefficacy, not only due to the ethnobotanical records show the selective use of separate plant parts for medicinal uses but because different plant parts and organs generally differ in their phytoconstituent (Kachura, 2018).

For quite a long time, the advancement of societies and their particular uses of medicinal plants have prompted the cutting-edge disclosure of

bioactive constituents and the exact relationship of various natural products to explicit physiological functions. With medicinal plants, such pharmacological activities are generally mediated by secondary metabolites, which vary widely in their structure and distribution among plant taxa. These phytochemicals are frequently the evolutionary components of plant–animal or plant–microbe interactions (e.g., for plant defense). Several herbivorous insects have adapted to these defenses and, in some cases, may sequester them for their protection. For example, *Longitarsus* beetles sequester and metabolize pyrrolizidine alkaloids found in Asteraceae host plants and use them for their defense, while the same phytochemicals effectively deter herbivory by another insect (Dobler et al., 2000; Macel et al., 2005). Plant bioactive compounds used as herbal medicine (or as pesticides) are rooted in, and in some cases comparable to, such co-evolution of plants and insects, providing another basis of reasoning for investigating the bioactivity of plant secondary metabolites (Kachura, 2018).

The phytochemical analysis of plants within the Asteraceae family has been studied comprehensively. There are several general phytochemical groups that are a feature of this family, including alkylamides. Further, various produce of these plants have already been used in several systems of traditional medicines; alkylamides are recorded in more than 100 spp. from 26 plant families, with the majority from the Asteraceae family (Boonen et al., 2012). The three most common species of *Echinacea* (Heliantheae) such as *Echinacea angustifolia*, *Echinacea pallida*, and *Echinacea purpurea*, contain a wide range of bioactive compounds, including alkylamides (Bauer et al., 1989; Woelkart et al., 2005). Alkylamides are secondary metabolites with anti-inflammatory properties, often acting as agonists to receptors in the endocannabinoid system (ECS). This mechanism is responsible for the significant immunomodulatory and anti-inflammatory properties of medicinal plants such as *Echinacea* (Raduner et al., 2006; Woelkart et al., 2005). Given the close taxonomic relationship of Heliantheae and Anthemideae tribes, it is possible that alkyl amides are present in several genera of Anthemideae and contribute to reduced soreness rampant in pulmonary diseases. It was hypothesized that higher levels of alkylamides exist in the most used North American Anthemideae species selected for pulmonary treatments. A systematic review of the online Alkamid database (Boonen et al., 2012) identified 92 alkylamide compounds isolated within the Anthemideae. Further, on comparing these data to North American Anthemideae, as preferred for pulmonary aid, a total of 21 distinct alkyl amides were recorded in two of the pulmonary species, viz., *Achillea millefolium* and *Artemisia dracunculus*.

According to this database, the majority of known alkylamides are recorded in *Achillea* spp., while only 03 have been extracted in *A. dracunculus*. However, the Alkamid database is dubious and an extensive list. Further phytochemical research should be completed on Anthemideae to provide updated reports (Kachura, 2018).

#### 1.4 THE GENUS *ACHILLEA*

*Achillea* procured its name after the legendary Greek person, Homer's saint Achilles,' who found the therapeutic miracles of this plant (Thieret, 2001) and disseminated it among his warriors to stanch the blood from their injuries. Its common name, Yarrow, began from the Scots language, meaning 'rough stream,' attributable to Scotland's Yarrow River (Armitage, 1987). The genus *Achillea* comprises of 200 types of perennial herbs distributed throughout Europe, North and West Asia, and North Africa (Gabbrielli et al., 1988).

*Achillea* commonly represents *Achillea millefolium*, and it roughly translates to Eurasia and is widely naturalized in temperate and boreal zones of the Northern Hemisphere, and slighter extent to southern regions. These plants are widespread and tend to become weedy and invasive (Armitage, 1987).

Yarrow's recorded standing for recuperating wounds made it famous among the military, and this affiliation prompted a large number of its common names: knight's milfoil, Herbe Militaris, staunchweed, bloodwort, and warrior's woundwort (Grieve, 1974; Leyel, 1972).

Yarrow has delighted in shifting prominence as a cure through the ages. Its ethics were recorded first by Dioscorides (Kremers, 1921) and later in numerous herbals and books on therapeutic plants (Angier, 1978; Grieve, 1974; Hutchens, 1969; Hylton, 1974; Krochmal & Krochmal, 1973; Levy, 1966; Lewis & Elvin-Lewis, 1977; Leyel, 1972; Moerman, 1977; Thomson, 1978; Tobe, 1969; Weiner, 1972). The dried leaves and blooming tops were true in the United States Pharmacopeia from 1836–1882 for tonic, energizer, and emmenagogue purposes (Vogel, 1970). Yarrow is as yet recorded in the pharmacopeias of Austria, Hungary, Poland, and Switzerland, and its unstable oil is recorded in the Romanian Pharmacopeia and The Extra Pharmacopeia (Wade, 1977). Some have asserted that the American plant, *A. lanulosa*, is more medically potent than its European counterpart (Millspaugh, 1974; Vogel, 1970).

## 1.5 CULTIVATION AND PROPAGATION

*Achillea* spp. are raised in many plant nurseries as a decorative plant. The plant is a normal component of butterfly nurseries and natural landscaping of different environments. The plant grows very well in drained soil with full sun but can also be grown in less ideal soil conditions (Anon, 2020).

Propagation through seed germination is the best method of plant cultivation. However, optimal seed germination occurs when the plantation is made at a distance of 30 to 46 cm (12–18 in), not deeper than 6 mm, and at an average temperature of 18°C to 24°C.

Some of the ornamental cultivars species are Calistoga (white), Credo, Cerise Queen, Island Pink (pink), Lachsschönheit (Galaxy Series), Lansdorferglut, Martina, Paprika, Red Beauty, Red Velvet, Saucy Seduction, Sonoma Coast (white) and Strawberry Seduction (red). Besides this, some of the hybrids species are Appleblossom, Fanal, Hoffnung, and Moonshine (Anon, 2020).

## 1.6 TRADE POTENTIAL OF *ACHILLEA*

Medical and aromatic plants have been an essential part of healthcare throughout since the origin of man on this planet (Schippmann et al., 2002). Recently, there has been a normal assessment that synthetic substances/manufactured materials that are frequently used in the food sector and drug industries cause several side effects and diseases. This has augmented worldwide demand for organic and natural forms of the medication. As a result, healing herbs through natural medicines are commonly used as a part of traditional systems of medicine worldwide. In Australia, 48.5% of the population (MacLennan et al., 1996), in Finland, 33% (Vaskilampi et al., 1993), in Denmark, 10% (Rasmussen, 1990), in Belgium, 31%, in France, 49% (Fisher & Ward, 1994), and in Canada 17% of the population (Wayne, 2001) lean toward alternative medication strategies to some extent one time each year, and consume home grown medications and healing herb. Earlier, local usage of these medicinally important plants was common as part of their traditions, but nowadays, these herbs have become an essential source of national and international trade marketing.

Literature reveals that 50,000–75,000 plant species are being used in traditional and modern systems of medicine globally (Schippmann et al., 2006). In Europe, at least 2000 medical and sweet-smelling spices are utilized in such areas as beauty care products, medication, color, natural tea,

healthful enhancements, alcohol, pesticides and fungicides, fundamental oil items, fragrances, seasoning fluids, and cleaning items. Roughly 1,200–1,300 of these spices are derived from species that are local to Europe (Kathe et al., 2003). Eastern Europe and Southeastern European countries play an important role in the global trade in herbs of Europe. In particular, Albania, Bulgaria, Poland, Hungary, and Turkey are essential source countries for such commodities (Lange, 2001). A great majority of medical and aromatic herbs are obtained from natural environments, including 90% of the natural products traded in Europe and the great majority of those present in Turkey (Coskun & Ozkan, 2005).

Accurate data on the trade volume and business worth of medicinally important plants is provided by the United Nations Comtrade data set. UN Comtrade has recorded exchange information for around 180 nations since 1962 (Lange, 2006). According to data for 2011, total global import value was \$3.05 billion US dollars, and total exports were \$2.86 billion US dollars (Akbulut & Bayramoglu, 2013).

*Achillea* has a wide array of medicinal uses like spasmolytic, choleric, treatment of wounds, and anti-inflammatory activities, making it known as an important medicinal plant (Benedek et al., 2007). In addition, some *Achillea* species were considered new ornamental plants (Armitage, 1992; Evenor & Reuveni, 2004). *Achillea* is also marketed as fresh fillers and dry flowers in flower arrangements (Small & Catling, 1999). *Achillea millefolium* plants are characterized as heavy metal accumulators that aid in phytoremediation (Radanovic et al., 2000). *A. millefolium* is used in beer, wine, and soft drink flavoring. It is an insect repellent that dissuades visits from some ants, flies, and beetles (Schwartz, 2006). Due to these properties, it is thought that the trade potential of yarrow is high.

## 1.7 PHYTOCHEMISTRY OF *ACHILLEA*

Phytochemical characterizations of *Achillea* spp. have revealed that this genus consists of several bioactive components. The main antispasmodic flavonoids, cynaroside I and cosmosiin II, were extracted from *Achillea millefolium* L. (Falk et al., 1975), and the primary natural proazulene, achillicin III, was recognized from the genus *Achillea* (Cuong et al., 1979).

Literature reveals that flavonoids, terpenoids, lignans, amino acid derivatives, unsaturated fats, and alkamides viz., p-hydroxyphenethylamide IV have effectively been recognized in *Achillea* species (Si et al., 2006). In this

way, the current chapter manages the therapeutic and industrial uses of the minor or uncommon constituents which have not yet been exposed properly. Among them, alkaloids, the lipophilic and nitrogen-containing compounds, are liable for insect spray, antiinflammation, and some immunological exercises of *Achillea* and *Echinacea* plants (Greger, 1984).

The genus *Achillea* consists of flavored species which produce strong essential oils and endures monoterpenes as the most common metabolites in different spp. Further, there are several research on significant amounts of sesquiterpenes in contrast to monoterpenes (Nemeth, 2005; Bakkali et al., 2008). There are also few reports on pharmacological investigations, and the majority of them perceived the presence of azulenogenous sesquiterpene lactones in the oil of *Achillea* species. Results show that tetraploid species are collecting proazulenes viz., achillicin III (Radusiene & Gudaityte, 2006). Further, yarrow (*A. tenuifolia* Lam.) seeds comprise a high essential oil yield, which is rich in linoleic acid (a poly-unsaturated fatty acid. This favors yarrow seed as a possible source of edible oil for consumption by human beings (Goli et al., 2008).

Recently, because of the presence of luteolin V, apigenin VI, and flavonoids, *A. millefolium* has been introduced as a novel source of natural dye for dyeing wool fabrics. Further, *A. millefolium* was also recorded to have an excellent source of agronomic potential as a color agent in Iran (Kiumarsi et al., 2009). In the plant, hydroxycinnamoyl forms of quinic acid were recorded as usual end metabolites of the shikimate-phenylpropanoid pathway, however, feruloyl caffeoylquinic acid derivatives VII have been isolated only from two types of *Achillea* (Radulovic et al., 2006). Further, from the airborne pieces of the *Achillea* spp., betonicine X, betaine XI, choline XII, proline VIII, and stachydrine IX have been identified as significant nitrogen-containing compounds (Mehlfuhrer et al., 1997; Saeidnia et al., 2004). Other than this, betaines, containing the super durable positive charge on the quaternary ammonium moiety, belong to the class of naturally occurring compounds and function as compatible solutes or osmoprotectants, have also been isolated (Wood et al., 2002). These constituents have revealed immuno-suppressive action in the test animals (Zhang et al., 1996; Hamidi et al., 2010).

## 1.8 ETHNOMEDICINAL USES OF *ACHILLEA*

Yarrow is one of the known oldest botanicals used among humans (*sensu lato*) and is one of the six medicinally important plants whose pollens were

recorded in Homo-neanderthalensis grave at Shanidar, dated to 65,000 B.P. (Leroi-Gourhan, 1975; Solecki, 1975; Leroi-Gourhan, 1998). The most established enduring writings to record the utilization of yarrow in European traditional medical practices are by Pliny the Elder and Dioscorides, both during the primary century A.D. These literatures put forth a lower line on the time of yarrow's use among Western cultures, while, concerning most botanicals, people use in an oral practice might have since a long time ago went before the plant's appearance in perceptive medication (Applequist & Moerman, 2011).

Dioscorides portrayed the spice Achilleios, or *Millefolium* (among different names), as being valuable to quit dying, including from wounds and unusual feminine dying, and diminish irritation; however, decoction can be used as douche for menstrual bleeding and could also be inebriated for diarrhea (Osbaldeston & Wood, 2000). Pliny's Natural History demonstrated that a plant is presumably recognizable as yarrow was recognized by names including achilleos, sideritis, and millefolia and that a few groups additionally utilized the previous two names for other few species, some very divergent in portrayal, with all being viewed as significant for wounds. Pliny likewise revealed *Achillea* to be helpful for "looseness of the bowels," bleeding, extreme menstruation (sometimes given as a sitz bath), and ear infection (Jones, 1956).

In the Persian language, Bumadaran is the well-known name of several *Achillea* species. The species are reported as anti-inflammatory, diaphoretic, diuretic, antispasmodic, tonic, and emmenagogic agents, as well as used for the treatment of pneumonia, hemorrhage, rheumatic pain, and wound healing properties in traditional Persian literature (Zargari, 1996; Saeidnia et al., 2005). However, in Spanish (New Mexico and Southern Colorado), *Achillea millefolium* L. is known as plumajillo, or "little feather," due to the shape of the leaves. Further, local Americans and early settlers utilized yarrow as an astringent, making it efficient in anti-bleeding and wound healing (Dodson & Dunmire, 2007).

*Achillea* species are quite possibly the most monetarily significant local plants of Anatolia. Additionally, in Turkey, natural teas arranged from some *Achillea* species are generally utilized for stomach agony and farting (Honda et al., 1996).

Comparable use of yarrow stays alive till day: usually, European people utilize are intended for gastrointestinal issues and loss of hunger, for feminine issues, and as a diaphoretic, and topically as a poultice for healing wounds, external bleeding, and for washing skin inflammations (Wichtl,



2004). However, Germany's Commission E authoritatively endorsed oral yarrow prescriptions just for gentle gastrointestinal aggravations, dyspepsia, and loss of craving (Blumenthal et al., 1998).

Italy utilized yarrow primarily for gastrointestinal conditions (Guarrera, 2006) and also for menstrual problems, urinary problems/diuretics, toothache, as well as a sedative. Further, in Hungary, the plant is well-known as cickafark or cat tail and has been utilized for internal sicknesses and pertains to wound and burn healing properties (Kolos & Kolosné, 1956). Furthermore, it is also used as a tea for treating bronchitis, diarrhea, vomiting, and urinary and kidney problems (Sulyok & Siklos, 1998).

Over 33% of the 125 records of traditional use of *Achillea* spp. (yarrow) In Britain and Ireland, treatment of blood-related ailments, including nosebleeds, bleeding wounds, uterine discharge, and hypertension; however, a large percentage is involved in respiratory infections, fevers, and rheumatic complaints (Allen & Hatfield, 2004).

In China, yarrow has been used for the treatment of various ailments such as treatment of sores and bleeding, wounds, hemorrhoids, dysmenorrhea, varicose veins, snakebite, and tuberculosis (Duke & Ayensu, 1985).

Chandler et al. (1982) compiled from 15 references a list of 30 medical uses for yarrow among 22 indigenous American tribes. The uses were diverse but could be gathered into four distinct classifications: (i) colds, fever, and sore throat; (ii) digestive problems; (iii) skin injuries or disorders, wounds, bruises, and bleeding conditions; and (iv) general tonic use.

Moerman's authoritative (1998) compilation identified 377 distinct medicinal use reports for yarrow by Native American groups, the most for any plant. The medicinal use of yarrow was used by more than 76 tribes. The wider uses reported by Moerman (1998) incorporated utilizations for skin issues and wounds, respiratory sicknesses and stomach-related issues, toothaches, and eye issues.

## 1.9 SUMMARY

Bioactivities of different *Achillea* species consist of angiogenic (Demirci et al., 2011), antifungal (Kordali et al., 2009; Amjad et al., 2014), antibacterial (Alfatemi et al., 2015), antimicrobial (Tunca-Pinarli et al., 2023; Bozyel et al., 2017; Azaz et al., 2008; Sokmen et al., 2004), hepatoprotective (Al-Said et al., 2016), herbicidal (Kordali et al., 2009), insecticidal (Tabanca et al., 2011; Khani, 2012), antioxidant (Tunca-Pinarli et al., 2023; Alfatemi et al.,

2015; Al-Said et al., 2016), antiradical (Sokmen et al., 2004), protective effects against oxidative stress (Baser, 2016; Dadkhah et al., 2015), estrogenic (Innocentia et al., 2007), antiulcer (Niazmand & Khoshnood, 2010; Potrich et al., 2010), antitumoral (Lopes et al., 2005), antisecretory (inhibiting intestinal motility) (Babaei et al., 2010), immunomodulatory (Shariffar et al., 2009), fibrinogenic (Hemmati et al., 2011), and anti-inflammatory (Salvagnini et al., 2006; Lakshimi et al., 2011).

The majority of these therapeutical uses have already been confirmed on the basis of investigational and clinical studies. The utilization of herbal teas from various *Achillea* species, particularly for the treatment of the gastrointestinal tract, is a usual process in traditional medicine (Skocibusic et al., 2004).

## KEYWORDS

- *Achillea* spp.
- alternative medicine
- antioxidant
- Asteraceae
- cultivation
- ethnomedicinal uses
- herbal drugs
- phytochemistry

## REFERENCES

- Akbulut, S., & Bayramoglu, M. M., (2013). The trade and use of some medical and aromatic herbs in Turkey. *Studies on Ethno-Medicine*, 7(2), 67–77.
- Alfatemi, S. M. H., Rad, J. S., Rad, M. S., Mohsenzadeh, S., & Teixeira Da, S. J. A., (2015). Chemical composition, antioxidant activity, and *in vitro* antibacterial activity of *Achillea wilhelmsii* C. Koch essential oil on methicillin-susceptible and methicillin-resistant *Staphylococcus aureus* spp. *3Biotech*, 5(1), 39–44.
- Allen, D. E., & Hatfield, G., (2004). *Medicinal Plants in Folk Tradition*. Timber Press: Portland, Oregon.
- Al-Said, M. S., Mothana, R. A., Al-Yahya, M. M., Rafatullah, S., Al-Sohaibani, M. O., Khaled, J. M., Alatar, A., et al., (2016). GC-MS analysis: *In vivo* hepatoprotective and

- antioxidant activities of the essential oil of *Achillea biebersteinii* Afan. growing in Saudi Arabia. *Evidence-Based Comp and Alt Med*. Article ID 1867048.
- Amjad, L., Mousavideh-mourdi, K., & Rezvani, Z., (2014). *In vitro* study on antifungal activity of *Achillea wilhelmsii* flower essential oil against twenty strains of *Candida albicans*. *Chiang Mai Journal of Science*, 14, 1058–1064.
- Angier, B., (1978). *Field Guide to Medicinal Wild Plants* (pp. 314–318). Stackpole Books, Harrisburg, PA.
- Anon., (2020). [https://en.wikipedia.org/wiki/Achillea\\_millefolium](https://en.wikipedia.org/wiki/Achillea_millefolium) (accessed on 31 August 2023).
- Anonymous, (2019a). *Dr. Duke's Phytochemical and Ethnobotanical Databases*. <https://phytochem.nal.usda.gov/phytochem/search/list> (accessed on 31 August 2023).
- Anonymous, (2019b). *Dandelion Taraxacum Officinale G. H. Weber Ex Wiggers*. <https://www.invasiveplantatlas.org/subject.html?sub=3887> (accessed on 31 August 2023).
- Applequist, W. L., & Moerman, D. E., (2011). Yarrow (*Achillea millefolium* L.): A neglected panacea? A review of ethnobotany, bioactivity, and biomedical research. *Economic Botany*, 65(2), 209–225.
- Armitage, A. M., (1987). The influence of spacing on field-grown perennial crops. *Hort. Sci.*, 22, 904–907.
- Armitage, A. M., (1992). Field studies of Achilles as a cut flower: Longevity, spacing, and cultivar response. *Journal of the American Society for Horticultural Science*, 117(1), 65–67.
- Azaz, A. D., Arabaci, T., Sangun, M. K., & Yildiz, B., (2008). Composition and the *in vitro* antimicrobial activities of the essential oils of *Achillea wilhelmsii* C. Koch. and *Achillea lycanica* Boiss & Heldr. *Asian Journal of Chemistry*, 20(2), 1238–1244.
- Babaei, M., Abarghoei, M. E., Akhavan, M. M., Ansari, R., Vafaei, A. A., Taherian, A. A., Mousavi, S., & Toussy, J., (2010). Antimotility effect of hydroalcoholic extract of yarrow (*Achillea millefolium*) on the guinea-pig ileum. *Pak. J. Biol. Sci.*, 10(20), 3673–3677.
- Bakkali, F., Averbeck, S., Averbeck, D., & Idaomar, M., (2008). Biological effects of essential oils: A review. *Food Chem Toxicol.*, 46, 446–475.
- Barkley, T. M., Brouillet, L., & Strother, J. L., (2006). *Asteraceae* (Vol. 19). In: *Flora of North America: North of Mexico*. Oxford University Press, USA.
- Barrett, B., (2003). Medicinal properties of Echinacea: A critical review. *Phytomedicine*, 10(1), 66–86.
- Baser, K. H. C., (2016). Essential oils of *Achillea* species of Turkey. *Nat. Volatiles & Essent. Oils*, 3(1), 1–14.
- Bauer, R., Remiger, P., & Wagner, H., (1989). Alkamides from the roots of *Echinacea angustifolia*. *Phytochemistry*, 28(2), 505–508.
- Benedek, B., Kopp, B., & Melizg, M. F., (2007). *Achillea millefolium* L. S.L.-is the anti-inflammatory activity mediated by protease inhibition? *J. Ethnopharmacol.*, 113, 312–317.
- Blumenthal, M., Busse, W. R., Goldberg, A., Gruenwald, J., Hall, T., Klein, S., Riggins, C. W., & Rister, R. S., (1998). *The Complete German Commission E Monographs: Therapeutic Guide to Herbal Medicines*. American Botanical Council: Austin, Texas.
- Boonen, J., Bronselaer, A., Nielandt, J., Veryser, L., De Tre, G., & De Spiegeleer, B., (2012). Alkamid database: Chemistry, occurrence, and functionality of plant N-alkylamides. *Journal of Ethnopharmacology*, 142(3), 563–590.
- Bozyel, M. E., Canli, K., Yetgin, A., Senturan, M., & Altuner, E. M., (2017). *In vitro* antimicrobial activity screening of *Achillea phrygia* and determination of the ethanol extract composition by gas chromatography/mass spectrometry. *Abstract Book, The Second*

- Japan-Turkey International Symposium on Pharmaceutical and Biomedical Sciences (Jatuspab-2)* (p. 108). Trabzon, Turkey.
- Chandler, R. F., Hooper, S. N., & Harvey, M. J., (1982). Ethnobotany and phytochemistry of yarrow, *Achillea millefolium*, Compositae. *Economic Botany*, 36, 203–223.
- Coskun, M., & Ozkan, A. M. G., (2005). Global phytochemistry: The Turkish frame. *Phytochemistry*, 66, 956–960.
- Cuong, B. N., Eszter, G. B., Lajos, R., Jozsef, T., Kalman, U., & Gizella, V. P., (1979). Achillicin, the first proazulene from *Achillea millefolium*. *Phytochemistry*, 18, 331.
- Dadkhah, A., Fatemi, F., Alipour, M., Ghaderi, Z., Zolfaghari, F., & Razdan, F., (2015). Protective effects of Iranian *Achillea wilhelmsii* essential oil on acetaminophen-induced oxidative stress in rat liver. *Pharm. Biol.*, 53(2), 220–227.
- Demirci, F., Kiyani, H. T., Demirci, B., & Baser, K. H. C., (2011). The *in vivo* angiogenic evaluation of *Achillea biebersteinii* Afan. and *Achillea teretifolia* Willd. essential oils. *Planta Medica*, 77(12), 1391–1391.
- Dempewolf, H., Rieseberg, L. H., & Cronk, Q. C., (2008). Crop domestication in the Compositae: A family-wide trait assessment. *Genet. Resour. Crop Evol.*, 55, 1141–1157.
- Dobler, S., Haberer, W., Witte, L., & Hartmann, T., (2000). Selective sequestration of pyrrolizidine alkaloids from diverse host plants by *Longitarsus* flea beetles. *Journal of Chemical Ecology*, 26(5), 1281–1298.
- Dodson, C., & Dunmire, W. W., (2007). *Mountain Wildflowers of the Southern Rockies*. University of New Mexico Press, New Mexico.
- Duke, J. A., & Ayensu, E. S., (1985). *Medicinal Plants of China*. Reference Publications; Algonac, Michigan.
- Evenor, D., & Reuveni, M., (2004). Micropropagation of *Achillea filipendulina* cv. 'parker.' *Plant Cell Tissue Organ Cult.*, 79, 91–93.
- Falk, A. J., Smolenski, S. J., Bauer, L., & Bell, C. L., (1975). Isolation and identification of three new flavones from *Achillea millefolium* L. *J. Pharm. Sci.*, 64, 1838–1842.
- Fisher, P., & Ward, A., (1994). Complementary medicine in Europe. *Br Med J.*, 309, 107–111.
- Gabbriellini, G., Loggini, G., Cioni, P., Giannaccini, B., & Mancuso, E., (1988). The activity of lavender essential oil against non-tubercular opportunistic rapid grown mycobacteria. *Pharmacol. Res. Commun.*, 20(5), 434–439.
- Goli, S. A. H., Rahimmalek, M., & Tabatabaei, B. E. S., (2008). Physicochemical characteristics and fatty acid profile of yarrow (*Achillea tenuifolia*) seed oil. *Int. J. Agric. Biol.*, 10, 355–357.
- Greger, H., (1977). Anthemideae-chemical review. In: Heywood, V. H., Harborne, J. B., & Turner, B. L., (ed s). *The Biology and Chemistry of the Compositae* (Vol. 2, pp. 899–941).
- Greger, H., (1984). Alkamides: Structural relationship, distribution, and biological activity. *Planta Med.*, 50, 366–375.
- Grieve, M. A., (1974). *Modern Herbal*. Hafner; New York.
- Guaâdaoui, A., Bouhtit, F., Cherfi, M., & Hamal, A., (2015). The preventive approach of biocompoundactives (2): A review of recent advances in common fruits. *Recent Advances in Common Fruits: International Journal of Nutrition and Food Sciences*, 4(2), 189–207.
- Guarrera, P. M., (2006). *Usi e Tradizioni Della Flora Italiana*. Medicina Popolare ed Etnobotanica. Aracne, Rome.
- Hamidi, H., Jahanian, R., & Pourreza, J., (2010). Effect of dietary betaine on performance, immunocompetence, and gut contents osmolality of broilers challenged with a mixed coccidial infection. *Asian J. Anim. Vet. Adv.*, 5, 193–201.

- Hemmati, A. A., Arzi, A., Adinehvand, A., Mostofi, N. E., Mozaffari, A. R., & Jalali, A., (2011). Yarrow (*Achillea millefolium* L.) extract impairs the fibrogenic effect of bleomycin in rat lungs. *J. Med. Plants Res.*, 5(10), 1843–1849.
- Honda, G., Yesilada, E., Tabata, M., Sezik, E., Fujita, T., Takeda, Y., Takaishi, Y., & Tanaka, T., (1996). Traditional medicine in Turkey VI. Folk medicine in West Anatolia: Afyon, Kutahya, Denizli, Mugla, Aydin provinces. *J. Ethnopharm.*, 53, 75–87.
- Hutchens, A. R., (1969). *Indian Herbarology of North America*. Merco; Windsor, Ontario.
- Hylton, W. H., (1974). *The Rodale Herb Book*. Rodale Press Book Division; Emmaus, PA.
- Innocenti, G., Vegeto, E., Dall'Acqua, S., Ciana, P., Giorgetta, M., Agradi, E., Sozzi, A., et al., (2007). *In vitro* estrogenic activity of *Achillea millefolium* L. *Phytomedicine*, 14, 147–152.
- Jones, W. H. S., (1956). [*Pliny, the Elder*] *Naturalis Historia, English and Latin*. Harvard University Press; Cambridge, Massachusetts.
- Kachura, A., (2018). *An Ethnobotanical, Pharmacological, and Phytochemical Analysis of Achillea Millefolium L. by Parts*. PhD Dissertation, Université D'Ottawa/University of Ottawa, Ottawa.
- Kathe, W., Honnef, S., & Heym, A., (2003). *Medicinal and Aromatic Plants in Albania, Bosnia-Herzegovina, Bulgaria, Croatia, and Romania*. Federal Agency for Nature Conservation; Bonn., BfN-Skripten, No. 91.
- Khan, N., Afaq, F., & Mukhtar, H., (2008). Cancer chemoprevention through dietary antioxidants: Progress and promise. *Antioxidants & Redox Signaling*, 10(3), 475–510.
- Khani, A., & Asghari, J., (2012). Insecticide activity of essential oils of *Mentha longifolia*, *Pulicaria gnaphalodes*, and *Achillea wilhelmsii* against two stored product pests, the flour beetle, *Tribolium castaneum*, and the cowpea weevil, *Callosobruchus maculatus*. *J. Insect Sci.*, 12(73), 1–10.
- Kiumarsi, A., Abomahboub, R., Rashedi, S. M., & Parvinzadeh, M., (2009). *Achillea Millefolium* is a new source of natural dye for wool dyeing. *Prog. Color Colorants Coat*, 2, 87–93.
- Kolos, E., & Kolosné, P. E., (1956). *Hazai gyogyövényeink* (2<sup>nd</sup> edn.). Tudományos és semeretterjeszto, Budapest.
- Kong, J. M., Goh, N. K., Chia, L. S., & Chia, T. F., (2003). Recent advances in traditional plant drugs and orchids. *Acta Pharmacologica Sinica*, 24(1), 7–21.
- Kordali, S., Cakir, A., Akcin, T. A., Mete, E., Akcin, A., Aydin, T., & Kilic, H., (2009). Antifungal and herbicidal properties of essential oils and n-hexane extracts of *Achillea gypsicola* Hub.-Mor. and *Achillea biebersteinii* Afan. (*Asteraceae*). *Ind. Crop. Prod.*, 29, 562–570.
- Kremers, R. E., (1921). The chemistry of the volatile oil of milfoil. *J. Amer. Pharm. Assoc.*, 10, 252–261.
- Krochmal, A., & Krochmal, C., (1973). *A Guide to the Medicinal Plants of the United States*. New York Times Book, New York.
- Lakshmi, T., Geetha, R. V., Roy, A., & Kumar, S. A., (2011). Yarrow (*Achillea millefolium* Linn.) a herbal medicinal plant with broad therapeutic use: A review. *Int. J. Pharm. Sci. Rev. Res.*, 9(2), 136–141.
- Lange, D., (2001). Financial instruments for nature conservation in central and 191 Eastern Europe. In: Heinze, B., Bäurle, G., & Stolpe, G., (eds.), *Trade in Medicinal and Aromatic Plants: A Financial Instrument for Nature Conservation in Eastern and Southeast Europe?* (pp. 157–171). Federal Agency for Nature Conservation, Bonn, BfNSkripten 50.

- Lange, D., (2006). *International Trade in Medicinal and Aromatic Plants. Actors, Volumes and Commodities, Medicinal and Aromatic Plants*. Springer Press; Netherlands.
- Leroi-Gourhan, A., (1975). The flowers were found with Shanidar IV, a Neanderthal burial in Iraq. *Science*, 190, 562–564.
- Leroi-Gourhan, A., (1998). Shanidar et ses fleurs. *Paléorient*, 24, 79–88.
- Levy, J. B., (1966). *Herbal Handbook for Everyone*. Faber and Faber; London.
- Lewis, W. H., & Elvin-Lewis, M. P. F., (1977). *Medical Botany: Plants Affecting Man's Health*. Wiley; Toronto.
- Level, C. F., (1972). *Culpepper's English Physician and Complete Herbal*. Wilshire Book; Hollywood, CA.
- Lopes, F. C. M., Benzatti, F. P., Junir, C. M. J., Moreira, R. R. D., & Carlos, I. Z., (2005). Effect of the essential oil of *Achillea millefolium* L. in the production of hydrogen peroxide and tumor necrosis factor- $\alpha$  in murine macrophages. *Rev. Bras. Cienc. Farm.*, 31(3), 401–405.
- Macel, M., Bruinsma, M., Dijkstra, S. M., Ooijendijk, T., Niemeyer, H. M., & Klinkhamer, P. G., (2005). Differences in effects of pyrrolizidine alkaloids on five generalist insect herbivore species. *Journal of Chemical Ecology*, 31(7), 1493–1508.
- MacLennan, A. H., Wilson, D. H., & Taylor, A. W., (1996). Prevalence and cost of alternative medicine in Australia. *The Lancet*, 347, 569–573.
- Mazed, M. A., Mazed, S., & Mazed, M. A., (2009). Nutritional supplements for the prevention of cardiovascular disease, Alzheimer's disease, diabetes, & regulation and reduction of blood sugar and insulin resistance. *U.S. Patent Application*, 12(390), 302.
- Mehlführer, M., Troll, K., Jurenitsch, J., Auer, H., & Kubelka, W., (1997). Betaines and free proline within the *Achillea millefolium* group. *Phytochemistry*, 44, 1067–1069.
- Merali, S., Binns, S., Paulin-Levasseur, M., Ficker, C., Smith, M., Baum, B., Brovelli, E., & Arnason, J. T., (2003). Antifungal and anti-inflammatory activity of the genus Echinacea. *Pharmaceutical Biology*, 41(6), 412–420.
- Millsbaugh, C. F., (1974). *American Medicinal Plants*. Dover Publishing; New York.
- Mjiqiza, S. J., Syce, J. A., & Obikeze, K. C., (2013). Pulmonary effects and disposition of luteolin and Artemisia Afra extracts in isolated perfused lungs. *Journal of Ethnopharmacology*, 149(3), 648–655.
- Moerman, D. E., (1977). *American Medical Ethnobotany: A Reference Dictionary*. Garland; New York.
- Moerman, D. E., (1998). *Native American Ethnobotany*. Timber Press; Portland, Oregon.
- Moerman, D. E., (2003). *Native American Ethnobotany Database*. Available from <http://naeb.brit.org/>.
- Nemeth, E., (2005). Essential oil composition of species in the genus *Achillea*. *J. Essent. Oil Res.*, 17, 501–512.
- Niazmand, S., & Khoshnood, E., (2010). The effects of *Achillea wilhelmsii* extract on rat's gastric motility at basal and vagal stimulated conditions. *Iran J. Basic Med. Sci.*, 14(2), 151–157.
- Osbaldeston, T. A., & Wood, R. P. A., (2000). *Dioscorides: De Materia Medica*. Ibis Press; Johannesburg.
- Potrich, F. B., Allemand, A., Da Silva, L. M., Dos Santos, A. C., Baggio, C. H., Freitas, C. S., Mendes, D. A. G. B., et al., (2010). The antiulcerogenic activity of hydroalcoholic extract of *Achillea millefolium* L. involvement of the antioxidant system. *J. Ethnopharmacol.*, 130, 85–92.

- Radanovic, D., Jakovljevic, M., & Mladenovic, S. A., (2000). Content of potentially toxic trace elements in some medicinal plants. In: Josif, P., (ed.), *Proc. of the First Conf. on Medic. & Aromatic Plants of SE European Countries* (pp. 481–488). VI Meeting: “Day of Medicinal Plants – 2000,” IMPR, Belgrade.
- Radulovic, N., Stojanovic, G., & Asakawa, Y., (2006). Hydroxycinnamoyl conjugates from the roots of *Achillea holosericea* Sibth. Et Sm. *Biochem. Syst. Ecol.*, 34, 83–87.
- Raduner, S., Majewska, A., Chen, J. Z., Xie, X. Q., Hamon, J., Faller, B., Altmann, K., H., & Gertsch, J., (2006). Alkylamides from *Echinacea* are a new class of cannabinomimetics cannabinoid type 2 receptor-dependent and-independent immunomodulatory effects. *Journal of Biological Chemistry*, 281(20), 14192–14206.
- Radusiene, J., & Gudaityte, O., (2006). Distribution of proazulenes and productivity in *Achillea millefolium* L. spontaneous populations. *Botucatu: Rev. Bras Pl. Med.*, 8, 155–158.
- Rasmussen, N. K., & Morgall, G. M., (1990). The use of alternative treatments in the Danish adult population. *Complementary Medicinal Research*, 4, 16–22.
- Rupp, R., (2011). How carrots won the trojan war. In: Deborah, B., (ed.), *Curious (But True) Stories of Common Vegetables*. Storey Publishing, ISBN: 978-1-60342-968-9.
- Saeidnia, S., Gohari, A. R., & Yassa, N., (2004). A search for betaine compounds within the Iranian *Achillea*. *Int. J. Biol. Biotech.*, 1, 719, 720.
- Saeidnia, S., Gohari, A. R., Yassa, N., & Shafiee, A., (2005). Composition of the volatile oil of *Achillea conferta* DC, from Iran. *Daru*, 13, 34–36.
- Salvagnini, L. E., Migliato, K. F., Isaac, V. L. B., Correa, M. A., Salgado, N. R. N., & Pietro, R. C. L. R., (2006). Evaluation of efficacy of preservatives associated with *Achillea millefolium* L. extract against *Bacillus subtilis*. *Braz. J. Microbiol.*, 37, 75–77.
- Schippmann, U., Leaman, D., & Cunningham, A. B., (2006). A comparison of cultivation and wild collection of medicinal and aromatic plants under sustainability aspects. In: Bogers, R. J., (ed.), *Medicinal and Aromatic Plants* (pp. 75–95). Dordrecht: Springer. Wageningen, UR Frontis Series No. 17.
- Schippmann, U., Leaman, J. D., & Cunningham, A. B., (2002). *Impact of Cultivation and Gathering of Medicinal Plants on Biodiversity: Global Trends and Issues*. Inter Departmental Working Group on Biological Diversity for Food and Agriculture; Rome.
- Schwartz, D., (2006). *Achillea Millefolium (Yarrow)*. <http://www.kingdomplantae.net/yarrow.php> (accessed on 31 August 2023).
- Shaikh, S. H., Malik, F., James, H., & Abdul, H., (2009). Trends in the use of complementary and alternative medicine in Pakistan: A population-based survey. *The Journal of Alternative and Complementary Medicine*, 15(5), 545–550.
- Sharififar, F., Pournourmohammadi, S. & Arabnejad, M., (2009). Immunomodulatory activity of aqueous extract of *Achillea wilhelmsii* C. Kosh. in mice. *Indian J. Exp. Biol.*, 47, 668–671.
- Si, X. T., Zhang, M. L., Shi, Q. W., & Kiyota, H., (2006). Chemical constituents of the plants in the genus *Achillea*. *Chem Biodivers.*, 3, 1163–1180.
- Simonetti, G., (1990). *Simon & Schuster's Guide to Herbs & Spices*. Fireside; New York.
- Skocibusic, M., Bezic, N., Dunkic, V., & Radonic, A., (2004). Antibacterial activity of *Achillea clavennae* essential oil against respiratory tract pathogens. *Fitoterapia*, 75, 733–736.
- Small, E., & Catling, P. M., (1999). *Achillea millefolium*. In: *Canadian Medicinal Crops* (pp. 6–14). NRC Research Press; Ottawa, Ontario, Canada.
- Sokmen, A., Sokmen, M., Daferera, D., Polissiou, M., Candan, F., Unlu, M., & Akpulat, H. A., (2004). The *in vitro* antioxidant and antimicrobial activities of the essential oil and methanol extracts of *Achillea biebersteinii* Afan. (*Asteraceae*). *Phytother. Res.*, 18, 451–456.

- Solecki, R. S., (1975). Shanidar IV, a Neanderthal flower burial in northern Iraq. *Science*, 190, 880, 881.
- Sulyok, K., & Siklos, L., (1998). *Lajor Atya Tanascai*. Hungalibri Kiado: Budapest.
- Tabanca, N., Demirci, B., Gurbuz, I., Demirci, F., Becnel, J. J., Wedge, D. E., & Baser, K. H. C., (2011). The essential oil composition of five collections of *Achillea biebersteinii* from Central Turkey and their antifungal and insecticidal activity. *Natural Product Communications*, 6(5), 701–706.
- Tamokou, J. D. D., Mbaveng, A. T., & Kuete, V., (2017). Antimicrobial activities of African medicinal spices and vegetables. In: *Medicinal Spices and Vegetables from Africa* (pp. 207–237). Academic Press.
- Thieret, J. W., (2001). *Yarrow*, *Encyclopedia Americana*. Grolier International Inc.; Danbury, Connecticut, USA.
- Thomson, W. A. R., (1978). *Medicines from the Earth, A Guide to Healing Plants*. McGraw-Hill; New York.
- Tobe, J. H., (1969). *Proven Herbal Remedies*. Provoker Press; St. Catharines, Ontario.
- Tunca-Pinarli, Y., Benek, A., Turu, D., Bozyel, M. E., Canli, K., & Altuner, E. M., (2023). Biological Activities and Biochemical Composition of Endemic *Achillea fraasii*. *Microorganisms*, 11(4), 978.
- Vaskilampi, T., Merilainen, P., & Sinkkonen, S., (1993). The use of alternative treatments in the Finnish adult population. In: Lewith, G. T., & Aldridge, D., (eds.), *Clinical Research Methodology for Complementary Therapies* (pp. 204–229). London: Hodder & Stoughton.
- Vogel, V. J., (1970). *American Indian Medicine*. Univ. Oklahoma Press; Norman, OK.
- Wade, A., (1977). *Martindale: The Extra Pharmacopeia* (27<sup>th</sup> edn.). Pharmaceutical Press; London.
- Watson, L. E., Evans, T. M., & Boluarte, T., (2000). Molecular phylogeny and biogeography of tribe Anthemideae (Asteraceae), based on chloroplast gene *ndhF*. *Molecular Phylogenetics and Evolution*, 15(1), 59–69.
- Wayne, J. M., (2001). Patterns of use alternative health care practitioners. *Health Reports*, 13, 9–21.
- Weiner, M. A., (1972). *Earth Medicine—Earth Food: Plant Remedies, Drugs, and Natural Foods of the North American Indians*. Collier MacMillan; London.
- WHO, (1999a). *Traditional, Complementary, and Alternative Medicines and Therapies*. Washington DC, WHO Regional office for the Americas/pan American health organization (Working group OPS/OMS).
- WHO, (1999b). *Consultation Meeting on Traditional Medicine and Modern Medicine: Harmonizing the Two Approaches*. Geneva, World Health Organization, (document reference (WP)TM/ICP/TM/001/RB/98-RS/99/GE/32(CHN)).
- WHO, (2002). *WHO Traditional Medicine Strategy 2002–2005*. World Health Organization, Geneva.
- Wichtl, M., (2004). *Herbal Drugs and Phytopharmaceuticals: A Handbook for Practice on a Scientific Basis* (3<sup>rd</sup> edn. [English]). Medpharm Scientific Publishers; Stuttgart, Germany.
- Woelkart, K., Xu, W., Pei, Y., Makriyannis, A., Picone, R. P., & Bauer, R., (2005). The endocannabinoid system as a target for alkaloids from *Echinacea angustifolia* roots. *Planta Medica*, 71(08), 701–705.
- Wood, K. V., Bonham, C. C., Miles, D., Rothwell, A. P., Peel, G., Wood, B. C., & Rhodes, D., (2002). Characterization of betaines using electrospray MS/MS. *Phytochemistry*, 59, 759–765.



Zargari, A., (1996). *Medicinal Plants* (4<sup>th</sup> edn., Vol. 3, pp. 106–117). Tehran University Publication; Tehran.

Zhang, F., Warskulat, U., & Haeussinger, D., (1996). Modulation of tumor necrosis factor- $\gamma$  release by anisoosmolarity and betaine in rat liver macrophages (Kupffer cells). *FEBS Lett.*, 391, 293–296.



# Taylor & Francis

Taylor & Francis Group

<http://taylorandfrancis.com>

## CHAPTER 2

---

# *Acorus calamus* L. (Sweet Flag): Bioactive Compounds, Medicinal Properties, and Biological Activity

SABYASACHI BANERJEE,<sup>1</sup> KARAN KUMAR DAS,<sup>2</sup> GOUTAM PAL,<sup>3</sup> and SANKHADIP BOSE<sup>4</sup>

<sup>1</sup>*Department of Phytochemistry, Gupta College of Technological Sciences, Ashram More, Asansol, West Bengal, India*

<sup>2</sup>*Bharat Technology, Jadurberia, Uluberia, Howrah, West Bengal, India*

<sup>3</sup>*Institute of Pharmacy, Kalyani, West Bengal, India*

<sup>4</sup>*School of Pharmacy, The Neotia University, Sarisa, West Bengal, India*

---

### ABSTRACT

*Acorus calamus* L. (Sweet flag) is a flowering plant species, the Acoraceae family's tall wetland monocot. It's a perennial herbaceous vine. These are the only plants that grow bear flowers in water. The various portions of this herb, such as rhizomes and leaves, are historically utilized in various herbal formulations to treat numerous ailments, inclusive of neuralgia, arthritis, diarrhea, kidney, and liver disorders, dyspepsia, eczema, sinusitis, cough, asthma, hair loss, bronchitis, and other disorders. In addition, it has also been found that this plant is active against the most common and troubling chronic ailments like cancer, heart diseases, and diabetes. Biochemical analyzation of the plant has uncovered an enormous number of secondary metabolites that might be accountable for its therapeutic benefits. The methods by which it exerts its therapeutic efficacy have been uncovered through basic scientific

study. Other than its pharmacological properties, it additionally acts as a pesticide and helps in phytoremediation. Many active components from this plant have been procured and characterized for their wider range of pharmacological actions. Moreover, investigating the pharmacological actions of individual components present in *A. calamus* would bring novel and safer alternative therapeutics for a wider range of ailments. In this chapter, the botanical descriptions, ethno-therapeutic uses, phytochemical components, and biological action of plant sections. And the molecular targets of sweet flag are included which might furnish as a suitable foundation for future research on this herb.

## 2.1 INTRODUCTION

*Acorus calamus* L. is likewise referred “calamus” or “sweet flag” which originates from the family called Acoraceae (Mukherjee et al., 2007; Chandra et al., 2017; Umamaheshwari et al., 2018). The description of this plant was found to be narrated in the papyrus VI of Chester Beatty, since 1300 BC (approximately). The primitive Egyptians once in a while referenced the herb in medicinal contexts, however this was mostly utilized in making fragrance (Manniche, 2006). The herb was acquainted with Britain in the late 16<sup>th</sup> century. Originally *Acorus calamus* grew up in Britain during leastways of 1596, as per the record of Catalogue, which is a list of plants was cultivated at Holborn in John Gerard’s Garden. Gerard says, “It prospereth exceedingly well in my garden, yet beareth neither blooms nor stalketh.” Gerard records the Latin appanage *Acorus verus*, yet it is apparent there was still suspicion on its veracity: in his ‘Herbal or General Historie of Plantes,’ 1597, he reported the common name of that plant in English, i.e., bastard calamus (Jackson, 1876). Sauer et al. announced the tuber to have been utilized by Indians of America (North) during the period of Europe discovering (Sauer, 1969). This plant has some other names also like myrtle flag, sweet sedge, flag root, cinnamon sedge, sweet root, sweet myrtle, myrtle sedge, and gladdon (Balakumbahan et al., 2010). This plant has long tenuous leaves, grass-like or sword-shaped, that fan from a pinkish base. Typically, the mid-vein is off-center. A tangerine-like soft scent is extracted from bruised leaves. The scape, sometimes called the flower stem, grows from the base of the outer leaves. Tiny yellowish-green to brown flowers pack the marginally bent spadix. 1–3 oblong seeded angular green berries yield the herb. The most critical component of this plant is the rhizomes. The rhizomes are branched, woody, light-brownish or occasionally orange-brownish in color, cylindrical

to flat with particular nodes and internodes. The rhizomes have a heavy, distinctive, and aromatic odor, and they taste bitter. Cream with a pinkish tinge is the transversely cut surface of the rhizome and is separated into smaller cortical and broader stellar areas. Microscopically, the epidermis comprises cells with intensely thickened borders that are radially prolonged. The cortical area consists of chains of slender-walled parenchymatous cells, with greater intercellular space, sheathed vascular collateral bundles, and fiber patches. With ample starch grains, the stellar area has single barrel-shaped endodermal cells. Endodermal cells are structured in barrels and have various starch grains. In the ground tissue of both cortex and stele, large oil cells with yellowish contents, cells containing dark-brownish oleoresin and starch grains are dispersed. In any cell of the stored row of cells running parallel to the fibers, calcium oxalate in the form of solitary polygonal crystals is available (Mukherjee et al., 2007).

The rhizomes and scented leaves of this plant are utilized as traditional medicine, apart from that dried rhizomes which are crushed into powder form containing a spicy flavor which is utilized as a substitute for cinnamon, nutmeg, and ginger for its odor (Umamaheshwari et al., 2018; Balakumbahan et al., 2010). Nowadays, an enormous population of developing nations are depending on the traditional medicines for their health needs (Chandra et al., 2017; Ramakrishna et al., 1984). The plant is very renowned for its medicinal value. The rhizomes have diverse different pharmacological properties like expectorant, antispasmodic, anthelmintic, carminative, aromatic, sedative, abdominal pain, dysentery (Umamaheshwari et al., 2018; Paithankar et al., 2011). Besides, it is a significant herb in Ayurveda medicine, and is utilized for rejuvenating brain and nervous system (Balakumbahan et al., 2010).

## **2.2 AREA AND PRODUCTION**

Calamus or sweet flag mostly found to be grown near to the locations of Indian villages, trails or camping places. It is thought that the origin of calamus is the central of Asia or in India and also surround areas of Himalayas. Because of plantation, calamus has spread all through the globe. Throughout the 16<sup>th</sup> century, it was known in the central Europe regions (Lokesh, 2004).

## **2.3 MARKETING AND TRADE**

Calamus is a trade item for numerous societies from a huge number of years. Calamus forms a valuable adjunct to several stimulants and tonics. In

addition to other respiratory disorders such as bronchitis, it forms a popular treatment for cold and cough. Sweet flag protects digestive system and functions over flatulent colic, vomiting, and dyspepsia. *A. calamus* used to depresses the CNS (central nervous system) and also a popular compound in the preparations for psycho-somatic ailments like epilepsy. The calamus vapors have insect repelling activity. Every year, importers, domestic consumers, producers, western medicine experts, Ayurvedic and Siddha medicine manufacturers rush to the markets to acquire this factory. Indeed, its domestic demand is great. As agriculture in India is excessively smaller, there is profound scope for the internal market itself.

Some point to be considered for *Acorus calamus*, like:

- Prices are determined according to the governing market rates.
- The yields rely upon appropriate implementation of package of practices.
- Financial aspects of cultivation extraordinarily enhance scale of operation.
- This action provides tax-free high returns. Also, various government support schemes are available.
- Economics may fluctuate time to time due to volatile medicinal plant market.

## 2.4 COMPOSITION AND USES

*Acorus calamus* L. comprises flavonoids, alkaloids, phenols, lectins, gums, mucilage, saponins, quinone, triterpenes (steroids), tannins, and sugars (Ahmad et al., 2007). There are numerous chemical and morphological variations of *A. calamus* in the Finnish and Czech gene bank collection. The plants gathered from the natural destinations in Czech Republic and make comparison to the calamus growing in Canada, Slovenia, and Finland, which are conserved in the Gene Bank collection in Finland. Calamus species from Slovenia, Finnish, and Czech were shown to be phenotypically and chemically very resembling. All of those illustrate *Acorus calamus* var. *calamus* of European triploid type. The mean essential oil content was produced from 1.91% and 1.50% of arid materials in the Czech Republic and Finland, respectively. According to the Czech Radix calami consistency level (minimum quantity is 2%), this quantity is not sufficient, but the carcinogen  $\beta$ -asarone material, which was formed in all of the examined sweet sedges at 9–21% in the essential oil, did not surpass the maximum recommended value of 0.5% of dry drug mass (Dušek et al., 2007) (Tables 2.1 and 2.2).

**TABLE 2.1** Morphological Characteristics from the Republic of Czech and Finland

Nation	Locality	Rhizome's		Cross-Sectional		Leaf Lengths		
		Cross-Sectional		Height of				
		Thickness (mm)		Rhizomes (mm)				
		$\bar{x}$	s	$\bar{x}$	s	$\bar{x}$	s	
Czech Republic	Horka na Moravě	19.0	1.8	–	–	1.1	0.1 m	
	Červený Kostelec	22.0	2.6	–	–	1.0	0.1 m	
	Opatov	22.0	1.8	–	–	1.1	0.1 m	
	Ospělov	17.0	1.9	–	–	0.8	0.1 m	
	Bojanov	15.0	4.3	14.0	3.5	1.1	0.2 m	
	Křemže	17.0	7.6	14.0	5.6	0.8	0.3 m	
	Pičín	19.0	6.8	16.0	3.6	1.0	0.1 m	
	Slavče	20.0	5.3	18.0	3.5	1.0	0.1 m	
	Stupná	15.0	3.5	13.0	2.5	1.2	0.1 m	
	Bohouškovice	25.0	5.1	21.0	4.1	1.1	0.2 m	
	Žehrovka-Nebákov	15.0	1.9	14.0	1.6	0.8	0.1 m	
	Rudice	17.0	4.8	15.0	3.8	0.9	0.1 m	
	Karolín	18.0	6.0	18.0	6.4	1.5	0.1 m	
	Lelekovice-Útěchov	21.0	3.6	18.0	2.5	1.2	0.2 m	
	Kostice	20.0	4.0	17.0	2.8	1.0	0.1 m	
	Lednice	18.0	6.5	15.0	4.5	1.0	0.2 m	
	Rybníště	20.0	1.6	–	–	1.2	0.2 m	
	Visalaje-Obidova	16.0	2.8	13.0	2.1	0.6	0.1 m	
	Staré Hamry	16.0	2.7	13.0	2.1	0.8	0.1 m	
	Horní Bečva	14.0	4.3	12.0	3.0	0.7	0.1 m	
	Karlovy Vary	23.0	3.5	18.0	3.1	0.8	0.1 m	
	Kamýk	18.0	10.6	16.0	10.4	0.8	0.1 m	
	Mýto	20.0	4.1	18.0	3.9	1.1	0.2 m	
Dolní Paseky	15.0	2.2	13.0	2.3	1.2	0.1 m		
<b>Mean</b>		<b>18.4</b>	<b>4.1</b>	<b>15.6</b>	<b>3.8</b>	<b>1.0</b>	<b>0.2 m</b>	
Finland	Marttila	11.7	3.9	20.1	2.1	0.9	0.1 mm	
	Aura	13.1	2.2	15.7	2.0	0.7	0.1 mm	
	Pori	16.6	1.3	22.0	2.4	0.8	0.1 mm	
	Paimio	15.5	4.1	19.9	1.3	0.8	0.1 mm	
	Piikkiö	12.9	2.7	18.5	1.3	0.7	0.1 mm	
	Turku I	18.4	3.9	20.3	2.4	0.8	0.1 mm	
	Turku II	15.6	2.0	19.3	1.7	0.8	0.1 mm	
	<b>Mean</b>		<b>14.8</b>	<b>2.9</b>	<b>19.4</b>	<b>1.9</b>	<b>0.8</b>	<b>0.1 mm</b>
	Ontario (CAN)	13.6	1.4	17.5	2.1	0.9	0.1 mm	
Zalec (SLO)	16	1.9	22.2	3.0	0.8	0.1 mm		

**TABLE 2.2** Chemical Features from Czech Republic and Finland

Nation	Elevation (m)	Locality	Oil Content (%)		$\beta$ -Asarone (%)	
			$\bar{x}$	s	$\bar{x}$	
Czech Republic	425	Bojanov	2.4	0.1	18.2	
	518	Slavče	1.5	0.1	14.8	
	380	Ospělov	1.3	0.2	11.3	
	435	Červený Kostelec	1.2	0.1	17.4	
	420	Pičín	2.1	0.0	19.8	
	430	Opatov	1.7	0.2	21.3	
	385	Horka na Moravě	1.8	0.1	18.4	
	528	Stupná	1.9	0.1	15.2	
	325	Žehrovka-Nebákov	1.6	–	18.9	
	572	Bohouškovice	2.8	0.1	20.3	
	521	Křemže	2.6	0.2	18.5	
	462	Karolín	2.5	0.4	14.1	
	463	Rybniště	1.7	0.2	17.9	
	155	Kostice	1.9	0.1	15.2	
	420	Rudice	1.4	0.1	17.6	
	312	Lelekovice-Útěchov	1.3	0.1	12.5	
	680	Horní Bečva	1.7	0.1	13.2	
	740	Visalaje-Obidova	1.3	0.1	12.6	
	173	Lednice	1.8	0.0	19.7	
	447	Karlovy Vary	2.1	0.1	18.2	
600	Staré Hamry	2.2	0.3	13.1		
500	Dolní Paseky	2.2	0.2	13.7		
443	Mýto	2.0	0.0	11.9		
472	Kamýk	2.9	0.1	12.8		
		<b>Mean</b>	1.9	0.1	16.1	
Finland	0	Turku I	1.3	0.1	9.0	
	0	Piikkiö	1.5	0.1	10.7	
	41	Aura	1.7	0.1	11.5	
	20	Paimio	1.2	0.1	10.0	
	40	Marttila	1.8	0.1	11.1	
	20	Pori	1.8	0.1	9.7	
	0	Turku II	1.9	0.1	9.7	
			<b>Mean</b>	1.5	0.1	10.2
		Reintroduction	Ontario (CAN)	1.1	0.1	Traces
		Reintroduction	Zalec (SLO)	1.3	0.1	10.0



The applications are as follows for the sweet flag plant: the rhizome is candied and turned into a sweet beef (Hedrick, 1972; Grieve, 1984). To extract the bitterness, it might be scraped and washed before being consumed fresh alike a fruit (Coon, 1975; Reid, 1977). It prepares a delicate vegetable when roasted (Emboden, 1979) and can likewise be utilized as a flavoring agent (Usher, 1974). The roots comprise around 1% essential oil, which is utilized in food preparations as a spice, and is also rich in starch (Triska, 1975). The root additionally comprises a bitter glycoside (Reid, 1977). The powdered dry rhizome is utilized for spicy flavor, as substitute of cinnamon, nutmeg, and ginger (Grieve, 1984; Harris, 1973). A pinch of rhizome powder enhances the flavor of tea (Manandhar, 2002). The small and tender inflorescence, because of its beauty, is often consumed by infants (Grieve, 1984). Fresh leaves comprise 0.078% of oxalic acid (Chopra et al., 1986). Calamus leaves may be utilized for flavoring custards, similarly as vanilla pods (Phillips et al., 1990). Young stems are eaten raw in the inner portion (Elias et al., 1982). It prepares a delicious salad (Facciola, 1998).

Calamus is used for various medicinal properties in Cree Indians of Northern Alberta, including as analgesic in headache or toothache, to maintain oral hygiene by cleaning and sterilizing the teeth, the fight the impacts of exhaustion or fatigue, and to help prevent/cure a hangover. Calamus has likewise be utilized for various valuable reasons from last 2000 years in Asia. The primitive Chinese utilized this to treat edema and constipation.

Ayurvedic medicine practice has utilized the magical root to heal fevers, asthma, bronchitis, and sedative in India. In addition, the root was used by the primitive Greeks and used in many other European cultures' traditional remedies.

Sweet flag was utilized in the holy incenses of both the primitive Egyptians and Sumerians and remnants of the herb were discovered onto the Tutankhamun tomb. The fragrant leaves were used as insecticides and efficient air-fresheners in houses and medieval churches by placing on the floors.

Calamus has a long history of therapeutical usage in a variety of pharmacognostical criteria. It is broadly utilized in modern herbal medicines as a mild tonic and aromatic stimulant (Grieve, 1984). In herbal drug system it is exceptionally worthy as a renovator for the nervous system, brain, and as a solution for digestive problems (Chevallier, 1996). The calamus root is aphrodisiac, anodyne, aromatic, diaphoretic, emmenagogue, carminative, febrifuge, hallucinogenic, expectorant, sedative, stimulant, hypotensive, stomachic, vermifuge, and mildly tonic (Chiej, 1984; Grieve, 1984; Launert,

1981; Mills, 1985; Lust, 1983; Chopra et al., 1986; Weiner, 1980). It is utilized internally to treat bronchitis, digestive disorders, sinusitis, and so on (Bown, 1995). It is mentioned to have amazing tonic powers to stimulate and normalize appetite. In smaller doses it diminishes stomach acidity while in larger doses it increases stomach secretion (Chevallier, 1996) and in this way, it is, suggested in anorexia nervosa treatment (Phillips et al., 1990). Calamus is also utilized externally in treatment of neuralgia, skin eruptions and rheumatic pains (Bown, 1995). The root infusion could bring about an abortion (Weiner, 1980) while chewing of root mitigates toothache (Weiner, 1980). In the folk medicinal system, it is applied to treat cancer, convulsions, arthritis, epilepsy, diarrhea, dyspepsia, etc. Chewing the root is reported to mask the taste for tobacco (Duke, 1985). Two to three years old roots are generally utilized as older roots tend to become hollow and tough (Grieve, 1984). They used to harvest during early spring or late autumn and are dried for future use (Grieve, 1984). The dry root mislays 70% of its weight, but it has an enhanced flavor and odor (Phillips et al., 1990). It does, however, deteriorate in case stored for long time (Phillips et al., 1990). From the roots, a homeopathic cure is made (Launert, 1981). It is also utilized to treat dyspepsia, flatulence, anorexia, and gall bladder disorders (Launert, 1981) (Table 2.3).

## 2.5 ORIGIN AND DISTRIBUTION

Present in ditches, river edges, marshes, and wetlands in wet soils and shallow water (Phillips et al., 1990, 1991). It is located in and naturalized in, Britain, Europe, Asia, New Guinea, Australia, South Africa, North America, Réunion (Clapham et al., 1962). In various subtropical and temperate regions of North America, Asia, and Europe, including India, this plant is used (Mukherjee et al., 2007). It is cultivated all over in India, climbing to altitude of around 2,200 meters. It is cultivated mainly in Shirmaur (Himachal Pradesh), Kashmir, Naga Hills and Manipur. It is routinely cultivated in the koratag (Umamaheshwari et al., 2018). *Acorus calamus* var *angustatus* is a tetraploid type that is native to Asian nations, from Japan to India along with Philippines as well as from Siberia to Indonesia. In the northern subarctic of North America and isolated disjunct areas throughout the Mississippi Valley, the diploid type *Acorus calamus* var *americanus* or *Acorus americanus* is present and diploids are also found in central Siberia (Buryatia), Mongolia, India's northern Himachal Pradesh and Pakistan's Gilgit-Baltistan. In certain parts of the USA (United States) and Canada, it is extinct. It may not be endemic to any of these countries, it is believed to have been spread through

**TABLE 2.3** Country Wise Ethnomedicinal Uses of *A. calamus*

Nation Name	Ailment Name	Plant Parts Used/Dosage Forms	Administration Route	References
India	Skin-diseases	<i>A. calamus</i> and <i>C. aromatica</i> rhizome paste are applied with <i>Argemone mexicana</i> seed paste.	Oral	Quraishi et al. (2017)
	Eczema	Rhizomes paste of sweet flag offered with rhizomes paste of <i>Curcuma aromatica</i> and <i>Azadirachta indica</i> leaves.		
	Cough, ulcer, scab, dermatitis, stuttering, fever, sores.	Rhizomes		Pradhan et al. (2008)
	Fever, cough, cold	Two teaspoon of herbal powder comprising sweet flag rhizomes, <i>Calonyction muricatum</i> flower pedicles, <i>Boerhaavia diffusa</i> roots, <i>Ipomoea muricata</i> seeds, <i>Cassia fistula</i> fruits pulp, Senna leaves, <i>Curcuma longa</i> rhizomes, black pepper, <i>Mentha arvensis</i> leaves and <i>Helicteres isora</i> fruits, is taken with lukewarm water.		Dwivedi et al. (2006)
		<i>A. calamus</i> rhizomes paste is given to children with mother's milk, <i>Calunarejan spinosa</i> , and <i>Myristica fragrance</i> fruits.		Sharma et al. (2004)
	Disorders in GIT	Rhizomes paste of sweet flag is given with cow milk.		Usher (1984)
	Flavoring, carminative, tonic, and head lice infestations.	Dried rhizome infusion (procured and stored throughout the autumn season).		Usher (1984); Ghosh (2008); Natarajan et al. (2000)
	Epilepsy, dysentery, kidney diseases, diarrhea, mental illnesses and liver diseases.	Rhizomes paste of sweet flag is served with honey.		Nisha et al. (2010)
	Wounds, fever, body pain.	Rhizomes		Ragupathy et al. (2008); Tomar (2009)
	Stimulant	<i>A. calamus</i> dry powder is given with honey.		Barbhuiya et al. (2009)

**TABLE 2.3** (Continued)

Nation Name	Ailment Name	Plant Parts Used/Dosage Forms	Administration Route	References
	Dysentery	Calamus rhizomes, freshly crushed, are combined with hot water and administered for three days		Rajith et al. (2010)
	Analgesic Gastrointestinal, emmenagogue, respiratory, anthelmintic	Rhizomes of <i>A. calamus</i> are given with cinchona bark. Rhizomes		Sher et al. (2011)
	Arthritis, paralysis Prolonger labor.	Castor oil is used to apply with rhizomes ash. Rhizomes are used in conjunction with saffron and horse milk.		
	Neurological disorder, respiratory, gastrointestinal, increases menstrual flow, contraceptive, analgesic.	Rhizomes		Poonam et al. (2009); Shrestha et al. (2003); Khatun et al. (2011)
	Analgesic, gastrointestinal, herpangina, respiratory, neurological disorder.			Dastur (1951)
	Injuries	Outer implementation of <i>A. calamus</i> rhizomes.	Dermal	Kadel et al. (2008)
	Stomach ache	Paste of the <i>A. calamus</i> rhizomes' ash.		Boktapa et al. (2010)
	Otitis externa	Roots paste of <i>A. calamus</i> is administered along with coconut husk extract.		Kingston et al. (2007)
	Cough, fever, and cancer	Juice of <i>A. calamus</i> roots is given with honey and <i>Myristica dactyloides</i> .		Yabesh et al. (2014)
	Lotion	<i>A. calamus</i> fresh leaves		Jain et al. (2007)
Pakistan	Diarrhea and colic	Whole plant	Oral	Satyavati et al. (1976)

**TABLE 2.3** (Continued)

Nation Name	Ailment Name	Plant Parts Used/Dosage Forms	Administration Route	References
Nepal	Cough, sore throat, headache, pain, and snake bite.	Rhizomes		Malhi et al. (1972)
	Blood pressure	<i>A. calamus</i> root infusion.		Jain (1968)
	Dysentery	Juice of rhizomes is given with hot water.		
	Neurological, respiratory	Rhizomes		Singh et al. (1979)
Malaysia	Rheumatism, dyspepsia, diarrhea, and hair loss.	Whole plant		Kirtikar et al. (1975)
Tibet	Cancer	Rhizomes		Burang (1979)
	Fever, gastrointestinal	Dried rhizomes are given with <i>Ferula foetida</i> , <i>Saussurea lappa</i> , <i>Terminalia chebula</i> , <i>Inula racemosa</i> , <i>Cuminum cyminum</i> , and <i>Zingiber officinale</i> .		Lama et al. (1979)
China	Gastrointestinal, respiratory, analgesic, neuroprotective, cancer, contraceptive	Rhizomes		Wallnofer et al. (1965); Agarwal et al. (1956); Duke et al. (1985)
	Detoxifications	Sweet flag rhizome along with <i>Alpinia galanga</i> , vinegar, <i>Zingiber purpureum</i> .		Perry et al. (1980)
	Anti-pyretic and ear disease	Rhizomes were administered together with squeezed <i>Coccinia cordifolia</i> stems and water.		
	Analgesic	The rhizome herbal baths.	External	
	Hemorrhage	Rhizomes paste		Boissya et al. (1980)
	Hallucinations	Rhizomes are applied by combining with <i>Podophyllum pleianthum</i> and Indian hemp.	Oral	Li (1977)
	Aphrodisiac	Rhizomes		Dragendor (1898)
	Fair skin	<i>Artemisia vulgaris</i> is administered with sweet flag leaves.	Dermal	Shih-Chen (1973)

**TABLE 2.3** (Continued)

Nation Name	Ailment Name	Plant Parts Used/Dosage Forms	Administration Route	References
Indonesia	Gastrointestinal	Rhizomes	Oral	Hirschhorn (1983)
England		Rhizomes blended with magnesium oxide and chalk.		Wren (1956)
	Gastrointestinal, antibacterial, analgesic	Rhizomes		Grieve (1971)
	Chronic catarrh, dysentery, and neurological.	Sweet flag rhizomes are administered along with <i>Gentiana campestris</i> L.		
		Rhizome		
	Malaria			Wheelwright (1974)
Europe	Obesity, influenza, gastrointestinal, respiratory			Moerman (1981); Jochle (1974)
South African Republic	Gastrointestinal, tooth powder, aphrodisiac, tonic			Watt et al. (1962)
Sweden	Liquor			Kantor (1916)
Germany	Increases menstrual flow, gastrointestinal.			Herrmann (1956); Burkill (1966)
Java	Lactation			Motley, 1994
Lithuania	Chest pain, diarrhea.	Leaves and rhizomes are taken with sugar.		Grieve (1971)
	Relieves pain, rheumatism, gout.	Decoction of leaves	External	Krochmal et al. (1975)
New Guinea	Miscarriage	Rhizomes	Oral	El'Yashevych et al. (1972)
Philippines	Gastrointestinal, rheumatism			Watt et al. (1962)

**TABLE 2.3** (Continued)

<b>Nation Name</b>	<b>Ailment Name</b>	<b>Plant Parts Used/Dosage Forms</b>	<b>Administration Route</b>	<b>References</b>
Russia	Syphilis, typhoid, fever, baldness, cholera.			Barton et al. (1877)
Thailand	Blood purifier, fever			Mokkhasamit et al. (1971)
Turkey	Wound healing, tuberculosis, cough Gastrointestinal		External and oral Oral	Krochmal et al. (1975) Harris (1972); Lindley (1838)
Arab countries	Gastrointestinal, tuberculosis			Caius (1986); Clymer (1963)
Brazil	Destroys parasitic worms.			Clymer (1963)
Argentina	Dysmenorrhea			Manfred (1947)
Korea	Improving memories as well as life span.			Kumar et al. (2013b)
United States	Gastrointestinal, tonic, abortifacient, stimulant, respiratory disorder			Dobelis (1986)
Sri Lanka	Worm infestation, cough	Rhizomes pastes are given with milk.		Napagoda et al. (2019)

areas of the USA by Pre-Columbian people (Motley, 1994; Packer et al., 1984).

According to the Global Biodiversity Information Facility, *Acorus calamus* L. is discovered regionally across 42 countries (Quraishi et al., 2017; Global Biodiversity Information Facility, 2020). The details of the nations where it is distributed are India, Nepal, USA, Japan, Germany, Bangladesh, Myanmar, Thailand, Cambodia, Sri Lanka, Philippines, Papua New Guinea, Malaysia, Indonesia, Vietnam, China, Mongolia, Kazakhstan, Uzbekistan, Georgia, Turkey, Italy, Bulgaria, Greece, Albania, Croatia, Hungary, Switzerland, France, Belgium, Netherland, Czechia, Poland, Belarus, Denmark, United Kingdom, Ireland, Norway, Sweden, Finland, Canada, Korea (Sharma et al., 2020).

## 2.6 BOTANY AND TAXONOMY

*Acorus calamus* L. having common name calamus, with many other common names internationally like, in English its known as sweet cane, sweet flag; in Spanish it's called Acoro; in French: Acore vrai, Roseau aromatique; in Portuguese: calamo-aromatico. Apart from that sweet flag are having some local common names, such as in Germany: Kalmus, in Italy: Acoro aromatic, in the Netherlands: Kalmoes, in Sweden: Kalmus (CABI, 2020).

It is a grass-kind of perennial, rhizome forming, that can grow up to two meters. This species generally located at perpetually wet territories like streams edge and around lakes and ponds, in ditches and seeps. It frequently shares habitation with the general cattail.

The cylindrical rhizome of calamus is aromatic, creeping, and widely branched, thick up to 2.5 cm, white internally and purplish brown to pale brown externally. During the rhizome formation, perennial that can develop to two meters resembles like an iris (Umamaheshwari et al., 2018).

Root comprises of long creeping roots which expanse exactly beneath the surface of soil (Umamaheshwari et al., 2018).

The leaves of the erect *A. calamus* are dense and very uniform in appearance like the iris, but the margins are pleated. A solitary prominent mid vein contains the sweet flag leaves, secondary veins on both sides that are marginally elevated and several other fine tertiary veins. It also distinguishes itself from *Acorus americanus*. In certain locations, the leaves are 0.7 to 1.7 cm wide, with an average width of 1 cm. Calamus leaves are sympodial, slightly narrower than vegetative leaves. The free leaves are wavy, alternate, and green; one to three in seeded cylindrical shaped and green colored and have a thin testa (Umamaheshwari et al., 2018).



If this plant is grown, the very seldom grown flowers are around 3–8 cm tall, cylindrical in form, greenish brown in color and surrounded by a multitude of rounded spikes. Tiny, sessile, thickly packed flowers and 5 to 10 cm of spadix. The spadix could achieve a length of between 4.9 and 8.9 cm during growth. Flowers rose on the basis of latitude during the early to late summer, growing wild in moist regions up to altitude 2,000 m in the Manipur, Himalayas, Naga Hills and in some areas of South India (Umamaheshwari et al., 2018).

The small fruits are berry-like; in ecotypes, chemical components differ and contain many seeds. In July, flowering and fruiting occur (Umamaheshwari et al., 2018).

The taxonomic data of *A. calamus* includes (CABI, 2020):

- **Domain:** Eukaryota.
- **Kingdom:** Plantae.
- **Phylum:** Spermatophyta.
- **Subphylum:** Angiospermae.
- **Class:** Monocotyledonae.
- **Order:** Arales.
- **Family:** Acoraceae.
- **Genus:** *Acorus*.
- **Species:** *Calamus*.

## 2.7 VARIETIES AND CULTIVARS

Some global crop varieties are there which includes:

1. ***Acorus calamus*:** Eurasia and Eastern North America are home to this species. This variety have five feet long leaves and four inch longer elliptical spadix. The plant is perennial and has subterranean rhizomes that grow slowly.
2. ***Acorus calamus* Variegatus:** This variety plant leaves have yellow and cream color.
3. ***Acorus gramineus* Argenteostriatus:** This is intrinsic to Japan. This plant's leaves are 18 inch tall, and the blooms are around three inches. There are clumps that are 2 feet thick and have a sluggish rate of growth.
4. ***Acorus gramineus*:** This variety has been found in Cascadia. It seems to be an ever-green herb.

5. ***Acorus gramineus* Golden Pheasant:** The leaf color of this variety is golden to chartreuse and 12 to 14 inches in height.
6. ***Acorus gramineus* Minimus Aureus:** The leafage of this plant variety is fine in texture and 4-inch height.
7. ***Acorus gramineus* Ogon:** The golden and green color of the varying leaves of this plant variety is 10 to 12 inch tall.
8. ***Acorus gramineus* Variegatus:** The white and green color of the varying leaves of this plant is 8–12 inches long.
9. ***Acorus gramineus* Yodo-No-Yuki:** The leaf color of this variety of plants is olive-green with a yellowish border.
10. ***Acorus gramineus* Hakuro-Nishiki:** The leaves of this variety of plants are yellowish-green in color.

## 2.8 SOIL AND CLIMATE

*Acorus calamus* L, generally referred to as the sweet flag, occurs with ample moisture or irrigation in almost a large range of soil. This could additionally be cultivated in marshy or waterlogged soils. *A. calamus* grows in 1,800-meter high to 900-meter low altitudes (Sharma et al., 2020). Preferrable pH of this herb ranges from 5.5–7.5 and requires sunny position (Huxley, 1992). The plants can withstand temperatures as low as – 25°C (Phillips et al., 1991). Preferable rainfall should be 70–250 cm. The Tropical to subtropical climate is found to be worthy for this crop. The land is prepared identic to irrigated paddy field. Second, in order to promote impounding water, the lands are dripped with farmyard compost and *Pongamia pinnata* Pierre green leaves compost. March to April is the strongest planting season (Lokesh, 2004).

## 2.9 PROPAGATION

Propagation is often carried out by rhizomes. First the rhizomes are harvested into small portions and then sprouted rhizomes are cultivated. During planting 44,400 per acre seed are used. As soon the seed gets ripen, it is planted in a cold weather. Stand the pot in about 3 cm of water. As soon as they are too large to work with, pot up young seedlings, holding them moist by fixing the containers in shallows water and overwintering in a cold or greenhouse infrastructure for the 1<sup>st</sup> year. In Britain seed is seldomly produced (Grieve,

1984; Clapham et al., 1962). During spring division starts since the growth start. Easily, it can be carried out effectively at any moment throughout the growth period and could be sown direct into its stable situations.

## 2.10 PLANTING, IRRIGATION, AND NUTRIENT MANAGEMENT

Developing shoots or living ends of *A. calamus* are procured from past crops upon harvest and stored in a moist or puddle area for 2–3 weeks. This plantation materials are then put in a cultivated land at (30 x 30) cm spacing (Lokesh, 2004). During sowing the rhizomes are sown at depth of 4 cm, and the method of sowing should be direct sowing of seeds or sprouted rhizomes on bed.

It is water-deep grain similar to irrigated paddy, but 10 to 11 months is the length of the sweet flag. So, this herb is much compatible where the water isn't scarce. In preliminary phase of this grain, ground is waterlogged with 5-centimeter-deep water. Since the grain started growing, depth of the water in ground is raised to 10 centimeter till 20 days prior harvest. The total water needed for the period of 10 months is 34.58 million liters (Lokesh, 2004).

When these plants block the rows in a dense canopy, the grain is weeded once every month for the initial four to five months (Lokesh, 2004).

Chemical fertilizers with 45: 12.5: 12.5 kg of NPK/hectare (typically urea/17 All/DAP) are utilized for the top dressing in two or three splitted dosing, 60 days after plantation (Lokesh, 2004). Apply 1/3 portion of nitrogen (N), full portion of phosphorus (P), and potash (K) as basal dose. Residual portion of nitrogen should be applied after 1- and 2-months post plantation (Lokesh, 2004).

## 2.11 PEST AND DISEASE MANAGEMENT

The common issue in cultivation is pests attack over crops. Likewise, some minor organisms namely *Cerataphis lataniae* (palm aphid), *Fusarium oxysporum* (basal rot), *Lasioderma serricorne* (cigarette beetle) usually attacks sweet flag. Apart from that another fungal pathogen is there, usually called *Gibberella intricans* (damping-off of safflower) (CABI, 2020).

### 2.11.1 SLUG DAMAGE

It is the harm due to the slug on the herb leaves. They feed themselves on fresh plant leaves. Metaldehyde or iron phosphate is applied to rescue the plant from slugs.

### **2.11.2 MEALY BUGS**

It's a kind of harm to the plants caused by *Pseudococcus* and *Lepidocephalus*. Yellowing and withering starts with the leaves. About 10 ml of Methyl parathion or 20 ml of Quinalphos is added to the shoots and roots of the herb in 10 liters of water.

### **2.11.3 LEAF SPOT**

The discolored spots occurred on the plant leaves are due to the fungus attack. The leaf spot should be regulated by the application of 10 g of Captan and 20 ml of Chlorpyrifos in 10 liters of water.

## **2.12 HARVESTING AND YIELD**

That is a symbol of crop maturity when the leaf tips have begun to turn yellowish. Rhizomes are close to the surface and grow from 30 to 60 cm in height. They were harvested between February and March, when the crop was 10–11 months old (Lokesh, 2004). The best temperature for harvesting is 15–20°C. The most conventional type of harvesting implements is small sickle, big sickle and darat (Verma, 1998).

The average rhizomes yield is 40 qt/ha (quintal/hectare). Better agronomic techniques, on the other hand, might improve production (Lokesh, 2004). In addition, for two continuous years, an examination was attempted to investigate the probability of increasing the yield of *A. calamus* L rhizome by altering the planting period (such as growing in rainy and autumn seasons), retaining separate distances, and harvested in various seasons. Calamus yields were considerably higher when planted in autumn (131.5 qt/ha) than in the rainy season (65.7 qt/ha) (Tiwari et al., 2012). Crop harvesting after one year resulted in greater rhizomes yield of 164.7 qt/ha and 93.7 qt/ha during the autumn and rainy seasons, respectively. In various yield pieces, a similar trend was also seen. Closer planting (20 x 20 cm, 30 x 20 cm) resulted in slightly higher rhizome yields (86.2 qt/ha, 81.2 qt/ha) than a larger 40 x 40 cm (70.3 qt/ha) spacing. This research shows the possibility of maximizing sweet flag rhizome yield by controlling planting and harvesting times while maintaining sufficient plant spacing (Tiwari et al., 2012).

## **2.13 POST-HARVEST HANDLING AND STORAGE**

They are harvested into parts that are 5 to 7.5 cm longer and then dried in the sun for one day then battered and rubbed. In the heat, this drying process and

eventual rubbing is followed 2 to 3 times before the leaf scales and fibrous roots are expelled. It's packed to be shipped after rubbing. Cultivators have been using hand-operated or power-operated equipment in recent days to spread the leafy scales and fibrous roots (Lokesh, 2004). It ought to be kept in a cool and dry place, but not >1 year. Following this, the roots lose the majority of their active principles.

## 2.14 PROCESSING AND CHARACTERIZATION OF PHYTO-CONSTITUENTS

The different phytochemical studies of calamus have been disclosed that it contains different phytochemical constituents. The constituents are sterols, phenylpropanoids, triterpene glycosides, sesquiterpenoids, triterpenoid saponins, monoterpenes, and alkaloids, essential oil containing calameon, calamen, asarone, clamenol, and sesquiterpenes. The plant additionally comprises a bitter glycoside namely acorine along with  $\alpha$ -pinene,  $\beta$ -pinene, eugenol, and camphene (Sharma et al., 2020; Mukherjee et al., 2007; Chandra et al., 2017; Imam et al., 2013).

The different studies of volatile oil of calamus obtained in mass spectrometry and gas chromatography has 145 components in the oil from triploid European *Acorus calamus* and 93 components in the oil from tetraploid Indian *Acorus calamus* (Sharma et al., 2020; Umamaheshwari et al., 2018). The theory constituents found in the volatile oil are 2,4,5-trimethoxy-1-propenylbenzene as  $\beta$ -asarone and  $\alpha$ -asarone, chemically classified as trans-and cis-isomers, respectively (Mukherjee et al., 2007; Baxter et al., 1960).

The oil from calamus also comprises lots of chemical compounds in different concentrations (Mukherjee et al., 2007; Raina et al., 2003; Oprean et al., 2001) like:  $\gamma$ -asarone, eugenyl acetate, methyl isoeugenol, isoeugenol, *p*-cymene, azulene, calamol, dipentene, methyl ether of eugenol, asaronaldehyde, methyleugenol, 1,8-cineole, terpinolene,  $\alpha$ -caryophyllene, hydrocarbons, and camphor (Mukherjee et al., 2007; Nigam et al., 1990; Srivastava et al., 1997; Mukherjee, 2002). In addition, the oil consists of fatty acids such as palmitic acid and its ester, heptylic acid, and butyric acid ester (Mukherjee et al., 2007; Chaudhry et al., 1957).

### 2.14.1 PHENYLPROPANOIDS

These are having an aromatic ring along with a structurally varied category of secondary plant metabolites derived from phenylalanine (C6–C3), such as

alpha-asarone,  $\beta$ -asarone, eugenol, isoeugenol, etc. (Banerjee et al., 2020a; Bose et al., 2020). Various phenylpropanoids from calamus rhizomes and leaves have been described. The important components of this plant are alpha and  $\beta$ -asarone discovered from the rhizome. There are also records of a collection of aromatic rhizome oils with different structures.

### **2.14.2 SESQUITERPENOIDS**

Around 44 sesquiterpenes, inclusive of lactones, were separated and recognized in sweet-flag rhizomes. Sesquiterpene lactones are formed from three units of isoprene and are made up of lactone rings. It is accepted that the alpha- $\beta$  unsaturated alpha-lactonic ring in sesquiterpene lactones is responsible for pharmacological activities (46–99).

### **2.14.3 MONOTERPENES**

These are the simplest class terpene (C-10) which is associate with 2 isoprene units (monocyclic, bicyclic, tricyclic, etc.) (Banerjee et al., 2020b). Monoterpenes may have diverse functional groups, as ketones, aldehydes, esters, phenols, ethers, and alcohols (Benaiges et al., 2007). These organic components spread the characteristic fragrance and flavor of calamus rhizomes and leaves (100–122).

### **2.14.4 TRITERPENOID SAPONINS**

Triterpenoid saponins comprise of a pentacyclic terpene (C-30) skeleton (Banerjee et al., 2019). Till now only 2 triterpenoid saponins (123, 124) have been recognized from sweet flag rhizomes.

### **2.14.5 OTHER COMPOUNDS**

To date, calamus rhizomes have been described with 1 xanthone glycoside (125), 2 alkaloids (126–127), 1 triterpene glycoside (128), 1 steroid (129), 12 amino acids (130–141), and 4 fatty acids (142–145).

The details of the chemical components of *A. calamus* along with their processing and characterization are portrayed in Table 2.4 and Figure 2.1.

**TABLE 2.4.** *A. calamus* Chemical Constituents Extracted from Various Plant Sections

Classification	Compounds No.	Chemical Ingredients	Characterization Techniques	Plant Parts	Extracts Used	References							
Phenylpropanoids	1	$\alpha$ -Asarone	GC-FID, GC-MS	Rhizome	n-hexane, aqueous, methanol, ethanol	Mukherjee (2002); Nigam et al. (1990); Kumar et al. (2010); Lee et al. (2011); Padalia et al. (2014)							
	2	$\beta$ -Asarone											
	3	$\gamma$ -Asarone											
	4	Eugenyl acetate	GC-MS		Aqueous extract		Mukherjee (2002); Nigam et al. (1990); Kumar et al. (2015)						
	5	Eugenol											
	6	Isoeugenol											
	7	Calamol											
	8	Azulene											
	9	Eugenol methyl ether											
	10	Dipentene											
	11	Asaronaldehyde											
	12	Terpinolene											
	13	1,8-cineole											
	14	Methyl eugenol						GC-FID, GC-MS	Aqueous extract	n-hexane, ethyl acetate	Srivastava et al. (1997)		
	15	Methyl isoeugenol										Hexane	Mukherjee (2002); Nigam et al. (1990); Kumar et al. (2015); Kim et al. (2011)
	16	(E)-Methyl isoeugenol											
	17	(E)-Isoeugenol acetate									Lee et al. (2011)		

**TABLE 2.4** (Continued)

Classification	Compounds No.	Chemical Ingredients	Characterization Techniques	Plant Parts	Extracts Used	References
	18	Cinnamaldehyde			n-hexane,	Srivastava et al. (1997)
	19	Eusarone			ethyl acetate	
	20	Cis-methyl isoeugenol				
	21	Cyclohexanone	GC-MS		Hexane	Kim et al. (2011)
	22	Isoasarone	NMR		Chloroform	Patra et al. (1981)
	23	Acorin				
	24	Safrole				
	25	Z-3-(2,4,5-trimethoxyphenyl)-2-propenal	FTIR, NMR		Ethanol	Saxena (1986)
	26	2,3-dihydro-4,5,7-trimethoxy-1-ethyl-2-methyl-3 (2,4,5-trimethoxyphenyl) indene				
	27	(Z)-asarone	GC-MS	Leaves	n-hexane	Radušienė et al. (2007)
	28	(E)-caryophyllene				
	29	Estragole		Rhizome	Aqueous	Haghighi et al. (2017)
	30	Carvacrol				
	31	2-cyclohexane-1-one				
	32	Naphthalene				
	33	$\gamma$ -Cadinene				
	34	Aristolene				
	35	1(5),3-aromadenedradiene				
	36	5-n-butyltetraline				



**TABLE 2.4** (Continued)

Classification	Compounds No.	Chemical Ingredients	Characterization Techniques	Plant Parts	Extracts Used	References
Sesquiterpenoids	37	4,5-dehydro-isolongifolene				
	38	Calarene				
	39	Isohomogenol				
	40	Zingiberene				
	41	$\alpha$ -Calacorene				
	42	5,8-dimethyl isoquinoline				
	43	Cyclohexane methanol				
	44	Longifolene				
	45	Isoelemicin				
	46	Calamene				Mukherjee (2002); Nigam et al. (1990); Kumar et al. (2015)
	47	Calameneol				
	48	Calameone				
	49	Preisocalamendiol				
	50	1,4-(trans)1,7(trans)-acorenone				Özcan et al. (2002)
	51	1,4-(cis)-1,7-(trans)-acorenone				
	52	2,6 diepishyobunone				
	53	$\alpha$ -Gurjunene				
54	$\beta$ -Gurjunene					
55	$\alpha$ -Cedrene				Haghighi et al. (2017)	
56	$\beta$ -Elemene					
57	$\beta$ -Cedrene				Özcan et al. (2002)	

**TABLE 2.4** (Continued)

Classification	Compounds No.	Chemical Ingredients	Characterization Techniques	Plant Parts	Extracts Used	References
	58	$\beta$ -Caryophyllene				
	59	Valencene				
	60	Viridiflorene				
	61	Caryophyllene oxide				
	62	$\delta$ -Cadinene				
	63	$\alpha$ -Curcumene				
	64	Elemol				
	65	Cedrol				
	66	Spathulenol				
	67	Acorenone				
	68	$\alpha$ -Cadinol				
	69	Shyobunone				Kumar et al. (2010); Özcan et al. (2002); Nawamaki et al. (1996); Zaugg et al. (2011)
	70	Isoshyobunone				Özcan et al. (2002); Nawamaki et al. (1996); Yamamura et al. (1971)
	71	Humulene oxide II	GC-FID, GC-MS			Lee et al. (2011); Özcan et al. (2002)
	72	$\alpha$ -Selinene				
	73	Humulene epoxide II				Lee et al. (2011)
	74	$\alpha$ -Bisabolol				

**TABLE 2.4** (Continued)

Classification	Compounds No.	Chemical Ingredients	Characterization Techniques	Plant Parts	Extracts Used	References
	75	Asaronaldehyde			Chloroform	Patra et al. (1981)
	76	Acorone			Hydro alcoholic	Zaugg et al. (2011)
	77	Neo-acorane A			Ethanol	Li et al. (2017)
	78	Acoric acid				
	79	Calamusin D				
	80	1,5-Guaiene-4,10-diol-6-one				Zhou et al. (2012)
	81	Calamusenone	GLC, IR, NMR		Petroleum ether	Nawamaki et al. (1996)
	82	Isocalamendiol				
	83	Dehydroxyiso-calamendiol				
	84	Epishyobunone				
	85	Dioxosarcoguaiacol	HPLC		Petroleum ether	Yamamura et al. (1971)
	86	7-tetracycloundecanol,4,4,11,11-tetramethyl	GC-MS		Ethanol	Kumar et al. (2010)
	87	4,7-Methano-4-naphth[1,8a-b]oxirene				
	88	Spathulenol				Haghighi et al. (2017)
	89	Vulgarol B				

**TABLE 2.4** (Continued)

Classification	Compounds No.	Chemical Ingredients	Characterization Techniques	Plant Parts	Extracts Used	References
	90	Tatanan A			95% ethanol	Yao et al. (2018)
	91	Acoramone				
	92	2-hydroxyacorenone				
	93	4-(2-formyl-5-methoxymethyl pyrrol-1-yl) butyric acid methyl ester				
	94	2-acetoxyacorenone				
	95	Acoramol				
	96	N-transferuloyl tyramine				
	97	Tatarinoid A				
	98	Tatarinoid B				
	99	Acortatarin A				
Monoterpenes	100	<i>p</i> -Cymene	GC-FID, GC-MS	Rhizomes, roots	Aqueous	Lee et al. (2011); Özcan et al. (2002); Haghghi et al. (2017)
	101	$\alpha$ -Pinene	GC-MS			Mukherjee (2002); Nigam et al. (1990); Kumar et al. (2015); Özcan et al. (2002)
	102	$\beta$ -Pinene				
	103	Camphene				Mukherjee (2002); Nigam et al. (1990); Kumar et al. (2015); Özcan et al. (2002); Haghghi et al. (2017)

TABLE 2.4 (Continued)

Classification	Compounds No.	Chemical Ingredients	Characterization Techniques	Plant Parts	Extracts Used	References
	104	<i>o</i> -Cymol				Haghighi et al. (2017)
	105	$\gamma$ -Terpinene				
	106	$\alpha$ -Terpinolene				
	107	Anethole				
	108	Thymol				
	109	Isoaromadendrene epoxide				
	110	Camphor		Rhizome, leaves, roots	Aqueous, hexane	Özcan et al. (2002); Radušiene et al. (2007)
	111	Sabinene		Roots	Aqueous	Özcan et al. (2002)
	112	Cis-linalol oxide				
	113	Cis-sabinene hydrate				
	114	Trans-linalol oxide				
	115	Terpinen-4-ol				
	116	$\alpha$ -Acoradiene				
	117	$\beta$ -Acoradiene				
	118	$\alpha$ -Terpineol				
	119	2-hexenal				
	120	Limonene				Özcan et al. (2002); Haghighi et al. (2017)
	121	Linalool				Özcan et al. (2002); Radušiene et al. (2007)

**TABLE 2.4** (Continued)

Classification	Compounds No.	Chemical Ingredients	Characterization Techniques	Plant Parts	Extracts Used	References
	122	Isoborneol		Leaves	Hexane	Radušiene et al. (2007)
Triterpenoid saponins	123	1 $\beta$ ,2 $\alpha$ ,3 $\beta$ , 19 $\alpha$ -Tetrahydroxyurs-12-en-28-oic acid-28-O- $\{\beta$ -D-glucopyranosyl (1-2)}- $\beta$ -D-galactopyranoside	NMR	Rhizome	Ethanol	Rai et al. (1998)
	124	3- $\beta$ ,22- $\alpha$ -24,29-Tetrahydroxyolean-12-en-3-O-( $\beta$ -Darabinosyl(1,3))- $\beta$ -D-arabinopyranoside				
Xanthone glycosides	125	4,5,8-trimethoxy-xanthone-2-O- $\beta$ -D-glucopyranosyl (1-2)-O- $\beta$ -D-galactopyranoside				Rai et al. (1999)
Alkaloids	126	Trimethoxyamphetamine,2,3,5	GC-MS			Kumar et al. (2010)
	127	Pyrimidin-2-one,4-[N-methylureido]-1-[4-methyl amino carbonloxy methyl]				
Triterpene glycoside	128	22-[(6-deoxy-L-rhamnopyranosyl oxy)-3,23-dihydroxy-, methyl ester, (3 $\beta$ ,4 $\beta$ ,20 $\alpha$ ,22 $\beta$ )	NMR	Root, Rhizomes	Ethyl acetate	Wu et al. (2007)
Steroids/Sterols	129	$\beta$ -daucosterol				

**TABLE 2.4** (Continued)

Classification	Compounds No.	Chemical Ingredients	Characterization Techniques	Plant Parts	Extracts Used	References
Amino acids	130	Arginine	HPLC	Roots	Ethanol	Vashi et al. (1987); Weber et al. (1994)
	131	Lysine				
	132	Phenylalanine				
	133	Threonine				
	134	Tryptophan				
	135	$\alpha$ -alanine				
	136	Asparagine				
	137	Aspartic acid				
	138	Norvaline				
	139	Proline				
	140	Tyrosine				
141	Glutamic acid					
Fatty acids	142	Myristic acid	GLC	Rhizome	Petroleum ether	Asif et al. (1984)
	143	Palmitic acid				
	144	Palmitoleic acid				
	145	Stearic acid				

*Abbreviation:* GC-MS: Gas chromatography–mass spectrometry; GC-FID: Gas chromatography–flame ionization detector; NMR: Nuclear magnetic resonance; GLC: Gas liquid chromatography; FTIR: Fourier-transform infrared spectroscopy; HPLC: High-performance liquid chromatography; and IR: Infrared spectroscopy.

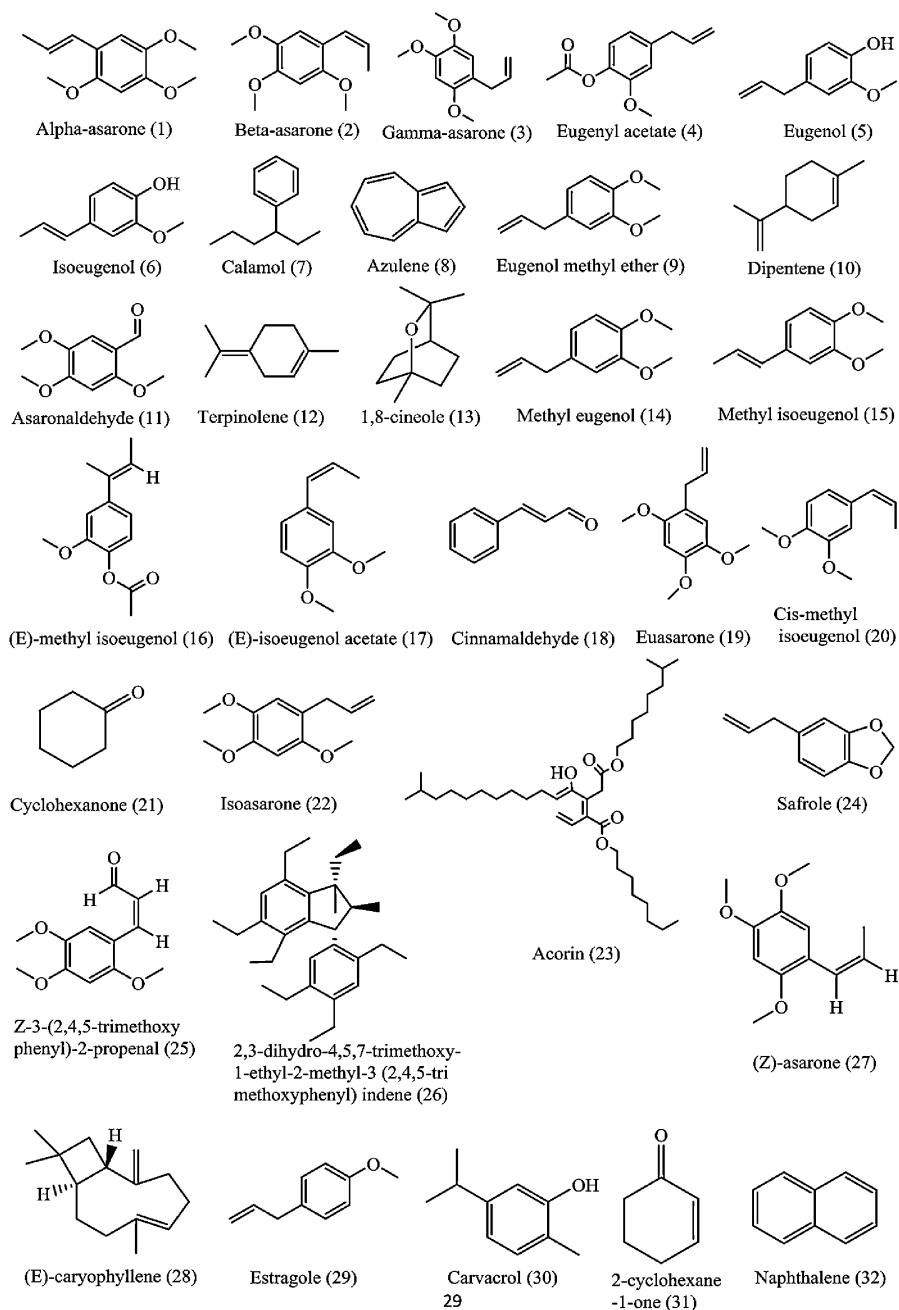


Figure 2.1 (Continued)



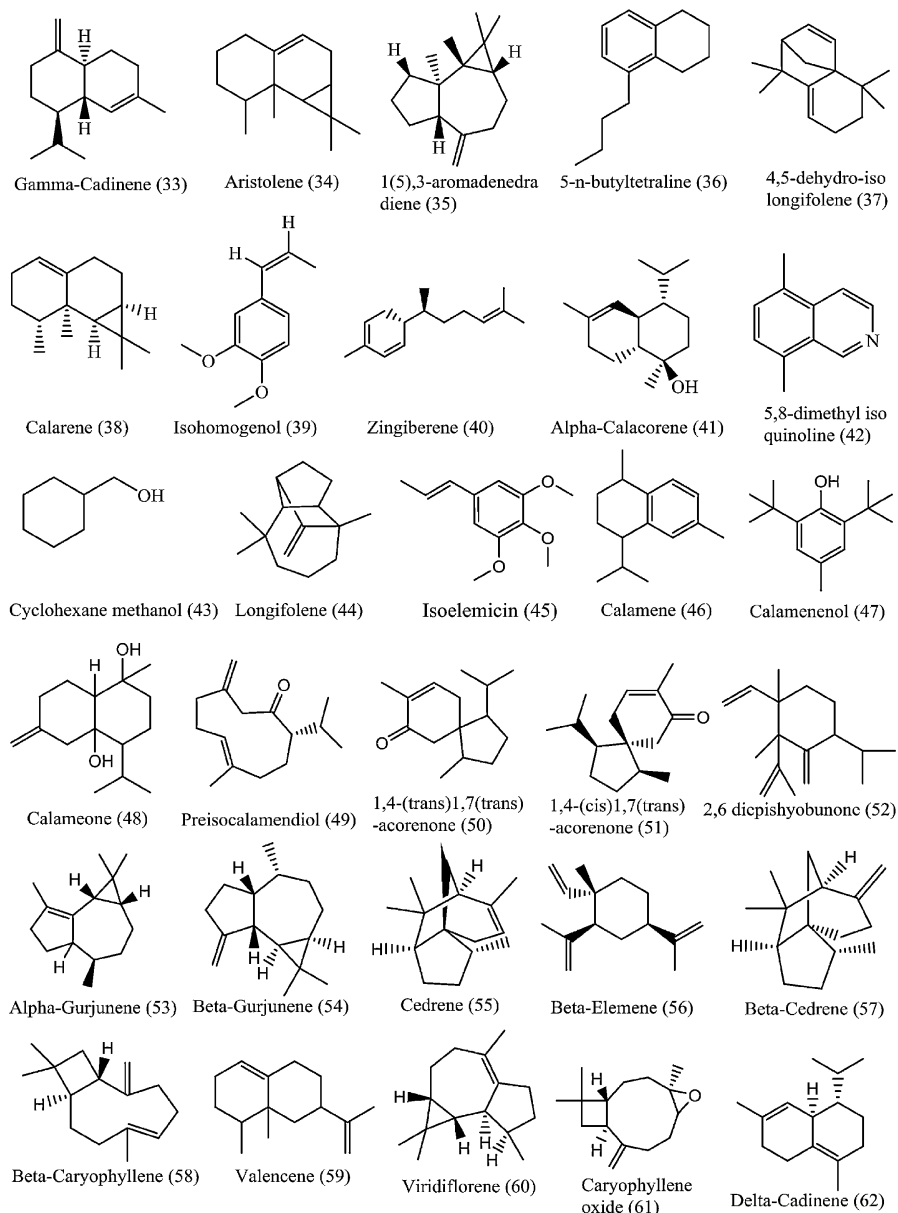


Figure 2.1 (Continued)

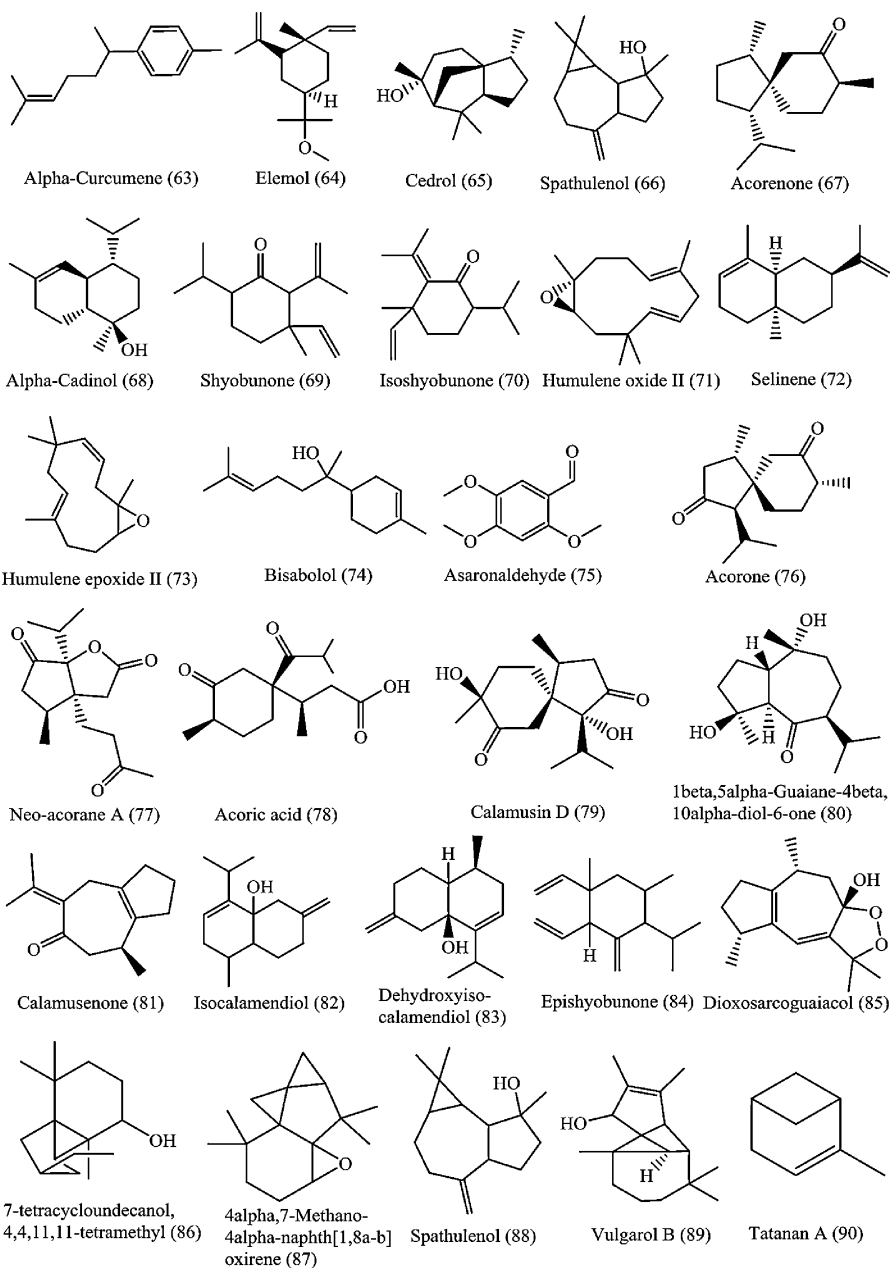


Figure 2.1 (Continued)

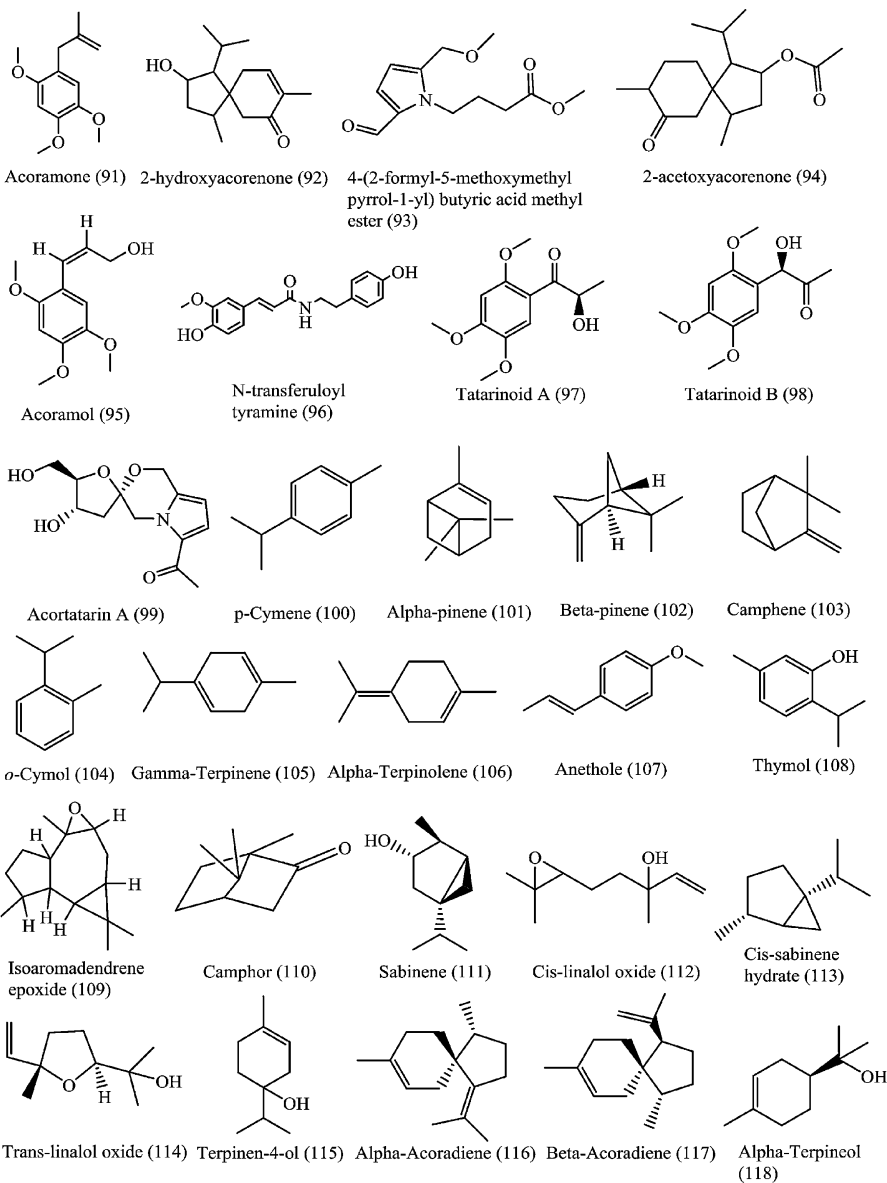
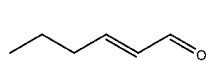
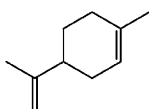


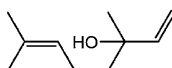
Figure 2.1 (Continued)



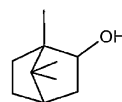
2-hexenal (119)



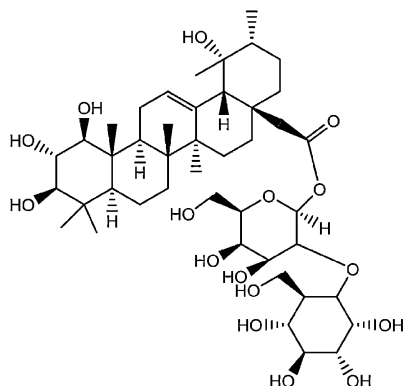
Limonene (120)



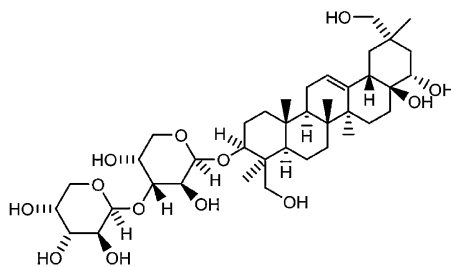
Linalool (121)



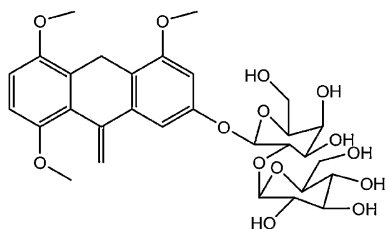
Isoborneol (122)



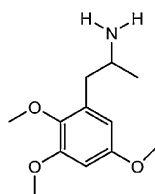
1beta,2alpha,3beta,19alpha-Tetrahydroxyurs-12-en-28-oic acid-28-O-((beta-D-glucopyranosyl (1-2))-beta-D-galactopyranoside) (123)



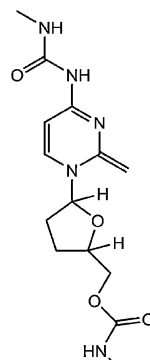
3-beta,22-alpha-24,29-Tetrahydroxyolean-12-en-3-O-(beta-D-arabinosyl(1,3))-beta-D-arabinopyranoside (124)



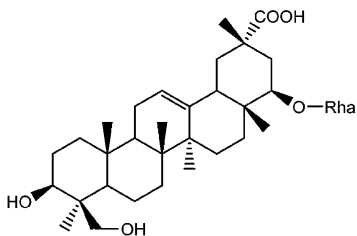
4,5,8-trimethoxy-xanthone-2-O-beta-D-glucopyranosyl (1-2)-O-beta-D-galactopyranoside (125)



Trimethoxyamphetamine, 2,3,5 (126)

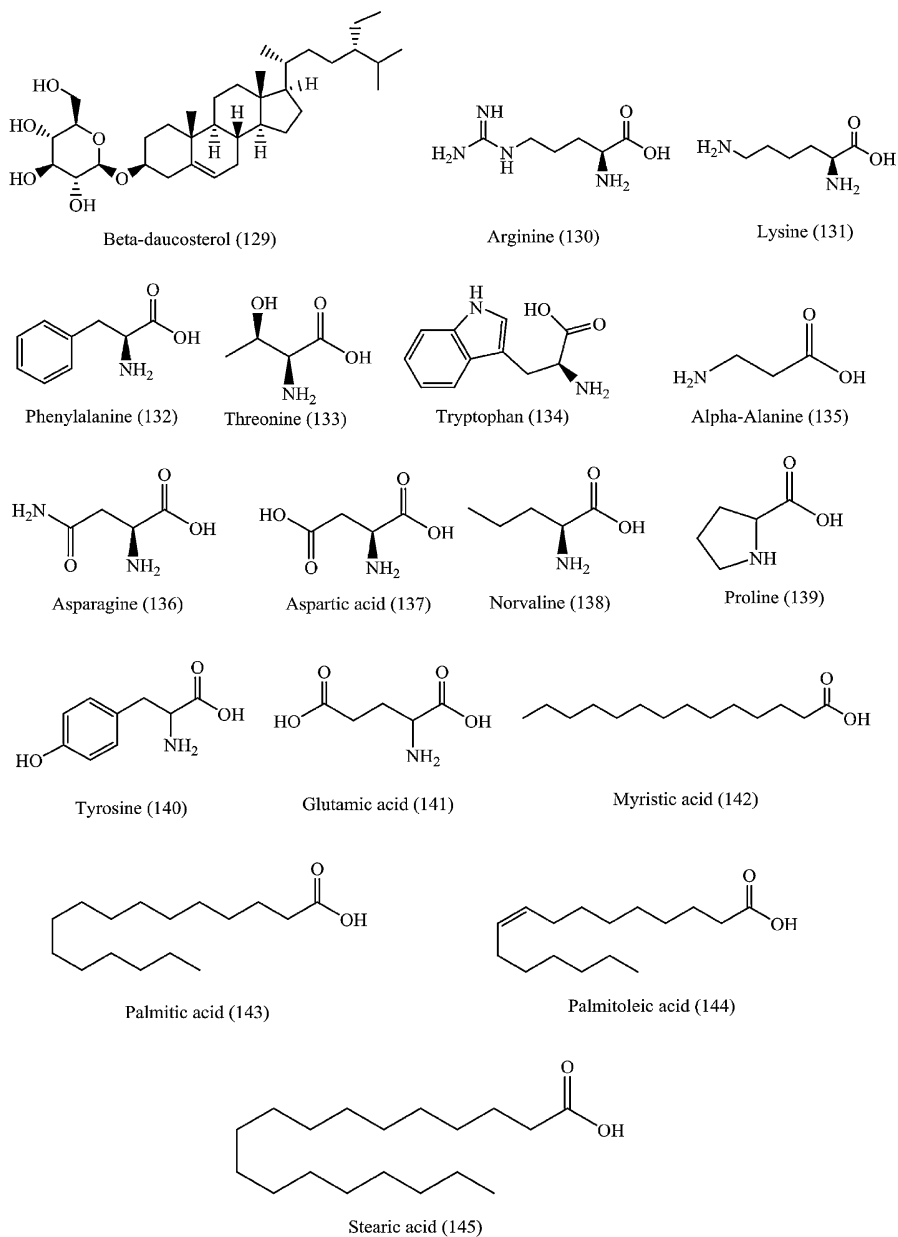


Pyrimidin-2-one, 4-[N-methylureido]-1-[4methyl amino carbonoxy methyl] (127)



22-[[6-deoxy-alpha-L-rhamnopyranosyl]oxy]-3,23-dihydroxy-, methyl ester, (3beta,4beta,20alpha,22beta) (128)

Figure 2.1 (Continued)



**FIGURE 2.1** Phytoconstituents obtained from *Acorus calamus*.

## 2.15 BIOLOGICAL ACTIVITIES OF *ACORUS CALAMUS*

### 2.15.1 ANTICANCER ACTIVITY

Now a day's cancer, a major non-infectious disorder is being treated with different medicinal herbs or plants. *Acorus calamus* is a well-known therapeutic plant which have an anticancer activity. The *Acorus calamus* rhizome extract possess antioxidant property. Antioxidants are the free radicals which have the ability to prevent and cure the cancer from extremely reactive oxygen compounds which is responsible for cancer. Sweet flag can be implemented in cancer treatment (Gaidhani et al., 2009). The ethanolic and methanolic extracts as well as essential oil of calamus rhizome was evaluated on human gastric cell line (AGS) (Haghighi et al., 2017). Liu et al. revealed in research that treatment with  $\beta$ -asarone diminished the occurrence and tumour formation number against genotoxic colonic chemical carcinogen 1,2-Dimethyl hydrazine in CRJ: CD-1 (ICR) mice (Das et al., 2019). Further research by Wu et al. demonstrates the impacts of  $\beta$ -asarone which suppresses the proliferation in gastric cancer cell and induced early apoptosis. Human colorectal cell lines HT-29 and SW-480 were treated with  $\beta$ -asarone and finally concluded  $\beta$ -asarone inhibits colorectal carcinogenesis (Das et al., 2019).

### 2.15.2 ANTIDIABETIC ACTIVITY

Diabetes, a ceaseless condition related with abnormally increase in sugar levels (glucose) in blood causes in absence or insufficient production of insulin or a disability of the body to appropriately utilize insulin. *Acorus calamus* is extensively utilized in the diabetes treatment in conventional folk medication. An antidiabetic study described that *A. calamus* methanolic extract when administered orally, showed a significant blood glucose level decrease in streptozotocin induced diabetic rat. Blood glucose levels were lowered after 21 days of extract therapy, while plasma insulin levels were dramatically increased (Prisilla et al., 2012).

Prashanth et al. studied that *A. calamus* extract decreases the blood glucose level significantly. Total 54 rats were taken for that experiment on 2 different phases. *A. calamus* extract in diverse doses like 100, 150, and 200 mg per kg to various groups and observed thoroughly. It was shown that *A. calamus* 150 mg/kg induces hypoglycemic action in both alloxan-induced diabetic and non-diabetic rats.

A minor drop in blood glucose level in fasted and glucose-fed normal mice with 200–800 mg/kg *A. calamus* extract was further examined after 1 hour after ingestion (Si et al., 2010a).

### **2.15.3 ANTIMICROBIAL ACTIVITY**

Both plant-based and synthetic products from different sources have been recognized over the past 2 decades and found *Acorus calamus* as one such herb alleged to have antimicrobial activity.  $\beta$ -asarone, an antibacterial component, was extracted from methanolic sweet flag leaves essence utilizing different chromatographic methods. Due to pathogens with multi-drug resistance, the clinical efficiency of existing antibiotics is being dangerous (Bandow et al., 2003). So, researchers are thinking to progress better herbal medicine against microbial infections (Manikandan et al., 2010; Murugaian et al., 2009). The study displayed potential antimicrobial action of methanolic *A. calamus* rhizome extract, like it is highly active against filamentous fungi (Phongpaichit et al., 2005).

It is clear from the experiment that *A. calamus* displays antibacterial and antifungal activity, which gives solid evidence of the application of this herb in various drugs (Kumar et al., 2014). Agar disc diffusion process (Bauer et al., 1996) was employed for antimicrobial bioassay. Several past and continuing investigations have shown that calamus rhizomes have antibacterial properties (Mungkornasawakul et al., 2000; McGaw et al., 2002; Grosvenor et al., 1995). It is also traditionally utilized as medicinal herb to treat bacterial infection in India (Panchal et al., 1989). From an *in-vitro* experiment of calamus it can be understood that the compound has remarkable antimicrobial activity (Kaithavalappil et al., 2015). Another experiment reported that *A. calamus* methanol extract displayed inhibition against *Salmonella typhi*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa* (Singh et al., 2011).

### **2.15.4 ANTI-INFLAMMATORY ACTIVITY**

Inflammation has been related with many diseases which bring the dangerous effect on the patients, that can cause a threat to his/her life. Numerous anti-inflammatory drugs are obtainable in the market to treat inflammation which are belonging to steroidal and non-steroidal anti-inflammatory drug (NSAIDS). But these drugs have many adverse effects, for example,

gastrointestinal complications, bleeding, and acute renal failure. For this reason, researchers have concentrated their focus on medicinal plants which have the anti-inflammatory property. *A. calamus* is one of the famed therapeutic herbs which have important anti-inflammatory property. The study had been conducted on plants and these plants had been screened for phytochemicals which have anti-inflammatory property (Chamlagai et al., 2016). In acute, chronic and immunological inflammation models, and compared to hydrocortisone action, an extract of the *Acorus calamus* rhizome was investigated. The *A. calamus* extract showed significant anti-inflammatory activity (Kumar et al., 2013a). From the research it is clear that the aqueous *A. calamus* leaves extract has anti-inflammatory action (Vengadesh et al., 2009). The *A. calamus* leaves extract was studied on HaCaT keratinocyte cell lines for anti-inflammatory effect (Kim et al., 2009). The calamus root and rhizome extract have been accounted for anti-inflammatory action (Valay et al., 2015). The anti-inflammatory function was demonstrated by the analysis of distilled saponins derived from water and methanolic extracts of *A. calamus* leaves (Shahzad et al., 2015).

### **2.15.5 ANTIDIARRHEAL ACTIVITY**

Diarrhea is a nationwide issue, particularly among kids. Many medicinal plants which are conveniently available had been portrayed to be efficient against diarrhea. Sweet flag is a kind of therapeutic plant that has anti-diarrheal properties. It was reported that *A. calamus* possess many medicinal benefits inclusive of anti-diarrheal property (Rajput et al., 2014). Water boiled with *A. calamus* ought to be given to patient suffering from diarrhea. In an experiment it significantly declines the severity caused by diarrhea. *A. calamus* are utilized in traditional folk medicine in order to treat diarrhea (Kapadia et al., 2012). Additional analysis revealed that aqueous and methanolic sweet flag extract displayed anti-diarrheal effect against diarrheal model induced by castor oil (Devi et al., 2014). The *A. calamus* rhizome is recognized in Ayurvedic medicine to have expectorant, aromatic stimulant, emetic, diuretics properties. It's utilized to treat a host of diseases, for example, diarrhea and dysentery (Kirtikar et al., 1987). From the study it is clear that the rhizomes of *A. calamus* is useful for diarrheal disorder (Jha et al., 1996). An examination was conducted to assess the action of calamus aqueous and methanol extract for anti-diarrheal effect (Mukherjee et al., 2007).



### 2.15.6 ANTHELMINTIC ACTIVITY

Helminthiasis, a macro-parasitic worm disease, is incurred by nematodes. It is amongst the maximal common infection in human affecting a large population worldwide. Many anthelmintics are available in the market but the existing drugs causes adverse effects and made the parasites to drug resistance. There are numerous medicinal herbs which have anthelmintic activity. *A. calamus* is one of such type of popular medicinal plant. The *Acorus calamus* fresh leaves extract is implemented to treat worm infections. The rhizomes and roots of this herbs have anthelmintic activity which is reported earlier (Deepa et al., 2008). The rhizomes infusion of calamus used to applied to children to offer relief from intestinal worms (Bhatt et al., 2015). Previous research on sweet flag rhizome extracts found that it has anthelmintic activity (Devi et al., 2014). A study discloses that aqueous *A. calamus* extract has strong anthelmintic effects in compared to standard Albendazole drug. The phenylpropanoid  $\beta$ -asarone of calamus rhizomes was displayed anthelmintic activity (McGaw et al., 2002). In India, powdered rhizome and rootstock are utilized as anthelmintic (Watt et al., 1962). The investigation indicated that the isolated  $\beta$ -asarone from sweet flag had a stronger anthelmintical impact compared to crude extraction (McGaw et al., 2002). Anthelmintic action was observed in ethyl acetate-chloroform extract of sweet flag rhizomes (Deepa et al., 2008). From the investigation it can be inferred that the *Acorus calamus* extract displayed significant anthelmintic effect at 100 mg/ml concentration (Deb et al., 2013).

### 2.15.7 ANTIADIPOGENIC ACTIVITY

Adipogenesis is defined as the procedure by which preadipocytes get separated into adipocytes. The adipocyte, usually termed as fat cells and lipocytes, is essential to the body's energy balance. Some medicinal herbs have antiadipogenic property, *A. calamus* is one of them. Hypolipidemic efficacy of 50% sweet flag rhizome alcoholic extract in conjunction with saponins.  $\alpha$ -asarone shows hypolipidemic activity and  $\beta$ -asarone restrain the separation of 3T3-L1 adipose tissues. The investigation indicated that  $\alpha$ -asarone of calamus has the inhibitory impact on 3T3-LJ adipose tissue cells (Si et al., 2010b) and asarone has been shown to suppress adipogenesis while promoting lipolysis in 3T3-LJ adipose tissues (Lee et al., 2004). The ethanolic  $\alpha$ -asarone extract had described to promote adipocytes differentiation

(Lee et al., 2004). The major antiadipogenic component of sweet flag oil was purified and identified as a  $\alpha$ -asarone (Lee et al., 2010).

In the last several years, researchers studying the antiadipogenic properties of *Acorus sp.* have shown that *Acorus calamus* is hypolipidemic in rats (Parab et al., 2002). Treatment of asarone significantly restrained the separation of 3T3-L1 preadipose tissues (Lee et al., 2010). Another study showed that  $\beta$ -asarone of calamus ethanol extract enhances differentiation in mouse adipocytes (Wu et al., 2007). The significant anti-adipocytes compound  $\beta$ -asarone repressed accumulation of lipid in a concentration dependent way (Lee et al., 2010).

### 2.15.8 NEURO-PROTECTIVE ACTIVITY

Central Nervous System (CNS) consists of interconnected networks to form on the basis of neuronal function including thinking, learning, and emotionality. Neuro protection is the active suppression of damaging neuro toxic conditions in the nervous system. The aim of neuro protection is to confine neuronal dysfunction after injury and give effort to maintain the integrity of cellular interaction inside the brain. Diverse medicinal herbs that can be utilized alone or in combinations as a neuro protective. *A. calamus* is one of those, which is having prominent action on CNS by improving memory, grasping power, intellect, and speech (Ray et al., 2016). An investigation reveals that  $\beta$ -asarone has neuroprotective action. It suppresses neuronal apoptosis by down regulating Bcl-W, Bcl2 and caspase-3 (Kim et al., 2011). The methanol and acetone sweet flag leaves extracts exhibit CNS depressant activity (Umamaheshwari et al., 2018). A study demonstrated that the rhizome and root of the herb have CNS depressant potency (Pandy et al., 2009). An effective neuroprotector that preserved memories by shielding the hippocampus was  $\beta$ -asarone (Venkatramaniah et al., 2016). *Acorus calamus* is a drug for epilepsy, cognition, enhancing intelligence in children and used to improve brain activities, as suggested by Caraka and Susruta. *Acorus calamus* can enhance memory and reduce stress, according to experimental and clinical research (Singh et al., 2011). Another experiment showed that  $\beta$ -asarone when administered orally, improved cognitive function (Geng et al., 2010). Rhizomes additionally have defensive mechanisms over acrylamide induced neurotoxicity (Shukla et al., 2002).

### **2.15.9 IMMUNOSUPPRESSIVE ACTIVITY**

Immunosuppressive is mostly or totally suppressing the immune response of an individual. Immunosuppressant is the operator that can repress or inhibit immune response, so to treat various autoimmune disorders. Presently the medical herbs and its products have been examined for immunomodulatory effects. Herb essences have been thoroughly researched for possible immunosuppressive effects. The experiment shows the immunosuppressive efficiency of *A. calamus* rhizome ethanolic extract (Mehrotra et al., 2003). *A. calamus* extract prevents the activation of the cells which have shown their immunosuppressive effect (Umamaheshwari et al., 2018). In another examination the immunomodulatory action of ethanolic calamus rhizomes extract has been assessed and positive response has been found (Bhatt et al., 2015). A study by McGaw et al. demonstrated *A. calamus* root, rhizome, and essential oils from rhizomes showed immunosuppressive action (McGaw et al., 2002). A study has described that the *A. calamus* rhizome ethanolic extract exhibit immunomodulatory actions (Mehrotra et al., 2003). Diverse *A. calamus* extracts are also utilized as immunosuppressive action over human lymphocytes (Divya et al., 2011). Inhibition of nitric oxide productions, that is essential in the immune systems, in the cell line after incubation with the extract and LPS for the production of nitric oxide (Mehrotra et al., 2003). Diverse investigation reports revealed numerous helpful bioactivities of calamus leaves and rhizomes extracts, essential oils, and separated phytochemicals, for instance, immunosuppressive. The components were seen as highly active in immunosuppressing (Reddy et al., 2018). *A. calamus* stimulates production of *in-vitro* IL-12 and Nitric oxide by murine macrophage (Devi et al., 2014).

### **2.15.10 INSECTICIDAL ACTIVITY**

Various synthetic pesticides have been employed to combat pests during the last five decades. Many synthetic pesticides are available but due to environmental issues and public health, alternatives of synthetic pesticides have been inquired about. According to watt et al. this plant is reported to be useful for insecticides. According to the findings of the study, the insecticidal effect of *A. calamus* rhizome ethanol extract. The study reflects ethanolic calamus extract might be used for limiting the harmful impacts of pesticides (Sharma et al., 2015). The powder of *A. calamus* and 2 bioactive compounds

namely alpha and beta-asarone have the repellency and toxicity against the red imported fire ant (RIFA). Sweet flag rhizome extracts in acetone, petroleum ether, and methanol exhibit insecticidal action. In between them petroleum ether calamus extract was found more toxic than that of other extracts in the insect species (Hossain et al., 2008). From the literature survey it has also been found that the *A. calamus* extract had significant insecticidal activity (Chauhan et al., 1987; Khan et al., 1986; Schmidt et al., 1994). According to one research, the essential oils from *A. calamus* rhizome and its constituent methyl eugenol, (E)-methylisoeugenol and alpha-asarone is potential insecticides for control of booklice. The *A. calamus* essential oils have been exhibited to have insecticidal effect over many insect species, e.g., termite, odontotermes, obesus (Tare et al., 2001), the kelpfly, *coelopa frigida* (Ocampo et al., 1986), the large grain borer, *prostephanus truh cates* (Schmidt et al., 1994). The plants rhizomes have insecticidal, repellent activity with bioactive compounds like alpha and beta-asarone (Schmidt et al., 1991; Hasan et al., 2006). The study showed that *A. calamus* may be effective in controlling the stored product in godown.

## 2.16 PRECLINICAL AND CLINICAL TRIALS

Many preclinical examinations have been performed on the sweet flag plant from a longer period. The performed experiments for preclinical trials are described in Table 2.5.

Furthermore, calamus has been investigated in clinical trials as a monotherapy and in conjunction with other medical plants, as well as in healthy volunteers and patients with distinct neurological and metabolic conditions. The effect of *A. calamus* on depression, obesity, coronary, and neuroprotection disorders has been supervised by most clinical trials. The data procured thus far may be found in chart given in Table 2.6.

## 2.17 COMMERCIAL/PHARMACEUTICAL PRODUCTS AVAILABLE

There are many herbal drug formulations obtainable in the market, manufactured by numerous companies, which are portrayed in Table 2.7 (Imam et al., 2013; Sharma et al., 2020).

**TABLE 2.5** Preclinical Trial Claims of *A. calamus* in Different Disorders

Activity	Plant Part Used	Extract Type	Dose	Animal Models	Results	References
Antidiabetic	Rhizomes	Methanol	50 mg/kg, 100 mg/kg, and 200 mg/kg, p.o.	STZ-induced rats	↓Lipid profile and blood glucose, ↑Plasma insulin, G6PD level and tissue glycogen.	Prisilla et al. (2012)
		Ethyl acetate	150 and 200 mg per kg, p.o.	Alloxan-induced rat	↓Blood glucose level	Prashanth et al. (2017)
			100 mg per kg, p.o.	Genetical obese diabetic C57BL/Ks db/db mice.	↓Triglycerides and serum glucose levels	Wu et al. (2009)
			100 mg per kg, i.g.	GLP-1 expressions and STZ-induced secretions	↓Blood glucose levels; ↑Secretion of GLP-1	Liu et al. (2015)
			6.25 µg, 12.5 µg, and 25 µg per ml.	<i>In vitro</i> HIT-T15 cell line and α-glucosidase enzyme.	↑Insulin secretion in HIT-T15 cells	Si et al. (2010)
Anti-obesity	Rhizomes	Ethanol and aqueous	400 and 800 mg per kg, p.o.	Glucose tolerance mice.	↓Serum glucose, and ↓level of glucose in blood	
			100 mg and 200 mg per kg	HFD-induced rats	↓ Serum cholesterol and triglycerides; ↑lipoprotein fraction levels	Parab et al. (2002)
		Diethyl ether	20 and 40 mg per kg, p.o.	HFD-induced rats	↑Plasma fibrinogen levels; ↓Total cholesterol and lower-density lipoprotein levels	D'Souza et al. (2007)
		Methanol	250 mg and 500 mg per kg	Triton-X-100-induced hyperlipidemic rats	Dose-dependent anti-hyperlipidemic effect	Kumar et al. (2016)
250 and 500 mg per kg, p.o.	HFD-induced rats		↓Total cholesterol, triglycerides, and LDL; ↑HDL cholesterol level	Arun et al. (2012)		

**TABLE 2.5** (Continued)

Activity	Plant Part Used	Extract Type	Dose	Animal Models	Results	References
Antihypertensive		Aqueous	100, 200, and 300 mg per kg, p.o.	HFD-induced rats	↓Serum glucose, leptin, and insulin levels; ↓ Elevated levels of triglyceride, lower-density lipoprotein, total cholesterol, very LDL cholesterol, phospholipids, and free fatty acid	Athesh et al. (2017)
		Ethyl acetate	250 mg per kg, p.o.	Clamping the left side kidney artery of rats for 4 h	↓ DBP and SBP, blood urea nitrogen, LPO, and creatinine; ↑Levels of NO, CAT, SOD, GPX	Patel et al. (2012)
		Crude extracts, n-hexane, and ethyl acetate	10, 30, and 50 mg per kg	Blood pressure reduction in normotensive anesthetized rats.	Relaxant effects mediated through Ca <sup>2+</sup> antagonism and NO pathways.	Shah et al. (2009)
Anti-inflammatory		Ethanol and $\alpha$ -asarone	100 and 9 mg per kg, p.o.	Dimethyl sulfoxide-induced noise stress to rats.	↓Destructive impact of stress enlightening the hippocampal morphologic change.	Sundaramahalingam et al. (2013)
	Leaves	Ethanol	100 mg/kg and 200 mg/kg	Carrageenan-induced rat paw oedema.	↓Histamine, 5-HT, and kinins	Jain et al. (2010)
Antioxidant	Rhizomes	$\alpha$ -asarone	3 mg, 6 mg, and 9 mg per kg, i.p.	Noise stress induced to rats.	↑SOD and LPO; ↓GPX, CAT, GSH, vitamin C and vitamin E, and protein thiol level.	Manikandan et al. (2005)
	Leaves and rhizomes.	Ethyl acetate and methanol.	200, 100, 80, 60, 40, 20, 10, and 5 $\mu$ g per ml	DPPH radical scavenging chelating ferrous ions, FRAP	Prominent DPPH scavenging action, chelating Fe <sup>2+</sup> ions, and reducing power.	Devi et al. (2011); Acuña et al. (2002)

**TABLE 2.5** (Continued)

Activity	Plant Part Used	Extract Type	Dose	Animal Models	Results	References
Anticonvulsant	Rhizomes	Ethanol	250, 500 mg per kg, p.o.	Acetaminophen-induced rats.	↓MDA; ↑SOD, GPX, CAT, GSH levels	Palani et al. (2010)
	Roots	Ethanol and $\alpha$ -asarone	35 mg and 20 mg per kg	Kainic acid-induced convulsions.	↓Neuroprotective; epileptic seizure; and regenerative ability	Venkatramaniah et al. (2019)
		Methanol	100 and 200 mg/kg, p.o.	PTZ-induced convulsion mice	↑Latency period; ↓PTZ-induced seizure time	Jayaraman et al. (2010)
Antidepressant	Rhizomes	Calamus oil	30, 100, and 300 mg/kg, p.o.	MES, PTZ, and MCS mice model.	Calamus oil is found stable	Kaushik et al. (2017)
		Ethanol	250, 500 mg/kg, p.o.	MES and PTZ-induced convulsion mice.	↓Hind limb extension and tonic flexion of forelimbs.	Chandrashekar et al. (2013)
		Methanol	250 and 150 mg per kg, p.o.	MES and PTZ-induced rats	↓Immobility time at 250 mg per kg, ineffective at 150 mg/kg	Yende et al. (2009)
			50 and 100 mg per kg, i.p.	TST and FST in mice model.	↓Immobility time in a dose-dependent manner.	Pawar et al. (2011)
	Leaves		50 and 100 mg per kg		↓Immobility time	Pushpa et al. (2013)
	Roots	Aqueous	100, 150, 200 mg/kg, p.o.			Shashikala et al. (2015)
	Rhizomes	Hydro-alcoholic extract.	75 mg/kg and 150 mg/kg, p.o.		↓Corticosteroid levels	De et al. (2013)
	Ethanol	72 mg/kg, p.o.	HPM and OFB test	No stimulation of postsynaptic 5-HT1A receptors.	Tripathi et al. (2010)	

**TABLE 2.5** (Continued)

Activity	Plant Part Used	Extract Type	Dose	Animal Models	Results	References
Neuroprotective		Acetone and methanol	5 mg/kg, 20 mg/kg, and 50 mg/kg, p.o.	Behavioral despair test	↓Spontaneous locomotor action	Pandy et al. (2009)
		$\beta$ -asarone	25, 50, and 100 mg/kg, p.o.	EPM and FST	↓Immobility time	Tiwari et al. (2014)
		Hydro-alcoholic	10 mg/kg	CCI of sciatic nerve-induced neuropathic pain of rat.	Significantly ameliorated CCI-induced nociceptive pain.	Muthuraman et al. (2012)
			100 and 200 mg/kg	CCI of sciatic nerve-induced peripheral neuropathy of rat.	⊥CCI-induced neuropathy by ↓oxidation and inflammation.	Muthuraman et al. (2013)
	Leaves	Acetone and methanol	20 and 50 mg per kg	Apomorphine-induced stereotypy and haloperidol-induced catalepsy of mice.	Reversed stereotypy induced by apomorphine and significantly potentiated catalepsy induced by haloperidol.	Vengadesh et al. (2009)
	Rhizomes	Ethanol	200 mg/kg and 300 mg/kg to rats.	Spontaneous electrical action and monoamine levels of brain.	Depressive response by altering electrical action, inclusive of changing brain monoamine levels.	Hazra et al. (2003)
		Hydro-alcoholic	25 mg/kg	MCAo-produced brain ischemia of rat.	Improvement in neurobehavioral performance; ↓GSH, SOD, and ↑LPO level.	Shukla et al. (2006)
		Ethanol	5 ppm, 10 ppm, 15 ppm, 20 ppm, 25 ppm concentration.	Methotrexate-induced stress of fruit flies.	↓Elevated SOD, ROS, GPX, and CAT levels.	Fathima et al. (2014)



**TABLE 2.5** (Continued)

Activity	Plant Part Used	Extract Type	Dose	Animal Models	Results	References
Cardioprotective		n-hexane, ethyl acetate	0.01 mg/ml	Guinea pig tracheal segments.	↓Force and contraction rates at higher concentrations.	Shah et al. (2010)
	Whole plant	Ethanol	100 mg and 200 mg per kg to rats.	DOX-induced myocardial toxicity.	↓Serum enzyme levels and protected myocardium from DOX's toxic effects.	Kumar et al. (2016)

*Abbreviation:* COX: cyclooxygenase; CCI: chronic constriction injury; CAT: catalase; DBP: diastolic blood pressure; DPPH: 2,2-diphenyl-1-picrylhydrazyl radical; DOX: doxorubicin; EPM: elevated plus maze; FST: forced swim test; FRAP: ferric reducing antioxidant power; GLP-1: glucagon-like peptide-1; GR: glutathione reductase; GPX: glutathione peroxidase; GSH: reduced glutathione; HFD: high-fat diet; HDL: high-density lipoproteins; HPM: high plus maze; i.p.: intraperitoneal; i.g.: intragastric; LDL: low-density lipoprotein; MCAo: middle cerebral artery occlusion; LPO: lipid peroxides; MCS: minimal clonic seizure; MES: maximal electroshock; MDA: malondialdehyde; NO: nitric oxide; p.o.: per oral; OFB: open field behavior; ROS: reactive oxygen species; PTZ: pentylenetetrazol; SOD: superoxide dismutase; SBP: systolic blood pressure; TST: tail suspension test; and STZ: streptozotocin.

**TABLE 2.6** Clinical Trial Claims of *A. calamus* in Different Diseases

Formulations of <i>A. calamus</i>	Study Objects	Study Designs	Interventions	Primary Endpoint	Outcomes	Quality of Evidence	References
Sweet flag rhizome powder	24 hyperlipidemic individuals (both sexes).	A randomized, single-blind control trial.	For one month, 500 mg of powder twice a day after meals.	Body perimeter, BMI, skinfold depth.	Significant decrease in fatigueness, skinfold depth, and excess hunger.	III	Singh et al. (2017)
Davaie Loban capsules (sweet flag, nut grass, ginger, incense, and black pepper).	24 patients of both sexes with Alzheimer's disease.	Randomized double-blind clinical trial.	For three months, 500 mg capsule three times each day.	CDR-SOB and ADAS-cog scores.	At 1 month and 3 months, significantly reduced the CDR-SOB and ADAS-cog scores.		Tajadini et al. (2015)
<i>A. calamus</i> hydro-alcoholic extract (70%).	33 patients of both sexes (20 males and 13 females) with anxiety disorder.	Non-randomized, open-labeled, single-armed study	For two months, one capsule of 500 mg extract twice a day after meals	BPRS score	Significantly decrease in anxiety as well as stress-related disorder.		Bhattacharyya et al. (2011)
Guduchyadi Medhya Rasayana, ( <i>A. calamus</i> , <i>Achyranthes aspera</i> , <i>Tinospora cordifolia</i> , <i>Embelia ribes</i> , <i>S. lappa</i> , <i>Convolvulus pluricaulis</i> , <i>T. chebula</i> , <i>Asparagus racemosus</i> , sugar, and cow ghee).	138 individuals with senile memory, all sexes, aged 55–75 years impairment.	Randomized, two-parallel-group study.	Three-gram granules three times a day post-meal for three months.	Mini-mental state examinations, serum acetylcholinesterase estimation, and BPRS score.	Significant improvements in recall memory, amnesia, cognitive impairment, concentration ability, stress, and depression.		Kulatunga et al. (2012)

**TABLE 2.6** (Continued)

Formulations of <i>A. calamus</i>	Study Objects	Study Designs	Interventions	Primary Endpoint	Outcomes	Quality of Evidence	References
<i>A. calamus</i> aqueous extract.	40 healthy participants, both sexes, aged 18–50 years, with an anesthetic premedicant.	Randomized, open-label, two-parallel-group research.	90 minutes prior to anesthesia, the control group received 0.2 mg intramuscular (IM) glycopyrrolate and a 0.2 mg IM 50 mg tablet of promethazine hydrochloride with water; the second group received 0.2 mg IM glycopyrrolate and 100 mg <i>A. calamus</i> extract.	Blood pressure, pulse rate, body temperature, respiratory rate.	The dried aqua extract has anti-hyperthermic and sedative properties without causing respiratory depression.		Pande et al. (2009)
Shankhapushpyadi Ghana Vati ( <i>A. calamus</i> , <i>Bacopa monnieri</i> , <i>C. pluricaulis</i> , <i>C. fistula</i> , <i>A. indica</i> , <i>T. cordifolia</i> , <i>Tribulus terrestris</i> , <i>S. lappa</i> )	20 hypertensive individuals of both sexes.	Randomized single-blind control trial.	One gram twice daily after a meal for two months.	DBP and SBP	Significant reduction in elevated DBP and SBP.		Mishra et al. (2012)
Brahmyadiyoga ( <i>A. calamus</i> , <i>Centella asiatica</i> , <i>Saussurea lappa</i> , <i>Rauvolfia serpentina</i> , <i>Nardostachys jatamansi</i> )	Ten individuals with schizophrenia, both sexes, aged 18–40 years.	Non-randomized, open label, singlearm study.	For three months, four pills after a meal three times a day.	Symptoms rating scale.	Significant effects as a hypnotic, brain tonic, tranquilizer, and sedative.		Ramu et al. (1983)

**TABLE 2.6** (Continued)

Formulations of <i>A. calamus</i>	Study Objects	Study Designs	Interventions	Primary Endpoint	Outcomes	Quality of Evidence	References
Vachadi Churna ( <i>A. calamus</i> , <i>Cedrus deodara</i> , <i>Cyperus rotundus</i> , <i>Aconitum Heterophyllum</i> , ginger, <i>T. chebula</i> ).	30 obese male and female patients ranging in age from 14 to 50 years.	Non-randomized, open-label, single-arm study.	For one month, three grams of powder with lukewarm water two times a day before meal.	Girth measurement of mid-thigh, BMI, chest, abdomen, and hip.	Significantly improved in body heaviness, extreme sleep, excessive hunger, and fatigueness.		Soni1 et al. (2012)
Vachadi Ghrita ( <i>A. calamus</i> , <i>Hedychium spicatum</i> , <i>T. cordifolia</i> , <i>C. pluricaulis</i> , <i>E. ribes</i> , ginger, <i>T. chebula</i> , <i>A. aspera</i> , and cow ghee).	90 healthy men and women between the ages of 40 and 50 for cognition assessment.	Non-randomized positive-control trial.	Ten grams twice daily with lukewarm water for 1 month.	Post Graduate Institute Memory Scale (PGIMS) test.	Marked improvement in mental equilibrium, holding of similar and different pairings, late-immediate memory, and digestion.		Pawar et al. (2018)
Bramhi Vati ( <i>A. calamus</i> , <i>C. pluricaulis</i> , <i>B. monnieri</i> , <i>Onosma bracteatum</i> , iron and copper pyrite, mercuric sulfide, <i>N. jatamansi</i> , <i>Piper nigrum</i> )	68 individuals with essential hypertension, all sexes, aged 20 to 70 years.	Randomized, double-blind, parallel-group comparative trial.	For one month, two 500 mg pills twice a day.	Hamilton anxiety rating scale, DBP, SBP, and MAP.	Significantly improved Hamilton anxiety rating scale, DBP, SBP, and MAP.		Mishra et al. (2019)
Tagaradi Yoga ( <i>A. calamus</i> , <i>N. Jatamansi</i> , <i>Valeriana wallichii</i> ).	24 individuals with insomnia, both sexes, ranging in age from 18 to 75 years.	Non-randomized positive-control trial.	For a fortnight, a 500 mg capsule of hydro-alcoholic extract was twice a day after meals.	Initiating sleeping time, sleep durations, and sleep quality.	Significantly improved initiation of sleeping time, sleep durations, and sleep quality.		Sharma et al. (2017)

**TABLE 2.6** (Continued)

Formulations of <i>A. calamus</i>	Study Objects	Study Designs	Interventions	Primary Endpoint	Outcomes	Quality of Evidence	References
<i>Acorus calamus</i> rhizome powder.	20 obese patients of both sexes.	Randomized single-blind trial.	250 mg rhizome powder twice daily for one month.	Body weight, height according to age, waist-hip ratio, and BMI.	Significantly improved extreme sleep, fatigue, body heaviness, and excess hunger.		Paradkar et al. (2019)
Bala compound ( <i>A. calamus</i> , <i>Embllica ocinalis</i> , <i>E. Ribes</i> , <i>Piper longum</i> , <i>T. cordifolia</i> , <i>C. rotundus</i> , <i>A. heterophyllum</i> , <i>Glycyrrhiza glabra</i> ).	24 neonates, both sexes, 2.5 to 3 kg b.w.	Randomized single-blind control trial.	5 drops 2 times a day orally for half a year.	Changes in serum immunoglobulin levels (IgA, IgG, and IgM).	Significantly improved levels of immunoglobulins after six months.	Ib	Appaji et al. (2009)
<i>Acorus calamus</i> rhizome powder	45 individuals with ischemic heart diseases.	Non-randomized positive-control trial.	For three months, three gms powdered rhizome twice a day.	Serum cholesterol levels, ECG	Improvements in chest discomfort, dyspnea on exertion, body mass index decrease, better ECG: lowered serum cholesterol as well as serum LDL, and higher serum HDL.		Mamgain et al. (1994)

**TABLE 2.7** Sweet Flag (*Acorus calamus*) Plant Formulations Available in the Market

<b>Formulation Name</b>	<b>Manufacturer</b>	<b>Manufacturer Address</b>
<i>Acorus calamus</i> herbal extract	Vidya Herbs Private Limited	Bangalore, Karnataka, India
Ayurvedic and herbal chemicals of <i>Acorus calamus</i>	Jenson Enterprises Pvt. Ltd.	Chengalpattu, Tamil Nadu, India
Scavon vet cream	The Himalaya Drug Company	Makali, Bangalore, India
Mentat tablets and syrup		
Abana		
Mentat tablets and syrup		
Muscle and Joint Rub		
Anxocare		
Erina-EP		
Himpyrin, Himpyrin Vet		
Varch oil	Herbotech Pharmaceuticals	Amritsar, India
Anxi-6	Kalhan Pharmaceuticals Private Limited	Jalandhar, India
Herbal preparations of <i>Acorus calamus</i>	Sydler Remedies Pvt. Ltd.	Mumbai, India
Ayurvedic preparations of <i>Acorus calamus</i>	Kebee Pharmachemie Private Limited	Andheri, Mumbai, India
Botanical insecticide (Vasambu)	Agricultural University and Bhuvicare Private Limited	Tirunelveli, Coimbatore, Tamil Nadu, India
Stresnil	Universal Pharmaceuticals Limited	Chennai, Tamil Nadu, India
Nervine tonic, antispasmodic	Salem Impex	Salem, Tamil Nadu, India
Calamus oil	Modern Natural Products	Mumbai, India
Natural oil of vacha	Bhagat Aromatics Limited	New Delhi, India
Insecticides	Ajinkya Chemtech Private Limited	Pune, India
Krush capsules	Prakruti Remedies Pvt. Ltd.	Karnataka (India)
Brainokan	Kangra Herb Pvt. Ltd.	Kangra, Himachal Pradesh, India
Calamus essential oil	Katyani Exports	Pitam Pura, New Delhi, India
Dark Forest Vekhand Powder	Simandhar Herbal Pvt. Ltd.	Dadar, Mumbai, India
Vacha powder capsule	Heilen Biopharm Pvt. Ltd.	Ahmedabad, Gujarat, India
Pilochek tablets and gel	Dabur India Limited	Ghaziabad, Uttar Pradesh, India
Brahm Rasayan		
Mahasudarsan Churna		
Janma Ghunti Honey		

**TABLE 2.7** (Continued)

<b>Formulation Name</b>	<b>Manufacturer</b>	<b>Manufacturer Address</b>
Brahmi Pearls capsules	Kerala Ayurveda Ltd.	Ernakulam, Kerala, India
GT capsules		
Histantin tablets		
Santhwanam oil		
Mahathikhaka Ghrita capsules		
Calamus root tincture	Florida Herbal Pharmacy	LLC Spanish Breeze Ct, Riverview, FL
Vacha capsules	DRWakde's Natural Health Care	London, United Kingdom
Vacha powder	Bixa Botanical	Vashi, Navi Mumbai, India
Amalth	Mcnow Biocare Private Limited	Noida, Uttar Pradesh, India.
Sunarin capsules	SG Phyto Pharma Pvt. Ltd.	Kolhapur, Maharashtra, India
Nilsin capsules		
Dr. Willmar Schwabe India <i>Acorus calamus</i> mother tincture	Dr. Willmar Schwabe India Pvt Ltd.	Noida, Uttar Pradesh, India.
Himalayan calamus root essential oil	Naturalis Essence of Nature	Bangalore, Karnataka, India
Calamus oil	Kazima Perfumers	Patparganj, Delhi, India
Winton tablets and syrup	Scortis Healthcare	Jaipur, Rajasthan, India
Chesol syrup	J&J Dechane Laboratories Pvt. Ltd.	Hyderabad, Telangana, India
Enzo fast	Naturava	Kharadi, Pune, India
Nervocare	Deep Ayurveda	S.A.S Nagar, Punjab, India
Antress tablets	Ayursun Pharma	Surat, Gujarat, India
Grapzone syrup	Alna Biotech Pvt Ltd.	Barwala, Haryana, India
Memocitive syrup	Aayursh Herbal India	Ahmedabd, Gujarat, India
Smrutihills capsules	Ayush Arogyam	Bengaluru, Karnataka, India
Gastrin capsules	Saravana Marundhagam	Chennai, Tamil Nadu, India
Pigmento tablets	Charak Pharma	Mumbai, Maharashtra, India
Paedritone drops		
Vacha Churna	Sadvaidyasala	Mysuru, Karnataka, India
Alert capsules	Vasu Healthcare	Vadodara, Gujarat, India
Brento tablets	Zandu Realty Limited	Mumbai, Maharashtra, India
Livotrit Forte		
Zanduzyme		
Vedic Slim	Vedic Bio-Labs Pvt. Ltd.	Bengaluru, Karnataka, India

**TABLE 2.7** (Continued)

<b>Formulation Name</b>	<b>Manufacturer</b>	<b>Manufacturer Address</b>
Hinguvachaadi Gulika	Nagarjuna Ayurvedic Group	Kalady, Kerala, India
Norbeepee tablet	AVN Ayurveda Formulations	Madurai, Tamil Nadu, India
Sooktyn tablet	Alarsin Pharma Pvt. Ltd.	Mumbai, Maharashtra, India
Deonac oil	Doux Healthcare Pvt. Ltd.	Panchkula, Haryana, India
Smrutisagar Rasa	Shree Dhootapapeshwar Limited	Mumbai, Maharashtra, India
Yogaraj Guggul		
Kankayan Bati	Baidyanath Pvt. Ltd.	Nagpur, India
Brahmi Ghrita		
Fat Go	Jolly Healthcare	Jaipur, Rajasthan, India
Divya Mukta Vati	Patanjali Ayurveda	New Delhi, India

## 2.18 TECHNOLOGY TRANSFER/PATENTS

Three patents are reported over the plant sweet flag. In between, all seems to be process patent. The specifics are shown in the chart beneath (Table 2.8).

## KEYWORDS

- *Acorus calamus*
- antidiarrheal activity
- calamus
- herbaceous perennial plant
- insecticidal activity
- sweet flag
- traditional medicine
- wetland monocot

## REFERENCES

Acuña, U. M., Atha, D. E., Ma, J., Nee, M. H., & Kennelly, E. J., (2002). Antioxidant capacities of ten edible North American plants. *Phytother. Res.*, 16, 63–65.



**TABLE 2.8** Patents Reported Over the Plant Sweet Flag (*Acorus calamus*)

Work Done	Special Features	Status	Inventor Name	Date of Patent	References
Processing for preparing 1-Propyl-2,4,5-trimethoxybenzene from toxic $\beta$ -asarone of <i>Acorus calamus</i> or from crude calamus oil containing $\beta$ -asarone.	The process comprises providing crude calamus oil or 3-asarone in a solvent; hydrogenating the solution in the existence of a catalyst; filtration of the catalyst and solvent removal at decreased arc, subjecting the reduced calamus oil to column of Silica gel chromatography utilizing an eluent to obtain 1-Propyl-2,4,5-trimethoxybenzene in liquid form with 85–97% purity.	Patented	Arun Kumar Sinha	04/03/2003	Sinha (2003a)
Process for producing pharmacologically active $\alpha$ -asarone out of toxicant $\beta$ -asarone-rich sweet flag oil.	Process for producing of highly pure and yields trans-2,4,5-trimethoxy cinnamaldehyde, $\alpha$ -asarone, 2,4,5-trimethoxy-phenyl propionone, from the 3-asarone or $\beta$ -asarone rich sweet flag oils comprising $\alpha$ and $\gamma$ -asarones by hydrogenation, following by treatments with dichlorodicyanobenzoquinone (DDQ) with/ without solid supports of alumina or silica gel in dried organic solvent and $\alpha$ -asarone could additionally be procured by treating the hydrogenated products of $\beta$ -asarone or $\beta$ -asarone rich sweet flag with DDQ in an aqua organic solution to achieve an intermediary product 2,4,5-trimethoxy phenyl propionone, which is then is lowered with sodium borohydride to achieve the desired 2,4,5-trimethoxy phenyl propanol and finally treated with a dehydration agent.	Patented	Arun Kumar Sinha; Ruchi Acharya; Bhupendra Prasad Joshi	08/07/2003	Sinha et al. (2003b)
Method of extracting for <i>Acorus calamus</i> root extracts oil including $\beta$ -asarone using Supercritical fluid extraction.	A technique for extraction of sweet flag root extract offers an essential oil comprising a plurality of $\beta$ -asarone by supercritical extracting by adding sweet flag root extract to CO <sub>2</sub> supercritical fluid utilizing a sub-solvent (ethanol) under pressure conditions of 40°C to 60°C and 200 to 400 bar, followed by a stage of concentrate the sweet flag extract.	Patented	Gwicheel Kim	16/10/2013	Kim (2013)

- Agarwal, S. L., Dandiya, P. C., Singh, K. P., & Arora, R. B., (1956). A note on the preliminary studies of certain pharmacological actions of *the Acorus calamus*. *J. Am. Pharm. Assoc.*, 45, 655–656.
- Ahmad, I., & Aqil, F., (2007). *In vitro* efficacy of bioactive extracts of 15 medicinal plants against ES $\beta$ L-producing multidrug-resistant enteric bacteria. *Microbiol. Res.*, 162(3), 264–275.
- Appaji, R. R., Sharma, R. D., Katiyar, G. P., & Sai, P. A., (2009). Clinical study of the immunoglobulin enhancing effect of “Bala compound” on infants. *Anc. Sci. Life*, 28, 18–22.
- Arun, K. S., & Augustine, A., (2012). Hypolipidemic effect of methanol fraction of *Acorus calamus* Linn. in diet-induced obese rats. In: *Prospects in Bioscience: Addressing the Issues* (pp. 399–404). Springer, Springer Science & Business Media: New Delhi, India.
- Asif, M., Siddiqi, M. T. A., & Ahmad, M. U., (1984). Fatty acid and sugar composition of *Acorus calamus* Linn. *Fette Seifen Anstrichm.*, 86, 24, 25.
- Athesh, K., & Jothi, G. (2017). Pharmacological screening of anti-obesity potential of *Acorus calamus* Linn. In high fat cafeteria diet fed obese rats. *Asian J. Pharm. Clin. Res.*, 10, 384–390.
- Balakumbahan, R., Rajamani, K., & Kumanan, K., (2010). *Acorus calamus*: An overview. *J. Med. Plants Res.*, 4(25), 2740–2745.
- Bandow, J. E., Brötz, H., Leichert, L. I. O., Labischinski, H., & Hecker, M., (2003). Proteomic approach to understanding antibiotic action. *Antimicrob. Agents Chemother.*, 47(3), 948–955.
- Banerjee, S., Banerjee, S., Jha, G. K., & Bose, S. (2020). *Barleria prionitis* L.: An illustrative traditional, phytochemical, and pharmacological review. *The Nat. Prod. J.*, 10, 1–17.
- Banerjee, S., Banerjee, S., Jha, G. K., & Bose, S. (2020). Conspectus of phytoconstituents and pharmacological activities of *Barleria lupulina* Lindl.: A review. *Curr. Trad. Med.*, 6, 1–10.
- Banerjee, S., Bose, S., Mandal, S. C., Dawn, S., Sahoo, U., Ramadan, M. A., & Mandal, S. K., (2019). Pharmacological property of pentacyclic triterpenoids. *Egypt. J. Chem.*, 62(special issue (part 1)), 13–35.
- Barbhuiya, A. R., Sharma, G. D., Arunachalam, A., & Deb, S., (2009). Diversity and conservation of medicinal plants in Barak valley, Northeast India. *Indian J. Tradit. Knowl.*, 8, 169–175.
- Barton, B. H., & Castle, T., (1877). *The British Flora Medica*. Chatto and Windus: Piccadilly, London, UK.
- Bauer, A. W., Kirby, W. M., Sherris, J. C., & Turck, M., (1966). Antibiotic susceptibility testing by a standardized single disk method. *Am. J. Clin. Pathol.*, 45(4), 493–496.
- Baxter, R. M., Dandiya, P. C., Kandel, S. I., Okany, A., & Walker, G. C., (1960). Separation of the hypnotic potentiating principles from the essential oil of *Acorus calamus* L. of Indian origin by liquid-gas chromatography. *Nature*, 185(4711), 466–467.
- Benaïges, A., & Guillén, P., (2007). Botanical extracts. *Anal. Cosmet. Prod.*, 345–363.
- Bhatt, D., Sharma, G. K., Soni, R., & Dashora, A. (2015). An overview of various properties and pharmacological studies of *Acorus calamus*. *Res. Rev. Pharm. Pharm. Sci.* e-ISSN 2320-1215.
- Bhattacharyya, D., Sur, T. K., Lyle, N., Jana, U., & Debnath, P. K., (2011). A clinical study on the management of generalized anxiety disorder with Vaca (*Acorus calamus*). *Indian J. Tradit. Knowl.*, 10, 668–671.

- Boissya, C. L., & Majumder, R., (1980). Some folklore claims from the Brahmaputra Valley (Assam). *Ethnomed.*, 6, 139–145.
- Boktapa, N. R., & Sharma, A. K., (2010). Wild medicinal plants are used by local communities of Manali, Himachal Pradesh, India. *Ethnobot. Leaflet*, 3, 259–267.
- Bose, B. C., Vijayvargiya, R., Saiti, A. Q., & Sharma, S. K., (1960). Some aspects of chemical and pharmacological studies of *Acorus calamus* Linn. *J. Am. Pharm. Assoc.*, 49, 32–34.
- Bose, S., Malik, J., & Mandal, S. C., (2020). Application of phytochemicals in pharmaceuticals. In *Advances in Pharmaceutical Biotechnology* (pp. 55–68). Springer, Singapore.
- Bown, D., (1995). *Encyclopaedia of Herbs and Their Uses*. Dorling Kindersley, London. ISBN 0-7513-020-31.
- Burang, T., (1979). Cancer therapy of Tibetan healers. *Comp. Med. East West*, 7, 294–296.
- Burkill, I. H., (1966). *Dictionary of the Economic Products of the Malay Peninsula* (Vol. 1). Ministry of Agriculture and Cooperatives, Kuala Lumpur, Malaysia.
- CABI, (2020). *Acorus calamus* (calamus). In: *Invasive Species Compendium*. Wallingford, UK: CAB International. Available online: [www.cabi.org/isc/datasheet/3037#topests](http://www.cabi.org/isc/datasheet/3037#topests) (accessed on 31 August 2023).
- Caius, J. F., (1986). *The Medicinal and Poisonous Plants of India*. Scientific Publishers: Jodhpur, India.
- Chamlagai, D., & Singh, B., (2016). Study of *in vitro* anti-inflammatory activity of ethnomedicinal plants of Sikkim *Viscum articulatum* and *Acorus calamus*. *Asian J. Pharm. Clin. Res.*, 9(3), 119–122.
- Chandra, D., & Prasad, K., (2017). Phytochemicals of *Acorus calamus* (Sweet flag). *J. Med. Plants Stud.*, 5(5), 277–281.
- Chandrashekar, R., Adake, P., & Rao, S. N., (2013). Anticonvulsant activity of ethanolic extract of *Acorus calamus* rhizome in Swiss albino mice. *J. Sci. Innov. Res.*, 2, 846–851.
- Chaudhry, S. S., Gautam, S. K., & Handa, K. L., (1957). *Composition of Calamus Oil from Calamus Roots Growing in Jammu and Kashmir* (pp. 183–186). Drug research laboratory: Jammu.
- Chauhan, S. P., Kumar, S. A., Singh, C. L., & Pandey, U. K., (1987). Toxicity of some plant extracts against rice moth *Corcyra cephalonica* (Stainton) (Lepidoptera). *Indian J. Entomol.*, 49(4), 532–534.
- Chevallier, A., (1996). *The Encyclopedia of Medicinal Plants* Dorling Kindersley. London. ISBN 9-780751-303148.
- Chiej, R., (1984). *Encyclopaedia of Medicinal Plants*. MacDonald, ISBN 0-356-10541-5.
- Chopra, R. N., Nayar, S. L., & Chopra, I. C., (1986). *Glossary of Indian Medicinal Plants (Including the Supplement)*. Council of Scientific and Industrial Research: New Delhi.
- Clapham, A. R., Tutin, T. G., & Warburg, E. F., (1962). *Flora of the British Isles*. Cambridge Univ. Press: United Kingdom.
- Clymer, R. S., (1963). *Nature's Healing Agents*. Dorrance and Company: Philadelphia, PA, USA.
- Coon, N., (1975). *The Dictionary of Useful Plants*. Rodale Press: USA; ISBN 0-87857-090-x.
- D'Souza, T., Mengi, S. A., Hassarajani, S., & Chattopadhyay, S., (2007). Efficacy study of the bioactive fraction (F-3) of *Acorus calamus* in hyperlipidemia. *Indian J. Pharmacol.*, 39, 196–200.
- Das, B. K., Swamy, A. V., Koti, B. C., & Gadad, P. C., (2019). Experimental evidence for the use of *Acorus calamus* (asarone) for cancer chemoprevention. *Heliyon*, 5(5), e01585.

- Dastur, J. F., (1951). *Medicinal Plants of India and Pakistan* (p. 12). D. B. Taraporevala Sons and Co. Ltd: Bombay, India.
- De, A., & Singh, M. S., (2013). *Acorus calamus* Linn. Rhizomes extract for antidepressant activity in mice model. *Adv. Res. Pharm. Biol.*, 3, 520–525.
- Deb, P. K. R., Ghosh, R., Das, S., & Bhakta, T., (2013). *In-vitro* anthelmintic activity of *Acorus calamus* leaves. *Asian J. Pharm. Clin. Res.*, 6(3), 135–137.
- Deepa, N., Sundaram, R. M., Devi, T. J., Jayapradha, V., Helan, P., & Valan, L. M. U., (2008). Anthelmintic activity of *Acorus calamus* L. *Nat. Prod.: An Indian Journal*, 4(3), 195–197.
- Devi, A. S., Bawankar, R., & Babu, S., (2014). Current status on biological activities of *Acorus calamus*: A review. *Int. J. Pharm. Pharm. Sci.*, 6(10), 66–71.
- Devi, S. A., & Ganjewala, D., (2011). Antioxidant activities of methanolic extracts of sweet-flag (*Acorus calamus*) leaves and rhizomes. *J. Herbs Spices Med. Plants*, 1, 1–11.
- Divya, G., Gajalakshmi, S., Mythili, S., & Sathivelu, A., (2011). Pharmacological activities of *Acorus calamus*: A review. *Asian J. Biomed. Pharm. Res.*, 4(1), 2231–2560.
- Dobelis, I. N., (1986). *Magic and Medicine of Plants*. The Reader's Digest Association Inc.: Pleasantville, New York, USA.
- Dragendor, G., (1898). *Die Heilpflanzen der Verschie Denen Volker und Zeiten*. F. Enke: Stuttgart, Germany.
- Duke, J. A., & Ayensu, E. S., (1985). *Medicinal Plants of China*. Reference Publications Inc.: Michigan; ISBN 0-917256-20-4.
- Dušek, K., Galambosi, B., Hethelyi, E. B., Korany, K., & Karlová, K., (2007). Morphological and chemical variations of sweet flag (*Acorus calamus* L.) in the Czech and Finnish gene bank collection. *Hortic. Sci. (Prague)*, 34(1), 17–25.
- Dwivedi, S. N., Dwivedi, S., & Patel, P. C., (2006). Medicinal plants are used by the tribal and rural people of Satna District, Madhya Pradesh, for the treatment of gastrointestinal diseases and disorders. *Nat. Prod. Rad.*, 5, 60–63.
- El'Yashevych, O. H., & Cholii, R., (1972). Some means of treatment in the folk medicine of L'Vov. *Farm. Zh.*, 27, 78.
- Elias, T., & Dykeman, P., (1982). *A Field Guide to N. American Edible Wild Plants*. Van Nostrand Reinhold: New York; ISBN 0442222009.
- Emboden, W., (1979). *Narcotic Plants Studio*. Vista: USA; ISBN 0-289-70864-8.
- Facciola, S., (1998). *Cornucopia II*. Kampong Publications: California; ISBN 0-9628087-2-5.
- Fathima, A., Patil, H. V., & Kumar, S., (2014). Suppression of elevated reactive oxygen species by *Acorus calamus* (vacha) a sweet flag in drosophila melanogaster under stress-full conditions. *Int. J. Pharm. Sci. Res.*, 5, 1431–1439.
- Gaidhani, S. N., Lavekar, G. S., Juvekar, A. S., Sen, S., Singh, A., & Kumari, S., (2009). *In-vitro* anticancer activity of standard extracts used in ayurveda. *Pharmacogn. Mag.*, 5(20), 425–429.
- Geng, Y., Li, C., Liu, J., Xing, G., Zhou, L., Dong, M., Li, X., & Niu, Y., (2010). Beta-asarone improves cognitive function by suppressing neuronal apoptosis in beta-amyloid hippocampus injection rats. *Biol. Pharm. Bull.*, 33(5), 836–843.
- Ghosh, A., (2008). Ethnomedicinal plants used in the West Rarrh region of West Bengal. *Nat. Prod. Rad.*, 7, 461–465.
- Global Biodiversity Information Facility, (2020). Available online: <https://www.gbif.org/> (accessed on 31 August 2023).
- Grieve, A., (1984). *Modern Herbal*. Penguin: USA; ISBN 0-14-046-440-9.
- Grieve, M., (1971). *A Modern Herbal* (Vol. II). Dover Publications Inc.: New York, USA.

- Grosvenor, P. W., Supriono, A., & Gray, D. O., (1995). Medicinal plants from Riau province, Sumatra, Indonesia. Part 2: Antibacterial and antifungal activity. *J. Ethnopharmacol.*, 45(2), 97–111.
- Haghighi, S. R., Asadi, M. H., Akrami, H., & Baghizadeh, A., (2017). Anti-carcinogenic and anti-angiogenic properties of the extracts of *Acorus calamus* on gastric cancer cells. *Avicenna J. Phytomed.*, 7(2), 145–156.
- Harris, B. C., (1972). *The Complete Herbal*. Barre Publishers: Barre, MA, USA.
- Harris, B. C., (1973). *Eat the Weeds*. Pivot Health.
- Hasan, M. U., Sagheer, M., Ullah, E., Ahmad, F., & Wakil, W., (2006). Insecticidal activity of different doses of *Acorus calamus* oil against *Trogoderma granarium* (Everts). *Pakistan J. Agri. Sci.*, 43(1, 2), 55–58.
- Hazra, R., & Guha, D., (2003). Effect of chronic administration of *Acorus calamus* on electrical activity and regional monoamine levels in rat brain. *Biog. Amines*, 17, 161–170.
- Hedrick, U. P., (1972). *Sturtevant's Edible Plants of the World*. Dover Publications: USA; ISBN 0-486-20459-6.
- Herrmann, G., (1956). Therapy with medicinal plants in present medicine. *Med. Monatsschr. Pharm.*, 10, 79.
- Hirschhorn, H. H., (1983). Botanical remedies of the former Dutch East Indies (Indonesia) I: Eumycetes, Pteridophyta, Gymnospermae, Angiospermae (Monocotyledones only). *J. Ethnopharmacol.*, 7, 123–156.
- Hossain, M. S., Zaman, S., Haque, A. B. M. H., Bhuiyan, M. P. I., Khondkar, P., & Islam, M. R., (2008). Chemical and pesticidal studies on *Acorus calamus* rhizomes. *J. Appl. Sci. Res.*, 4(10), 1261–1266.
- Huxley, A., (1992). *The New RHS Dictionary of Gardening*. MacMillan Press: New York, USA; ISBN 0-333-47494-5.
- Imam, H., Riaz, Z., Azhar, M., Sofi, G., & Hussain, A., (2013). Sweet flag (*Acorus calamus* Linn.): An incredible medicinal herb. *Int. J. Green Pharm.*, 7(4), 288–296.
- Jackson, B. D., (1876). *A Catalogue of Plants Cultivated in the Garden of John Gerard* (pp. 1, 23). London: Private Printing.
- Jain, A., Roshnibala, S., Kanjilal, P. B., Singh, R. S., & Singh, H. B., (2007). Aquatic /semi-aquatic plants used in herbal remedies in the wetlands of Manipur, Northeastern India. *Indian J. Tradit. Knowl.*, 6, 346–351.
- Jain, D. K., Gupta, S., Jain, R., & Jain, N., (2010). Anti-inflammatory activity of 80% ethanolic extract of *Acorus calamus* Linn. leaves in albino rats. *Res. J. Pharm. Tech.*, 3, 882–884.
- Jain, S. K., (1968). *Medicinal Plants*. National Book Trust: New Delhi, India.
- Jayaraman, R., Anitha, T., & Joshi, V. D., (2010). Analgesic and anticonvulsant effects of *Acorus calamus* roots in mice. *Int. J. PharmTech Res.*, 2, 552–555.
- Jha, R. R., & Verma, S. K., (1996). Ethnobotany of Sauria Pahanas of Santhal pargana, Bihar. *Ethnobot.*, 8, 31–35.
- Jochle, W., (1974). Menses-inducing drugs: Their role in antique, medieval and renaissance gynecology, and birth control. *Contraception*, 10, 425–439.
- Kadel, C., & Jain, A. K., (2008). Folklore claims on snakebite among some tribal communities of Central India. *Indian J. Tradit. Knowl.*, 7, 296–299.
- Kaithavalappil, S. S., Vellaichamy, G., Nagappan, K., & Sreekanth, D., (2015). *In-vitro* antimicrobial activity and phytochemical analysis of *Acorus calamus* rhizomes. *Res. Pharm. Health Sci.*, 1(1), 1–5.

- Kantor, W., (1916). Quack abortifacients and declining birth rate. *Therap. Monatsh.*, 30, 561–568.
- Kapadia, M. D., & Kharat, A. R., (2012). Anti-diarrheal activity of leaves of *Acorus calamus*. *Int. J. Pharm. Sci. Res.*, 3(10), 3847.
- Kaushik, R., Jain, J., Yadav, R., Singh, L., Gupta, D., & Gupta, A. (2017). Isolation of  $\alpha$ -asarone from *Acorus calamus* Linn. and evaluation of its anticonvulsant activity using MES and PTZ models in mice. *Pharmacol. Toxicol. Biomed. Rep.*, 3, 21–26.
- Khan, M. I., (1986). Efficacy of *Acorus calamus* L. rhizome powder against pulse beetle (*Callosobruchus chinensis* L.). *Pakistan Vet. Res. J.*, 10, 72–74.
- Khatun, M. A., Harun-Or-Rashid, M., & Rahmatullah, M., (2011). Scientific validation of eight medicinal plants used in traditional medicinal systems of Malaysia: A review. *Am. Eurasian J. Sustain. Agric.*, 5, 67–75.
- Kim, G., (2013). Korea Intellectual Property Office (KR). *Method of Extracting Irises Containing a Large Amount of Beta-Asaron Using a Supercritical Fluid Extraction Method*. 10-2013-0113820.
- Kim, H., Han, T. H., & Lee, S. G., (2009). Anti-inflammatory activity of a water extract of *Acorus calamus* L. leaves on keratinocyte HaCaT cells. *J. Ethnopharmacol.*, 122(1), 149–156.
- Kim, W. J., Hwang, K. H., Park, D. G., Kim, T. J., Kim, D. W., Choi, D. K., Moon, W. K., & Lee, K. H., (2011). Major constituents and antimicrobial activity of Korean herb *Acorus calamus*. *Nat. Prod. Res.*, 25(13), 1278–1281.
- Kingston, C., Nisha, B. S., Kiruba, S., & Jeeva, S., (2007). Ethnomedicinal plants used by indigenous communities in a traditional healthcare system. *Ethnobot. Leaflet*, 11, 32–37.
- Kirtikar, K. R., & Basu, B. D., (1975). *Indian Medicinal Plants* (Vol. IV). M/S. Bishen Singh Mahendra Pal Singh: Dehradun, India.
- Kirtikar, K. R., & Basu, B. D., (1987). *Indian Medicinal Plants* (Vol. IV, pp. 1229–1230). Good. IV; Dehradun, India, M/S Bishen Sing, Mahendra Pal Sing Publishers.
- Krochmal, A., & Krochmal, C., (1975). *A Guide to the Medicinal Plants of the United States*. Quadrangle/The New York Times Book Co., New York, USA.
- Kulatunga, R. D. H., Dave, A. R., & Baghel, M. S., (2012). Clinical efficacy of Guduchyadi Medhya Rasayana on senile memory impairment. *Ayu*, 33, 202–208.
- Kumar, A., & Vandana, (2013). Medicinal properties of *Acorus calamus*. *J. Drug Deliv. Ther.*, 3(3), 143–144.
- Kumar, G., Nagaraju, V., Kulkarni, M., Kumar, B. S., & Raju, S., (2016). Evaluation of the antihyperlipidemic activity of methanolic extract of *Acorus calamus* in fat diet induced rats. *Asian J. Med. Pharm. Sci.*, 4, 71–76.
- Kumar, H., Song, S. Y., More, S. V., Kang, S. M., & Kim, B. Y., (2013). Traditional Korean East Asian medicines and herbal formulations for cognitive impairment. *Molecules*, 18, 14670–14693.
- Kumar, M. S., & Hiremath, V. S. M. A., (2016). Cardioprotective effect of *Acorus calamus* against doxorubicin-induced myocardial toxicity in albino Wistar rats. *Indian J. Health Sci. Biomed. Res.*, 9, 225–234.
- Kumar, S. N., Aravind, S. R., Sreelekha, T. T., Jacob, J., & Kumar, B. D., (2015). Asarones from *Acorus calamus* in combination with azoles and amphotericin b: A novel synergistic combination to compete against human pathogenic candida species *in-vitro*. *Appl. Biochem. Biotech*, 175, 3683–3695.

- Kumar, S. S., Akram, A. S., Ahmed, T. F., & Jaabir, M. M., (2010). Phytochemical analysis and antimicrobial activity of the ethanolic extract of *Acorus calamus* rhizome. *Orient. J. Chem.*, 26, 223–227.
- Kumar, V., Singh, R., & Joshi, V., (2014). Antimicrobial activity of rhizome extract of *Acorus calamus* against different micro-organisms. *Octa J. Biosci.*, 2(1), 59–63.
- Lama, S., & Santra, S. C., (1979). Development of tibetan plant medicine. *Sci. Cult.*, 45, 262–265.
- Launert, E., (1981). *Edible and Medicinal Plants*. Hamlyn: London; ISBN 0-600-37216-2.
- Lee, J. Y., Lee, J. Y., Yun, B. S., & Hwang, B. K., (2004). Antifungal activity of  $\beta$ -asarone from rhizomes of *Acorus gramineus*. *J. Agric. Food Chem.*, 52(4), 776–780.
- Lee, M. H., Chen, Y. Y., Tsai, J. W., Wang, S. C., Watanabe, T., & Tsai, Y. C., (2011). Inhibitory effect of  $\beta$ -asarone, a component of *Acorus calamus* essential oil, on inhibition of adipogenesis in 3T3-L1 cells. *Food Chem.*, 126(1), 1–7.
- Lee, S. H., Kim, K. Y., Ryu, S. Y., Yoon, Y., Hahm, D. H., Kang, S. A., et al., (2010). Asarone inhibits adipogenesis and stimulates lipolysis in 3T3-L1 adipocytes. *Cell. Mol. Biol.*, 2010(56), 1215–1222.
- Li, H. L., (1977). Hallucinogenic plants in Chinese herbals. *Harv. Univ. Bot. Mus. Leaflet.*, 25, 161–177.
- Li, J., Zhao, J., Wang, W., Li, L., Zhang, L., Zhao, X. F., & Li, S. X., (2017). New acorane-type sesquiterpene from *Acorus calamus* L. *Molecules*, 22, 529.
- Lindley, J., (1838). *Flora Medica*. Paternoster-Row: London, UK.
- Liu, Y. X., Si, M. M., Lu, W., Zhang, L. X., Zhou, C. X., Deng, S. L., & Wu, H. S., (2015). Effects and molecular mechanisms of the antidiabetic fraction of *Acorus calamus* L. on GLP-1 expression and secretion *in-vivo* and *in-vitro*. *J. Ethnopharmacol.*, 166, 168–175.
- Lokesh, G. B., (2004). Sweet flag (*Acorus calamus*)—Cultivation and Economics aspects. *Nat. Prod. Radiance*, 3(1), 19, 20.
- Lust, J., (1983). *The Herb Book*. Bantam Books: New York, USA; ISBN 0-553-23827-2.
- Malhi, B. S., & Trivedi, V. P., (1972). Vegetable antifertility drugs of India. *Q. J. Crude Drug Res.*, 12(3), 1922–1928.
- Mangain, P., & Singh, R. H., (1994). Control clinical trial of the Lekhaniya drug Vaca (*Acorus calamus*) in case of ischemic heart diseases. *J. Res. Ayurveda Siddha*, 15, 35–51.
- Manandhar, N. P., (2002). *Plants and People of Nepal*. Timber Press: Oregon; ISBN 0-88192-527-6.
- Manfred, L., (1947). *Siete Mil Recetas Botánicas a Base de Mil Trescientas Plantas*. Edit Kier: Buenos Aires, Argentina.
- Manikandan, S., & Devi, R. S., (2005). The antioxidant property of  $\alpha$ -asarone against noise-stress-induced changes in different regions of rat brain. *Pharmacol. Res.*, 52, 467–474.
- Manikandan, S., Devi, R. S., Srikumar, R., Thangaraj, R., Ayyappan, R., Jegadeesh, R., & Hariprasath, L., (2010). *In vitro* antibacterial activity of aqueous and ethanolic extracts of *Acorus calamus*. *Int. J. App. Biol. Pharma. Technol.*, 1, 1072–1075.
- Manniche, L., (2006). *An Ancient Egyptian Herbal* (p. 74). American University in Cairo Press: Cairo; ISBN 977 416 034 7.
- McGaw, L. J., Jager, A. K., & Van, S. J., (2002). Isolation of beta-asarone, an antibacterial and anthelmintic compound, from *Acorus calamus* in South Africa. *S. Afr. J. Bot.*, 68(1), 31–35.
- Mehrotra, S., Mishra, K. P., Maurya, R., Srimal, R. C., Yadav, V. S., Pandey, R., & Singh, V. K., (2003). Anticellular and immunosuppressive properties of ethanolic extract of *Acorus calamus* rhizome. *Int. Immunopharmacol.*, 3(1), 53–61.

- Mills, S. Y., (1985). *The Dictionary of Modern Herbalism*. Thorsons Publishing Group: United Kingdom.
- Mishra, D., & Tubaki, B. R. (2019). Effect of Brahmi vati and Sarpagandha Ghana vati in management of essential hypertension – a randomized, double blind, clinical study. *J. Ayurveda Integr. Med.*, 10, 269–276.
- Mishra, J., Joshi, N. P., & Pandya, D. M., (2012). A comparative study of Shankhpushpyadi Ghana Vati and Sarpagandhadi Ghana Vati in the management of “essential hypertension.” *Ayu*, 33, 54–61.
- Moerman, D. E., (1981). *Geraniums for the Iroquois*. Reference Publications Inc.: Algonac, MI, USA.
- Mokkhasamit, M., Ngarmwathana, W., Sawasdimongkol, K., & Permiphath, U., (1971). Pharmacological evaluation of Thai medicinal plants. *J. Med. Assoc. Thail.*, 54, 490–504.
- Motley, T. J., (1994). The ethnobotany of sweet flag, *Acorus calamus* (Araceae). *Econ. Bot.*, 48, 397–412.
- Mukherjee, P. K., (2002). *Quality Control of Herbal Drugs: An Approach to Evaluation of Botanicals* (pp. 692–694). Business Horizons: New Delhi, India.
- Mukherjee, P. K., Kumar, V., Mal, M., & Houghton, P. J., (2007). *Acorus calamus*.: Scientific validation of Ayurvedic tradition from natural resources. *Pharm. Biol.*, 45(8), 651–666.
- Mungkornasawakul, P., Supyen, D., Jatisatienr, C., & Jatisatienr, A., (2001). Inhibitory EFFECT of *Acorus calamus* L. extract on some plant pathogenic molds. In: *International Conference on Medicinal and Aromatic Plants. Possibilities and Limitations of Medicinal and Aromatic Plant* (Vol. 576, pp. 341–345).
- Murugaian, P., Srikumar, R., & Thangaraj, R., (2009). Survey of arbuscular mycorrhizal fungi associated with sugarcane in South India. *Agric. Sci. Digest*, 29(2), 19–22.
- Muthuraman, A., & Singh, N., (2011). Attenuating effect of *Acorus calamus* extract in chronic constriction injury induced neuropathic pain in rats: An evidence of anti-oxidative, anti-inflammatory, neuroprotective and calcium inhibitory effects. *BMC Complement. Altern. Med.*, 11, 1–14.
- Muthuraman, A., & Singh, N., (2012). Neuroprotective effect of saponin rich extract of *Acorus calamus* L. in rat model of chronic constriction injury (CCI) of sciatic nerve-induced neuropathic pain. *J. Ethnopharmacol.*, 142, 723–731.
- Napagoda, M. T., Sundarapperuma, T., Fonseka, D., Amarasiri, S., & Gunaratna, P., (2019). Traditional uses of medicinal plants in Polonnaruwa District in North Central Province of Sri Lanka. *Scientifica*, 2019, 1–12.
- Natarajan, B., Paulsen, B. S., & Korneliusson, V., (2000). An ethnopharmacological study from Kulu District, Himachal Pradesh, India: Traditional knowledge compared with modern biological science. *Pharm. Boil.*, 38(2), 129–138.
- Nawamaki, K., & Kuroyanagi, M., (1996). Sesquiterpenoids from the *Acorus calamus* as germination inhibitors. *Phytochemistry*, 43(6), 1175–1182.
- Nigam, M. C., Ateeque, A., & Misra, L. N., (1990). GC-MS examination of essential oil of *Acorus calamus*. *Indian Perfumer*, 34(4), 282–285.
- Nisha, M. C., & Rajeshkumar, S., (2010). Survey of crude drugs from Coimbatore city. *Indian J. Nat. Prod. Resour.*, 1, 376–383.
- Ocampo, R. V., & Hsia, M. T. S., (1986). The influence of calamus oil and asarone analogs on the reproduction of *Oncopeltus fasciatus* (Dallas). *Philipp. Ent.*, 6(5), 495–515.



- Oprean, R., Oprean, L., Tamas, M., Sandulescu, R., & Roman, L., (2001). Essential oils analysis. II. Mass spectra identification of terpene and phenylpropane derivatives. *J. Pharm Biomed. Anal.*, 24(5, 6), 1163–1168.
- Özcan, M., Akgül, A., & Chalchat, J. C., (2002). Volatile constituents of the essential oil of *Acorus calamus* L. grown in Konya province (Turkey). *J. Essent. Oil Res.*, 14, 366–368.
- Packer, J. G., & Ringius, G. S., (1984). The distribution and status of *Acorus* (*Araceae*) in Canada. *Canad. J. Bot.*, 62, 2248–2252.
- Padalia, R. C., Chauhan, A., Verma, R. S., Bisht, M., Thul, S., & Sundaresan, V., (2014). Variability in rhizome volatile constituents of *Acorus calamus* L. from Western Himalaya. *J. Essent. Oil Bear. Plants*, 17, 32–41.
- Paithankar, V. V., Belsare, S. L., Charde, R. M., & Vyas, J. V., (2011). *Acorus calamus*: An overview. *Int. J. Biomed. Sci.*, 2, 518–529.
- Palani, S., Raja, S., Kumar, R. P., Parameswaran, P., & Kumar, B. S., (2010). Therapeutic efficacy of *Acorus calamus* on acetaminophen induced nephrotoxicity and oxidative stress in male albino rats. *Acta Pharm. Sci.*, 52, 89–100.
- Panchal, G. M., Venkatakrishna-Bhatt, H., Doctor, R. B., & Vajpayee, S., (1989). Pharmacology of *Acorus calamus* L. *Indian J. Exp. Biol.*, 27(6), 561–567.
- Pande, D. N., & Mishra, S. K., (2009). Vacha (*Acorus calamus*) is an ayurvedic premedicant. *Ayu*, 30, 279–283.
- Pandy, V., Jose, N., & Subhash, H., (2009). CNS activity of methanol and acetone extracts of *Acorus calamus* leaves in mice. *J. Pharmacol. Toxicol.*, 4(2), 79–86.
- Parab, R. S., & Mengi, S. A., (2002). Hypolipidemic activity of *Acorus calamus* L. in rats. *Fitoterapia*, 73(6), 451–455.
- Paradkar, S. R., & Pardhi, S. N., (2019). Clinical evaluation of lekhaniya effect of vacha (*Acorus calamus*) and musta (*Cyperus rotundus*) in medoroga w.s.r to obesity: A comparative study. *Res. Rev. J. Pharmacogn.*, 3, 1–8.
- Patel, P., Vaghasiya, J., Thakor, A., & Jariwala, J., (2012). Antihypertensive effect of rhizome part of *Acorus calamus* on renal artery occlusion induced hypertension in rats. *Asian Pac. J. Trop. Dis.*, 2, S6–S10.
- Pawar, M., & Magdum, P., (2018). Clinical study of assessment of the therapeutic potential of Vachadi ghrita, a medicated ghee formulation on healthy individual's cognition. *Int. J. Pharm. Sci. Res.*, 9, 3408–3413.
- Pawar, V. S., Anup, A., Shrikrishna, B., & Shivakumar, H., (2011). Antidepressant-like effects of *Acorus calamus* in forced swimming and tail suspension test in mice. *Asian Pac. J. Trop. Biomed.*, 1, S17–S19.
- Perry, L. M., & Metzger, J., (1980). *Medicinal Plants of East and Southeast Asia*. MIT Press: Cambridge, UK.
- Phillips, R., & Foy, N., (1990). *Herbs*. Pan Books Ltd.: London; ISBN 0-330-30725-8.
- Phillips, R., & Rix, M., (1991). *Perennials* (Vol. 1, 2). Pan Books: London, United Kingdom; ISBN 0-330-30936-9.
- Phongpaichit, S., Pujenjob, N., Rukachaisirikul, V., & Ongsakul, M., (2005). Antimicrobial activities of the crude methanol extract of *Acorus calamus* Linn. *Songklanakarin J. Sci. Technol.*, 27(2), 517–523.
- Poonam, K., & Singh, G. S., (2009). Ethnobotanical study of medicinal plants used by the Taungya community in Terai Arc Landscape, India. *J. Ethnopharmacol.*, 123, 167–176.

- Pradhan, B. K., & Badola, H. K., (2008). Ethnomedicinal plant use by Lepcha tribe of Dzongu valley, bordering hangchendzonga biosphere reserve, in North Sikkim, India. *J. Ethnobiol. Ethnomed.*, 4(1), 22.
- Prashanth, D., & Ahmed, F. Z., (2017). Evaluation of the hypoglycemic activity of methanolic extract of *Acorus calamus* (Linn). roots in alloxan-induced diabetes rat model. *Int. J. Basic Clin. Pharmacol.*, 6, 2665–2670.
- Prisilla, D. H., Balamurugan, R., & Shah, H. R., (2012). Antidiabetic activity of methanol extract of *Acorus calamus* in STZ induced diabetic rats. *Asian Pac. J. Trop. Biomed.*, 2(2), S941–S946.
- Pushpa, V. H., Padmaja, S. K., Suresha, R. N., Vaibhavi, P. S., Kalabharathi, H. L., Satish, A. M., & Naidu, S., (2013). Antidepressant activity of methanolic extract of *Acorus calamus* leaves in albino mice. *Int. J. Pharm. Tech.*, 5, 5458–5465.
- Quraishi, A., Mehar, S., Sahu, D., & Jadhav, S. K., (2017). *In vitro* mid-term conservation of *Acorus calamus* L. via cold storage of encapsulated microrhizome. *Braz. Arch. Biol. Tech.*, 60, 1–9.
- Radušienė, J., Judžentienė, A., Pečiulytė, D., & Janulis, V., (2007). Essential oil composition and antimicrobial assay of *Acorus calamus* leaves from different wild populations. *Plant Genet. Resour.*, 5, 37–44.
- Ragupathy, S., Steven, N. G., Maruthakkutti, M., Velusamy, B., & Ul-Huda, M. M., (2008). Consensus of the ‘Malasars’ traditional aboriginal knowledge of medicinal plants in the Velliangiri holy hills, India. *J. Ethnobiol. Ethnomed.*, 4, 8–16.
- Rai, R., Gupta, A., Siddiqui, I. R., & Singh, J., (1999). Xanthone glycoside from the rhizome of *Acorus calamus*. *Indian J. Chem.*, 38, 1143, 1144.
- Rai, R., Siddiqui, I. R., & Singh, J., (1998). Triterpenoid saponins from the *Acorus calamus*. *Indian J. Chem.*, 37, 473–476.
- Raina, V. K., Srivastava, S. K., & Syamasunder, K. V., (2003). The essential oil composition of *Acorus calamus* L. from the lower region of the Himalayas. *Flavour Frag. J.*, 18(1), 18–20.
- Rajith, N. P., & Ramachandran, V. S., (2010). Ethnomedicines of Kurichyas, Kannur district, Western Ghats, Kerala. *Indian J. Nat. Prod. Resour.*, 1, 249–253.
- Rajput, S. B., Tonge, M. B., & Karuppaiyl, S. M., (2014). An overview of traditional uses and pharmacological profile of *Acorus calamus* Linn. (Sweet flag) and other *Acorus* species. *Phytomed*, 21(3), 268–276.
- Ramakrishna, Y., Manohar, A. I., Mamata, P., & Shreekanth, K. G., (1984). Plants and novel antitumor agents: A review. *Indian Drugs*, 21, 173–185.
- Ramu, M. G., Senapati, H. M., Janakiramaiah, N., Shankara, M. R., Chaturvedi, D. D., & Murthy, N. N., (1983). A pilot study of the role of brahmyadiyoga in chronic unmada (schizophrenia). *Anc. Sci. Life*, 2, 205–207.
- Ray, C., Gupta, M., & Ghosh, A. (2016). Evaluation of the neuroprotective activity of Aswagandha and Vacha in combination with ayurvedic Medhya Rasayana *in-vivo*. *Int. Ayu. Med. J.*, 4(10), 2914–2922.
- Reddy, B. M., Lakshmi, B. V. S., & Dhanpal, C. K. (2018). Current status on biological activities of calamus: A review. *Int. J. Adv. Pharm. Med. Bioallied Sci.*, 6(1), 46–52.
- Reid, B. E., (1977). *Famine Foods of the Chiu-Huang Pen-ts'ao*. Southern Materials Centre: Taipei.
- Satyavati, G. V., Raina, M. K., & Sharmal, M., (1976). *Medicinal Plants of India* (Vol. I, pp. 14–16). Indian Council of Medical Research: New Delhi, India.

- Sauer, C. O., (1969). *Agricultural Origins and Dispersals (Bowman Memorial Lectures)* (2<sup>nd</sup> edn., p. 56). Massachusetts Institute of Technology Press: Cambridge, Massachusetts.
- Saxena, D. B., (1986). Phenyl indane from *the Acorus calamus*. *Phytochemistry*, 25(2), 553–555.
- Schmidt, G. H., & Strelake, M., (1994). Effect of *Acorus calamus* (L.) (*Araceae*) oil and its main compound  $\beta$ -asarone on *Prostephanus truncatus* (Horn) (*Coleoptera: Bostrichidae*). *J. Stored Prod. Res.*, 30(3), 227–235.
- Schmidt, G. H., Risha, E. E., & El-Nahal, A. K. M., (1991). Reduction of the progeny of some stored-product *Coleoptera* by vapors of *Acorus calamus* oil. *J. Stored Prod. Res.*, 27(2), 121–127.
- Shah, A. J., & Gilani, A. H., (2009). Blood pressure-lowering and vascular modulator effects of *Acorus calamus* extract are mediated through multiple pathways. *J. Cardiovasc. Pharmacol.*, 54, 38–46.
- Shah, A. J., & Gilani, A. H., (2010). The bronchodilatory effect of the *Acorus calamus* (Linn.) is mediated through multiple pathways. *J. Ethnopharmacol.*, 131, 471–477.
- Shahzad, N., Alam, M. A., Sultana, N., & Abdullah, A. K., (2015). Phytochemical and pharmacological studies of Vaj Turki (*Acorus calamus* Linn.) and Unani description: A review. *Int. J. Pharma Sci. Res.*, 6(10), 1241–1244.
- Sharma, P. K., Chauhan, N. S., & Lal, B., (2004). Observations on the traditional phytotherapy among the inhabitants of Parvati valley in western Himalaya, India. *J. Ethnopharmacol.*, 92(2, 3), 167–176.
- Sharma, S., Kumar, A., & Verma, G., (2015). Insecticidal and gerotoxic potential of *Acorus calamus* rhizome extract against *Drosophila melanogaster*. *Asian J. Pharm. Clin. Res.*, 8(4), 113–116.
- Sharma, V., Sharma, R., Gautam, D. S., Kuca, K., Nepovimova, E., & Martins, N., (2020). Role of Vacha (*Acorus calamus* Linn.) in neurological and metabolic disorders: Evidence from ethnopharmacology, phytochemistry, pharmacology and clinical study. *J. Clin. Med.*, 9(4), 1176.
- Sharma, Y., Upadhyay, A., Sharma, Y. K., & Chaudhary, V. (2017). A randomized clinical study to evaluate the effect of Tagaradi yoga in the management of insomnia. *Indian J. Tradit. Knowl.*, 16, S75–S80.
- Shashikala, G. H., Prashanth, D., Jyothi, C. H., Maniyar, I., & Manjunath, H. (2015). Evaluation of the antidepressant activity of aqueous extract of roots of *Acorus calamus* in albino mice. *World J. Pharm. Res.*, 4, 1357–1365.
- Sher, Z., Khan, Z., & Hussain, F., (2011). Ethnobotanical studies of some plants of Chagharzai valley, district Buner, Pakistan. *Pak. J. Bot.*, 43, 1445–1452.
- Shih-Chen, L., (1973). *Chinese Medicinal Herbs*. Georgetown Press: San Francisco, CA, USA.
- Shrestha, P. M., & Dhillion, S. S., (2003). Medicinal plant diversity and use in the highlands of Dolakha district Nepal. *J. Ethnopharmacol.*, 86, 81–96.
- Shukla, P. K., Khanna, V. K., Ali, M. M., Maurya, R. R., Handa, S. S., & Srimal, R. C., (2002). Protective effect of *Acorus calamus* against acrylamide-induced neurotoxicity. *Phytoh. Res.*, 16(3), 256–260.
- Shukla, P. K., Khanna, V. K., Ali, M. M., Maurya, R., Khan, M. Y., & Srimal, R. C., (2006). Neuroprotective effect of *Acorus calamus* against middle cerebral artery occlusion-induced ischemia in rat. *Hum. Exp. Toxicol.*, 25, 187–194.

- Si, K. T., Noto, F. K., Nagaoka, M., Li, J., Battle, M. A., Duris, C., North, P. E., et al., (2010b). Highly efficient generation of human hepatocyte-like cells from induced pluripotent stem cells. *Hepatology*, 51(1), 297–305.
- Si, M. M., Lou, J. S., Zhou, C. X., Shen, J. N., Wu, H. H., Yang, B., He, Q. J., & Wu, H. S., (2010a). Insulin releasing and alpha-glucosidase inhibitory activity of ethyl acetate fraction of *Acorus calamus* *in vitro* and *in vivo*. *J. Ethnopharmacol.*, 128(1), 154–159.
- Si, M. M., Lou, J. S., Zhou, C. X., Shen, J. N., Wu, H. H., Yang, B., & Wu, H. S., (2010). Insulin releasing and alpha-glucosidase inhibitory activity of ethyl acetate fraction of *Acorus calamus in-vitro* and *in-vivo*. *J. Ethnopharmacol.*, 128, 154–159.
- Singh, A. K., Ravishankar, B., Sharma, P. P., & Pandaya, T. (2017). Clinical study of the anti-hyperlipidaemic activity of Vacha (*Acorus calamus* Linn) W.S.R to sthaulya. *Int. Ayurvedic Med. J.*, 5, 1–8.
- Singh, M. P., Malla, S. B., Rajbhandari, S. B., & Manandhar, A., (1979). Medicinal plants of Nepal retrospect's and prospects. *Econ. Bot.*, 33, 185–198.
- Singh, R., Sharma, P. K., & Malviya, R., (2011). Pharmacological properties and ayurvedic value of Indian Buch plant (*Acorus calamus*): A short review. *Adv. Biol. Res.*, 5(3), 145–154.
- Sinha, A. K., (2003a). Council of scientific and industrial research (CSIR). *Process for the Preparation of 1-Propyl-2, 4, 5-Trimethoxybenzene from Toxic  $\beta$ -Asarone of Acorus Calamus or from Crude Calamus oil Containing  $\beta$ -Asarone*. U.S. Patent 6,528,041.
- Sinha, A. K., Joshi, B. P., & Acharya, R., (2003b). Council of scientific and industrial research (CSIR). *Process for the Preparation of Pharmacologically Active  $\alpha$ -Asarone from Toxic  $\beta$ -Asarone Rich Acorus Calamus Oil*. U.S. Patent 6,590,127.
- Soni, P., & Sharma, C., (2012). A clinical study of Vachadi Churna in the management of obesity. *Int. J. Ayurveda Allied Sci.*, 1, 179–186.
- Srivastava, V. K., Singh, B. M., Negi, K. S., Pant, K. C., & Sunjea, P., (1997). Gas chromatographic examination of some aromatic plants of Uttar Pradesh hills. *Indian Perfumer*, 41(4), 129–139.
- Sundaramahalingam, M., Ramasundaram, S., Rathinasamy, S. D., Natarajan, R. P., & Somasundaram, T., (2013). Role of *Acorus calamus* and alpha-asarone on hippocampal dependent memory in noise stress exposed rats. *Pak. J. Biol. Sci.*, 16, 770–778.
- Tajadini, H., Saifadini, R., Choopani, R., Mehrabani, M., Kamalinejad, M., & Haghdoost, A. A., (2015). Herbal medicine Davaie Loban in mild to moderate Alzheimer's disease: A 12-week randomized, double-blind placebo-controlled clinical trial. *Complement. Ther. Med.*, 23, 767–772.
- Tare, V., (2001). Bioactivity of some medicinal plants against chosen insect pests/vectors. *J. Med. Aromatic Plant Sci.*, 22, 120–124.
- Tiwari, N., Mishra, A., Bhatt, G., & Chaudhary, A., (2014). Isolation of principle active compound of *Acorus Calamus*. *In-vivo* assessment of pharmacological activity in the treatment of neurobiological disorder (stress). *J. Med. Clin. Res.*, 2, 2201–2212.
- Tiwari, R. K. S., Das, K., Pandey, D., Tiwari, R. B., & Dubey, J., (2012). Rhizome yield of sweet flag (*Acorus calamus* L.) as influenced by planting season, harvest time, and spacing. *Int. J. Agron.*, 2012.
- Tomar, A., (2009). Folk medicinal uses of plant roots from Meerut district, Uttar Pradesh. *Indian J. Tradit. Knowl.*, 8, 298–301.
- Tripathi, A. K., & Singh, R. H., (2010). Experimental evaluation of the antidepressant effect of Vacha (*Acorus calamus*) in animal models of depression. *Ayu*, 31, 153–158.

- Triska, Dr., (1975). *Hamlyn Encyclopaedia of Plants*. Hamlyn: London, United Kingdom; ISBN 0-600-33545-3.
- Umamaheshwari, N., & Rekha, A., (2018). Sweet flag: (*Acorus calamus*)-an incredible medicinal herb. *J. Pharmacog. Phytochem.*, 7(6), 15–22.
- Usher, G., (1974). *A Dictionary of Plants Used by Man*. Constable and Company Ltd.: London, United Kingdom; ISBN 0094579202.
- Usher, G., (1984). *Spilanthes Acmella, a Dictionary of Plants Used by Man* (p. 38). CBS Publishers and Distributors: New Delhi, India.
- Valay, S., Ragavendra, M., Sushma, M., & Rao, V. U. M. (2015). *Calamus aromaticus* medicinal review. *Int. J. Pharm. Res. Biomed. Anal.*, 4(2), 10–14.
- Vashi, I. G., & Patel, H. C., (1987). Chemical constituents and antimicrobial activity of *Acorus calamus* Linn. *Comp. Physiol. Eco.*, 12, 49–51.
- Vengadesh, K., George, T., VinothKumar, R., Nancy, J., Kalaivani, M., & Vijayapandi, P., (2009). Neuromodulatory effect of *Acorus calamus* leaves extract on the dopaminergic system in mice. *Int. J. PharmTech Res.*, 1(4), 1255–1259.
- Venkatramaniah, C., & Praba, A. M. A., (2019). Effect of beta asarone – the active principle of *Acorus Calamus* in neuroprotection and nerve cell regeneration on the pyramidal region of the hippocampus in mesial temporal lobe epileptic rat models. *J. Neurosci.*, 5, 19–24.
- Venkatramaniah, C., Praba, A. M. A., & Ismail, B. M., (2016). Neuroprotective role of *Acorus calamus* and Its active principle beta asarone in retaining the memory of rats using 8 arm radial maze. *Int. J. Anat. Res.*, 4(2), 2238–2244.
- Verma, L. R., (1998). *A Glimpse of Indigenous Technology Knowledge of Watersheds Management in Upper North-West Himalayas of India*. (Participatory Watershed Management Training in Asia (PWTMA) Program GCP/RAS/IGI/Net, FAO (UN), UN, Kathmandu, Nepal); iv+97.
- Wallnofer, H., & Rottauscher, A., (1965). *Chinese Folk Medicine and Acupuncture*. Bell Publishing Co. Inc.: New York, USA.
- Watt, J. M., & Breyer-Brandwijk, M. G., (1962). *The Medicinal and Poisonous Plants of Southern and Eastern Africa* (pp. 600, 601). E. & S. Livingstone Ltd.: London, UK.
- Weber, M., & Brändle, R., (1994). Dynamics of nitrogen-rich compounds in roots, rhizomes, and leaves of the sweet flag (*Acorus calamus* L.) at its natural site. *Flora*, 189, 63–68.
- Weiner, M. A., (1980). *Earth Medicine, Earth Food*. Ballantine Books: New York, USA; ISBN 0-449-90589-6.
- Wheelwright, E. G., (1974). *Medicinal Plants and Their History*. Dover Publications Inc.: New York, USA.
- Wren, R. C., (1956). *Potter's New Cyclopaedia of Botanical Drugs and Preparations*. Sir Isaac Pitman and Sons Ltd.: London, UK.
- Wu, H. S., Li, Y. Y., Weng, L. J., Zhou, C. X., He, Q. J., & Lou, Y. J., (2007). A Fraction of *Acorus calamus* L. extract devoid of  $\beta$ -asarone enhances adipocyte differentiation in 3T3-L1 cells. *Phytother. Res.*, 21, 562–564.
- Wu, H. S., Zhu, D. F., Zhou, C. X., Feng, C. R., Lou, Y. J., Yang, B., & He, Q. J., (2009). Insulin sensitizing activity of ethyl acetate fraction of *Acorus calamus* L. *in-vitro* and *in-vivo*. *J. Ethnopharmacol.*, 123, 288–292.
- Yabesh, J. M., Prabhu, S., & Vijayakumar, S., (2014). An ethnobotanical study of medicinal plants used by traditional healers in Silent Valley of Kerala, India. *J. Ethnopharmacol.*, 154, 774–789.

- Yamamura, S., Iguchi, M., Nishiyama, A., Niwa, M., Koyama, H., & Hirata, Y., (1971). Sesquiterpenes from *Acorus calamus* L. *Tetrahedron*, 27(22), 5419–5431.
- Yao, X., Ling, Y., Guo, S., Wu, W., He, S., Zhang, Q., Zou, M., Nandakumar, K. S., Chen, X., & Liu, S, (2018). Tatanan A from the *Acorus calamus* L. root inhibited dengue virus proliferation and infections. *Phytomedicine*, 42, 258–267.
- Yende, S. R., Harle, U. N., Bore, V. V., Bajaj, A. O., Shroff, K. K., & Vetal, Y. D., (2009). Reversal of neurotoxicity-induced cognitive impairment associated with phenytoin and phenobarbital by *Acorus calamus* in mice. *J. Herb. Med. Toxicol.*, 3, 111–115.
- Zaugg, J., Eickmeier, E., Ebrahimi, S. N., Baburin, I., Hering, S., & Hamburger, M., (2011). Positive GABAA receptor modulators from the *Acorus calamus* and structural analysis of (+)-dioxosarcoguaiaicol by 1D and 2D NMR and molecular modeling. *J. Nat. Prod.*, 74, 1437–1443.
- Zhou, C. X., Qiao, D., Yan, Y. Y., Wu, H. S., Mo, J. X., & Gan, L. S., (2012). A new anti-diabetic sesquiterpenoid from the *Acorus calamus*. *Chin. Chem. Lett.*, 23, 1165–1168.

## CHAPTER 3

---

# *Ocimum spp.* (Basil): An Incredible Plant

MOUMITA MALAKAR<sup>1</sup> and DEBASHIS MANDAL<sup>2</sup>

<sup>1</sup>*Department of Horticulture, Central University of Tamil Nadu, Neelakudy, Thiruvarur, Tamil Nadu, India*

<sup>2</sup>*Department of Horticulture, Aromatic and Medicinal Plants, Mizoram University, Aizawl, Mizoram, India*

---

### ABSTRACT

Basil (*Ocimum basilicum* L.), coined from the Greek word ‘*basileus*’ or ‘king,’ is a popular aromatic plant that belongs to the family Lamiaceae and contains countless herb and shrub species. The common basil is known as ‘Tulsi’ in India and Nepal widely used as folk medicine. Furthermore, it has a significant role in Ayurveda and for culinary purposes over the centuries. This herb is a reservoir of medicinal compounds which boosted its involvement to heal various diseases and disorders but the therapeutic significance of wide array of phytomolecules yet to be corroborated. It possesses central nervous system (CNS) depressant, anticancer, cardiac stimulant, hepatoprotective, hypoglycaemic, hypolipidemic, immunomodulator, analgesic, anti-inflammatory, antimicrobial, antioxidant, antiulcerogenic, chemomodulatory, and larvicidal activities. Different plant parts of *Ocimum basilicum* chiefly used for essential oil extraction as a source of methyl eugenol (78.02%),  $\alpha$ -cubebene (6.17%), nerol (0.83%) and  $\epsilon$ -muurolene (0.74%) components. It is characterized for high content of methyl eugenol. In general, leaves of *Ocimum sp.*, especially employed for chemical and essential oil extraction both eventually contribute for 80% of patents. Volatile oil of *O. Minimum* holds geranyl acetate (69.48%), terpinen-4-ol (2.35%) and octan-3-yl-acetate (0.72%) are imperative essential oil constituents. In this

backdrop, range of molecular attributes viz. sequencing of whole nuclear and chloroplast genomes and metabolic potency of this scared herb will be indeed vital. So, the development of new active principle and nutraceutical will be indeed a fascinating venture using basil plant components for drug developments against emerging disease vectors.

### 3.1 INTRODUCTION

Among all essential culinary items Basil (*Ocimum basilicum* L.) is the most vital annual herb resides to Lamiaceae family (so-called mint family) (Agarwal et al., 2013). The genus *Ocimum* has 50–150 species but variations in range of phonological traits (like whole plant morphology, growth habit, flower color, leaf, and stem characteristics and biochemical composition, etc.) cause uncertainty to calculate the exact number of species under the genus *Ocimum* (Svecova & Neugebauerova, 2010). The tropical regions of Asia and Central and South Africa are considered to be its native place (Ghosh, 1995). Some other plants, namely ‘Basil Thyme’ [*Acinos arvensis* (Lam.) Dandy] and ‘Wild Basil’ (*Clinopodium vulgare* L.) create confusion with the ‘Sacred Basil’ (*Ocimum* sp.) for their identical common name. Reclassification of taxonomic sections of this genus had been made by few plant systematists for enormous diversity caused for its geitonogamous nature (Paton, 1992).

Vernacular names of basil plants usually vary based on location. *O. basilicum* it is typically known as ‘Basil,’ ‘Common Basil’ or ‘Sweet Basil’ in English while in India specifically in Hindi and Bengali, it is popular as ‘*babuitulsi*.’ Several other common names of basil are ‘*Basilica*’ (in French and Italian), ‘*Basilikumor*’ (in German), ‘*Rehan* or *Rihan*’ (in Arabic) and ‘*Albahaca*’ (in Spanish) (Kritikar & Basu, 2003; Bilal et al., 2012). However, most common basil is sweet basil (*O. basilicum*) contains more than 160 named existing cultivars vary according to their flavor, scent, and uses. Aroma ranges from cinnamon, liquor ice, and lemon to anise. Popular examples include *O. basilicum* var. ‘Cinnamon,’ *O. basilicum* var. ‘Dark Opal’ and holy basil (the species *O. tenuiflorum* L., previously known as *O. sanctum* L.).

Basil plants are commonly shrubby or herbaceous though some regular varieties are annuals too while the occurrence of perennial varieties (e.g., *O. tenuiflorum*) in warm tropical regions were also evident (Simon et al., 1999; Tilebeni, 2011). Their size varies from 20 cm to 3 m based on species. Taxonomically laminas are smooth, shiny, hairy or curly while hues of dorsal and



ventral surface ranges from green–blue or purple and white–purple–lavender (Meyers, 2003). Wide array of forms, colors, and sizes (Svecova & Neugebauerova, 2010) and frequent growing in public parks and home gardens elevated basil's ornamental and economic importance globally.

The extensive prevalence of antioxidant activities of this annual herb (Yanishieva et al., 2006) served for human health benefits since time immemorial. It is significantly used as culinary herbs also. The antioxidant richness led to involve them in Mediterranean cuisines. Apart from its culinary importance it's a major essential oil producing species (Grayer et al., 2002). To formulate cosmetic and pharmaceutical products, the extracts of basil are imperative (Unerie et al., 1998). It has antioxidant, antimicrobial, and antitumor activities for presence of phenolic acids, flavonol-glycosides (Javanmardi et al., 2002; Kividompolo & Hyotylainen, 2007) and aromatic compounds (Gutierrez et al., 2008; Hussain et al., 2008). Redox properties are key reasons for antioxidant activity of phenolic compounds played major role to absorb and neutralize free radicals, to quench singlet and triplet oxygen or to decompose peroxidizes (Asami et al., 2003). Antioxidant capacities of phytochemicals proved to lower incidence and mortality rates of cancer in several human populations. The presence of phenyl propanoids like eugenol, chavicol, and their derivatives or terpenoids like monoterpene alcohol linalool, methyl cinnamate, and limonene facilitated the commercial status of basil oils concentrated mainly in leaves and flowers; while trace amounts available in branches and stems (Svecova & Neugebauerova, 2010). Decisively, the versatility of basil plants greatly influenced by their origin, source, and growing conditions while morphological and chemical variations also determined by ecological factors.

### 3.2 AREA AND PRODUCTION

The aromatic plant 'Basil' was derived from Greek, '*Basilica*' means 'Royal Plant.' The Indian subcontinent is its place of origin while distribution and successful cultivation is evident in the entire South-East Asian tropics. Owing to the multifaceted utilities (perfumery and cosmetic industries, folk medicines, etc.) of *Ocimum*'s essential oils, in India around 25,000 ha areas are occupied under this crop with an annual production of 250–300 tons of its oil.

Basils' habitat distribution is fascinating. Among the *Ocimum* genus *O. basilicum* dispersed in the warmer parts up to 1,800 m altitude from sea

level while *O. sanctum* (Common name: ‘Sacred basil’ or ‘Holy basil’), an emblem of sanctity as per Hindu mythology has widest distribution throughout the Indian sub-continent, ascending up to 1,800 m in the Himalayas and in Andaman and Nicobar Islands. Africa, South America (Brazil) and Asia – these 3 are the key centers of origin for this genus while France, Italy, Bulgaria, Egypt, Hungary, South America, Comoro Islands, Thailand, India, Haiti, and Guatemala are the key producers of basil. Uttar Pradesh (UP) is one of the states in India produce French basil significantly (Lupton et al., 2016).

Basils are commercially grown in USA’s western and southern states including Arizona, California, Florida, New Mexico, and North Carolina especially for having congenial climatic condition. For low production statistics the United States import this larger ‘herb’ from Mexico (Meyers, 2015).

Huge demand of basil oil mandating its rapid production. Although many small-scale growers involve in basil oil production but not at national status, in fact the absolute figure of its production is unidentified. The total production of basil oils was approx. 93–95 tons per annum during 1990s. Out of this amount 55 tons were obtained from *O. gratissima* L. and 43 tons from *O. basilicum*. *O. canum* (Syn. *O. americanum* L.), commonly known as ‘Simms’ also contributed 100 kg of oil per annum during that time. Among many basil oil producing countries, India (15 tons), Bulgaria (7 tons), Egypt (5 tons), Pakistan (4.5 tons), the Comoros (4.5 tons), Israel (2 tons), the former Yugoslavia (1 tons), the USA (1 tons), Madagascar (1 tons), Réunion and Albania (each 0.5 tons), Hungary (0.3 tons) and Argentina (0.2 tons) (Lawrence, 1993; Hiltunen & Holm, 1999) are at pinnacle. According to Robbins & Greenhalg (1979), USA followed by Germany, France, Netherlands, and UK also secured top position concerning basil oil production.

Dried basil is not so popular but still has meagre demand although the current global statistic of its production is unavailable. Desiccated basils are produced in India, California, and chiefly in Mediterranean regions. They are majorly consumed to meet the domestic need due to their less international demand. USA was considered as the world’s largest user of dried basil (according to Import statistics) (Putievsky & Galambosi, 1999).

### 3.3 MARKETING AND TRADE

European countries have huge demand for basil. Since 1990, Europe is the highest (830–880 t year<sup>-1</sup>) importer of basil herb. Among all European countries, France (300–350 t year<sup>-1</sup>), UK (250 t year<sup>-1</sup>), Germany (200 t year<sup>-1</sup>)

and the Netherlands (80 t year<sup>-1</sup>) are the topmost basil importers. Egypt among the Western European countries is the greatest supplier of this herb (Putievsky & Galambosi, 1999).

To have noteworthy contribution in international essential oil trade, range of cultivars or chemotypes from diversified geographic origin of *O. basilicum* are essential to upgrade the richness of essential oils since the climate play vital role on chemical composition and yield quantity of essential oil (Simon et al., 1990; Marotti et al., 1996). The European type (Italy, French or Sweet basil) produces supreme quality oils in terms of finest odor for having linalool and methyl-chavicol as key constituents (Simon et al., 1990). Egyptian and European basil are almost identical regarding their chemical composition but the former one contains relatively higher percent of methyl chavicol. The essential oils produced by Comoro Islands, Thailand, Madagascar and Vietnam are known to contain high concentrations of methyl-chavicol (Marotti et al., 1996) while India, Guatemala, Pakistan (Marotti et al., 1996) and Eastern Europe produce methylcinnamate-rich essential oils (Simon et al., 1990). Furthermore, Java (Simon et al., 1990), Russia and North Africa's (Marotti et al., 1996) essential oils are characterized for eugenol-richness (Vieira & Simon, 2000).

### 3.4 COMPOSITION AND USES

Basil, considered as 'Culinary' herbs proved to have antioxidant activities (Yanishieva et al., 2006) suggesting their potential role for human health benefits. It is a popular ingredient in many Mediterranean food preparations. Its essential oil extracts (Grayer et al., 2002) are also used in the manufacturing of cosmetic and pharmaceutical products (Unerie et al., 1998). It has antioxidant, antimicrobial, and anti-tumour activities for presence of phenolic acids and aromatic compounds (Gutierrez et al., 2008; Hussain et al., 2008).

Phenyl propanoids, like eugenol, chavicol, and their derivatives or terpenoids like monoterpene alcohol linalool, methyl cinnamate, and limonene are the key components; contribute significantly for high economic value of basil oil. Redox properties of phenolic compounds enact vital role to absorb and neutralize free radicals, to quench singlet and triplet oxygen or to decompose peroxides (Asami et al., 2003). Moreover, these phytochemicals are potential to decrease the incidence and death rates of cancer in several human populations.

Geographical occurrence has significant influence on the qualitative and quantitative profiles of different basil varieties, for example, 'Purple Opaal' variety (Beatovic et al., 2015; Klimánková et al., 2008) is highly enriched with phenolic compounds while 'Red Rubin' variety (Seidler-Lozykowska & Król, 2008; Švecová, 2006) is a potential essential oil extractor. Linalool – the chief component of essential oils extracted from European basil varieties (Beatovic et al., 2015; Seidler-Lozykowska & Król, 2008; Marotti et al., 1996; Nurzyska-Wierdak et al., 2013). Additionally, geraniol (12.6%), 1,8-cineole (4.1%) and epi- $\alpha$ -cadinol (3.8%) are also present in the extract. Other key components in basil oil are linalool, methyl chavicol, eugenol, bergamotene, and methyl cinnamate (Klimánková et al., 2008), methylchavicol, camphor, citral, limonene, methylcinnamate, caryophyllen, anethol, terpinen-4-ol, myrcene, thymol, ocimene, and cinnamaldehyde (Švecová & Neugebauerová, 2010). Wide variations in linalool concentrations and other essential oil components extracted from this herb's range of plant parts (flowers, leaves, and stems) are evident (Chalchat & Özcan, 2008). Estragole (58.26%), fenchone (10.1%), limonene +  $\beta$ -phellandrene (19.41%), and  $\alpha$ -phellandrene (4.37%) are main components of oil extracted from basil blooms, while estragole (52.60%), limonene (13.64%), exo-fenchyl acetate (10.99%), fenchone (5.70%),  $\alpha$ -phellandrene (4.15%), and endo-fenchyl acetate (1.30%) are found in basil leaf oil. Recent research revealed the positive impact of jasmonic acid (JA) on the plant yield, production, and composition of essential oils of 'Lettuce leaf' basil jasmonic acid (JA) on the plant yield, production, and composition of essential oils of 'Lettuce leaf' basil (Złotek, 2016).

Apart from its use as flavoring agent in culinary, basil is sometimes good for mild nervous disorders and for mitigating wandering rheumatic pains. Basil leaves have some healing effect on the central neural system whereas powdered dried leaves, in snuff form are curative for nervous headaches (Waldstein, 2006). For example, ethanolic extracts using leaf of *O. sanctum* could reduce the total acetylcholine content (noise induced stress results in its elevated content) and enhance acetylcholinesterase activity of cerebral cortex, corpus striatum, hypothalamus, and hippocampus of brain (Sembulingama et al., 2005), possibly through the antioxidant activity (Samson et al., 2007). These properties are due to the presence of volatile compounds present in basil plant. For example, sesquiterpenes eugenol and 1,8-cineole found in *O. gratissimum* could eradicate range of stress-induced symptoms (Mukherjee et al., 2005). Folk infusion using fresh basil herb found optimal for obstructions of internal organs. The efficacy of basil infusions to arrest

vomiting and allaying nausea is well proven. Furthermore, the therapeutic properties of basil seeds could successfully cure the poison of snakes and warts too.

According to Tohti et al. (2006), the dose-dependent treatment by ADP caused the inhibition of platelet aggregation in rats but the effect of ADP and basil extracts together as a procoagulant and anticoagulant (like thrombin) was impactful. In fact, an aqueous extract of basil@ 75 mg kg<sup>-1</sup> day<sup>-1</sup> (approx.) could also bring the similar effect of aspirin@ 8.8 mg kg<sup>-1</sup> day<sup>-1</sup> (approx.).

Sweet basil is quite low in fat and calorie contents but highly enriched in minerals and vitamin A. About 2.5 g of fresh basil leaves (5 nos. approx.) contain 96.6 IU, 3.85 mg and 11.55 mg of vitamin A, calcium (Ca) and potassium (K) respectively but very low calories (<1). It contains meagre amount of range of vitamins especially vitamin C and also protein, fiber, and minerals. About 2.0–68.0 ppm of raw extracts of sweet basil leaves and 0.01–50 ppm of its essential oil could be used as this species of basil was enlisted under GRAS (generally recognized as safe), US department of Agriculture. Overall, the recommended doses of its essential oil will be only effective whereas imprudent consumption may cause carcinogenic effect (Hanif et al., 2011; Hosseini-Parvar et al., 2015).

‘Tulsi’ is an imperative herb in ayurvedic medicine used for several millennia to heal many ailments like stress relieving, and for respiratory, gastrointestinal, kidney, dermatological, and ophthalmological treatments in India exclusively while range of blood disorders could be also healed using its phytoformulation (Singletay, 2018). Human trials demonstrated the usefulness of Tulsi in the treatment of metabolic disorders, in modulation of the immune system, and in improving neuro-cognition. Leaves of *O. viridae* (commonly known as ‘Fever Plant’) native of Western Africa, has febrifugal properties as its leaves decoction could be a remedy for the fevers if drink like tea. The aroma of leaves is also used as remedial measures, for example *O. canum*, *O. gratissimum* (in India) and *O. crispum* (in Japan) used for cold treatments owing to the sweet scent of leaves while *O. teniflorum* is considered as aromatic stimulant in Java and *O. guineense* utilized to heal bilious fever. Due to its fragrance and aroma, ‘tulsi’ is also the most acclaimed ‘kitchen herb.’

Leaves and flowers of sweet basil are the most vital plant parts used as tonic and vermifuge in traditional folk medicine. For example, the raw extracts of these 2 plant parts are employed as first aid treatment for wasp stings and snakebites. Basil tea is good for treatment of nausea, flatulence,

and dysentery while to mitigate mental fatigue, colds, spasm, and rhinitis its leaf and bloom-derived essential oils are unparallel. According to Ahmad et al. (2002) basil contains central nervous system (CNS) depressant, anti-cancer, cardiac stimulant, hepatoprotective, hypoglycaemic, hypolipidemic, immunomodulator, analgesic, anti-inflammatory, antimicrobial, antioxidant, antiulcerogenic, chemomodulatory, and larvicidal activities. Eugenol (1-hydroxy-2-methoxy-4-allylbenzene), the active constituents found in *O. sanctum* L. chiefly responsible for the therapeutic potentials (Pattanayak et al., 2010).

Basil contains vitamin C (25 mg of vit C per 100 g of its edible portions), vitamin A, minerals viz. Ca, Zn, Fe (Anbarasu & Vijayalakshmi, 2007) and range of phytonutrients like protein@ 4.2 g, fat@ 0.5 g, carbohydrate@ 2.3 g, calcium@ 25 mg, phosphorous@ 287 mg, iron@ 15.1 mg (Pattanayak et al., 2010). It accelerates the efficient digestion, absorption, and use of nutrients from food and other herbs.

Basil is a common culinary ingredient. This herb is a mandatory component in Italian dishes 'pesto.' Apart from that it is used to flavor foods such as vegetables, poultry, and fish. The preserved basil in vinegar or olive oil adds a delightful flavor for salad dressings while edible basil flowers could be a striking addition to salads and other dishes (Grieve, 1931; Grieve & Marshall, 198). They could be a fine flavoring agent for jelly, honey, tea, and liquor. For potpourri and sachets, it also used as an aromatic herb. Except these, basil oil is a mandatory inclusion in wide cosmetic items viz. Lotions, shampoos, perfumes, and soaps. For its attractive foliage and flowers, it often included in ornamental flower garden.

*Tulsi* is very popular throughout the world for its medicinal properties. Different plant parts of this 'whole-plant-use-herb' are used as folk medicine in pan world exclusively in India. In Bangladesh, the importance of traditional, plant-based medicines is always hugely admired. For cough, cold, leg swelling, fever, bronchitis, gastric disorders, headache, nausea, and skin diseases, the water-based extracts made from basil leaves are hugely acclaimed. Especially, in Chuadanga, the extracts prepared from whole herb used to heal array of ailments. Although, Himalayan regions are sufficiently enriched of highly diversified floras but in some parts like Himachal Pradesh (H.P.), Nepal and Central Himalayan region basil plant parts like fresh leaves (enhance mental power) and desiccated leaves with 'ghee' (heal dysentery, piles, stomach disorders, etc.) still used hugely. At Makwanpur (Nepal), a concoction prepared from basil leaf extracts and flower heads of *Leucas cephalotes* is most effective to cure high fever while decoction of basil leaves

after blending with *Piper nigrum* and ‘Palmgur’ also found most effective to reduce high fever temperature. Sometimes, dehydrated basil leaves are also consumed as vegetables especially at Central Himalayan Region for blood purification purpose. The decoction of different plant parts (especially leaves inflorescence’s apex portion and roots) is also an effective antidote in snake bite poisoning significantly used in India. In Southern India (like Tamil Nadu [T.N.], Andhra Pradesh [A.P.] and Karnataka), basil is considered as a vital member of plant-based medicine’s community. Concoction of basil leaf extracts and onion bulbs is used to treat cough, cold, headache, etc., in T.N. Medicinal formulations especially ‘basil leaves + garlic + leaves of *Achyranthes aspera* + pepper’ and ‘basil leaves + fruits of *Trychosanthes dioica* + blooms of *Leucas indica* + leaves of *Aristolochia bracteate*’ used popularly to heal typhoid fever in A.P. while goat urine extracts of basil leaves with coconut oil and mildly warm concoction of fresh basil leaves extract with leaves of *Catharanthus roseus* could be effective enough to cure skin allergy and ear boils, respectively in Karnataka. As an antidote for scorpion bite, basil leaves paste is quite well-known in A.P. In North-East province, pharmaceutical formulations made by basil is highly acclaimed. For example, to treat Diarrhea, fever, dysentery, and skin infections, fresh basil leaf juice along with black pepper are used in Tripura, in Arunachal Pradesh decoction and paste of basil leaves used for inflammations and wound cuts, in Assam decoction of leaves used to heal stomach ache and headache. Powdery form of basil leaves mixed with honey also used for diabetic treatment and antidote for snake bite in Assam. For effective ringworm treatment, leaf extracts of basil are widely used in Uttar Pradesh (U.P.) province. Topical application of basil leaf extractions blended with *Bruguiera gymnorrhiza* and coconut oil is of great ethnomedicinal importance for body and mind rejuvenation purposes used in Nicobar Island (Singh & Chowdhury, 2018).

Based on tree bibliographic search, it is evident that basil as folk medicine is popular since time immemorial. Jamshidi & Cohem (2017); Leelahagul et al. (1992); & Akbarian et al. (2016) reported that consumed extracts of basil whole plant, seeds, and leaves at the dose rate of 300 mg–6 g/day may improve blood sugar and lipid profiles. The identical dose rate could also potentially reduce stress, anxiety, depression, and cause significant mental performance (Jamshidi & Cohen, 2017; Satoh & Sugawara, 2003 & Sugawara et al., 1999). While notable improvement in immune responses and lowering down the asthmatic symptoms could also be achieved (Jamshidi & Cohen, 2017). Essential oil and extract-based oral formulations at the dose rate of 250 mg/day could potentially improve oral health and hearing

(like low plaque deposition, reduced gingival inflammation and bleeding, quick recovery from jaw fractures, etc.) (Pate & Venkatakrishna Bhatt, 1988; Agarwal & Nagesh, 2011; Gupta, 2014; Hosamane, 2014; Pereira et al., 2014; Pimenta, 2014; Mohammad et al., 2014). According to many researchers (Rasal & Akhtar, 2011; Balambar et al., 1985; Orafidiya et al., 2002; Martin & Ernst, 2003) 3% cream formulated using essential oil of leaves could decrease wrinkling and improve acne problems.

### 3.5 ORIGIN AND DISTRIBUTION

'Basil' (member of the large mint family [Lamiaceae]) is cultivated across the world but prefers tropical to sub-tropical condition for its easy thrives. In India, Pakistan, Iran, Thailand, and other countries of Asia more than 5,000 perennial wild species of basil are found to be grown (Albuquerque, 1996). Some parts of Africa and Pacific islands also possess patch of basil plants. Its center of origin is assumed to be not in exactly India but in more East part of the globe. According to the ancient literature of 807 A.D. Hunan region of China could be the most probable place of their origin as some evidence of its use during that era was found. Its acceptance as indoor plant in Western countries is noteworthy to mitigate the frost injury of this tropical herb. Significant medicinal values of *Tulsi* are the probable cause of its eventual migration from India to Europe and America via Middle East during 16<sup>th</sup> and 17<sup>th</sup> century, respectively (Darrah, 1972).

Warm climatic condition is the best suited for its cultivation even though it has wide angel climatic adaptability. Warm temperature regime, sufficient sunlight and moisture level – these three are key factors for its successful thrives but its susceptibility to frost makes it inappropriate for outdoor cultivation. Basil is cultivated widely in several countries like India, Pakistan, Comoros Islands, Madagascar, Haiti, Guatemala, Reunion, Thailand, Indonesia, Russia (Georgia, East Caucasus), South Africa, Egypt, Morocco, France, Israel, Bulgaria, USA (Arizona, California, New Mexico), Italy, Hungary, Poland, Germany, Greece, Slovakia, Turkey, and other Balkan countries (Putievsky & Galambosi, 1999).

### 3.6 BOTANY AND TAXONOMY

Basil is a popular, tender, annual or rarely perennial herb used basically for its aromatic leaves. Depending on the variety, height varies from 30 cm (0.98 ft)



to 150 cm (4.9 ft). Hues of laminas are richly green, surface pubescent, shape ovate, but leaf sizes and shapes differ significantly based on the cultivar. Leaf sizes range from 3 cm (1.2 inches) to 11 cm (4.3 inches) in length and between 1 cm (0.39 inches) and 6 cm (2.4 inches) in width (<https://plantvillage.psu.edu/topics/basil/infos>). Leaves of some species are greyish-green on ventral surface having dotted dark oil cells (Albuguerque, 1996; Darrah, 1974; Morales & Simon, 1996). It grows about 1 m height in a bushy form having central taproot system, has an obtusely quadrangular stem, labiates, small, white colored flowers in whorl fashion. Flowers emerge from axils of leaves. Calyx has round; spreading upper lobe emerges from the central inflorescences which arise from central stem atop the plant.

*Ocimum minimum* (commonly known as 'Bush Basil') attains the height > 6 inches usually propagated by seed. Leaves are characteristically ovate, entire, and produce white blooms in whorled fashion at towards the top but its height is smaller than sweet basil. This type of basils is basically of 2 types viz. one having black-purple leaves while other possesses variable leaves. Concerning the low temperature susceptibility, bush basil is hardier than the garden basil although both are native of India. Both of them bloom during July and August (Darrah, 1972; Martins et al., 1999; Morales & Simon, 1996). Leafy tops of bush basil are a mandatory item for seasoning and in salads like sweet basil.

Generally, basil is herbaceous plant. Mostly, *O. basilicum* has upright stem with branched habit. The stem is square in shape (thickness approx. 0.6–0.9 cm) with glabrous texture usually green colored but purple color is often found. Leaves are ovate (2.5–5 cm long), apex acute, entire to slightly toothed margin, petiolate (length 1.3–2.5 cm long), simple with opposite phyllotaxy and contain oil glands (emits strongly fragrant volatile oil). The inflorescence is usually racemose, sometimes terminal raceme. It has stalked bracts which are ovate in shape with acute apex, green colored calyx (5 mm in length) almost envelopes the pedicillate fruits, calyx has long lower (with 2 central teeth) and short upper (rounded in shape) lips formed by fusion of 5 sepals, corolla (generally 8–13 mm long) hues are species/cultivar-specific (may be white, pink, purple, etc.) with glabrous/slightly pubescent texture and superior ovary is common, fruits composed of 4 achenes while seeds are ellipsoid in shape, pitted, approximately 2 mm long and black in color (Bilal et al., 2012).

'Wild basil'/'Hedge basil or Clamint' (botanically known as *Calamintha clinopodium*), is found throughout the North Temperate Zone. It is usually dry in nature and used as bush for demarcation purpose in England and Scotland.

In Ireland, wild basil is somewhat rare. It is a weak-looking, straggling plant, though stems are erect and thickly wrapped with soft hairs (Darrah, 1972; Grieve, 1999; Pushpangadan & Bradu, 1995). Leaf phyllotaxy is opposite, short-stalked, ovate-obovate shaped positioned on the four-angled stem. Flower opening occurs during July to September. Overall, it's an aromatic herb emits mild thyme like fragrance.

*O. basilicum* basically contains all commercial cultivars. According to Darrah (1974, 1980), *O. basilicum* cultivars are of 7 types viz. (i) 'Tall slender types' (belong to 'Sweet' basil group); (ii) 'Large leafed and robust types' (belong to 'Italian' basil group [regionally known as 'Lettuce leaf']); (iii) 'Dwarf types' (belong to short and small leafed 'Bush' basil); (iv) 'Compact types' (belong to 'Thai' basil [*O. basilicum* var. *thyrsiflora*] group); (v) 'Purple colored basil' (belong to 'Sweet' basil group); (vi) 'Purple types' (belong to 'Dark Opal' [hybrid between *O. basilicum* and *O. forskolei*] group, possess clove-like aroma); and (vii) 'Lemon-flavored basil' (belong to *O. basilicumcitriodorum* group) (Morales & Simon, 1996).

On the other hand, according to the great diversity in chemical composition and geographical sources of different species and varieties, they've been classified into four major types as here under.

- 1. European or Sweet Basil:** The extracted oil of this type is characterized mainly for having methyl chavicol and linalool, but no camphor. It includes French and American Sweet basil oils have high demand for its high quality and finest odor. Distillation takes place in France, Italy, Bulgaria, Egypt, Hungary, South Africa and occasionally in the United States.
- 2. Reunion Basil:** Chief chemical constituents of extracted oil from this type are methyl chavicol and camphor (in meagre amount) without any linalool content. Distillation of its oil is made in Reunion Island, Comoros, Malagasy Republic, Thailand, and Seychelles.
- 3. Methyl Cinnamate Basil:** This oil contains methyl chavicol, linalool, and methyl cinnamate in sufficient quantity, usually distilled in India, Haiti, Guatemala, and a few African countries.
- 4. Eugenol Basil:** Eugenol, the key chemical component of this oil. Distillation is often made in U.S.S.R. and North African countries (especially Egypt and Moracco).

Around nine species are recorded in Eugenol basil from India, of which three are exotic. The more important of these species are:

i. *Ocimum basilicum* Linn (2n = 48) (English/French/Sweet Basil).

It has the following subspecies and varieties:

- a. *O. basilicum* Linn. Subsp. *minima* Danert (Syn. *O. minima* Linn).
- b. *O. basilicum* Var. *Majus* Benth.
- c. *O. basilicum* Var. *Difforme* Benth (Curly-leaved basil).
- d. *O. basilicum* Var. *Purpurascens* Benth (Violet-red basil).
- e. *O. basilicum* Var. *Glabratum* Benth (Common white basil).
- f. *O. basilicum* Var. *Pilosum* Benth (Syn. *O. pilosum* Roxb.).
- g. *O. basilicum* Var. *Crispa*.
- h. *O. basilicum* Var. *Thyrisiflora*.
  - i. *O. basilicum* Var. *Darkopal*.
  - ii. *O. americanum* Linn. (Syn. *O. canum* Sims.) (Hoary basil).
  - iii. *O. gratissimum* Linn. (Shrubby basil).
  - iv. *O. kilimandscharicum* Guerke (camphor basil).
  - v. *O. sanctum* Linn. (Sacred or Holy basil).
  - vi. *O. viridae* Willd (Fever plant of Sierra Leone).

Of the above listed species, *Ocimum basilicum* Linn. Is the only commercially cultivated species in India.

Varieties like RRL-011, Vikarsudha, Kusumohak, and Cim-Saumya have been released from different institute.

➤ **Scientific Classification:**

- **Kingdom:** Plantae.
- **Phylum:** Magnoliophyta.
- **Class:** Magnoliopsida.
- **Order:** Lamiales.
- **Family:** Lamiaceae.
- **Genus:** *Ocimum*.
- **Species:** *O. basilicum*.

### 3.6.1 TAXONOMIC HISTORY OF OCIMUM SPECIES

Throughout the tropical and sub-tropical areas (Asia, Africa, and Central and South America) approximately 30–160 numbers of species of these annual and perennial herbs are distributed (Darrah, 1980; Paton et al., 1999). Growth habit, color, and chemical composition of aromatic substances – these 3 are the basic criterias to distinguish between various species of *Ocimum* sp. but

meagre diversities are the basic circumscription for appropriate identification. *O. africanum* Lour (Syn. *O. x citriodorum* Vis.), *O. americanum* L. (Syn. *O. canum* Sims.), *O. basilicum* L., *O. minimum* L., *O. gratissimum* L. and *O. tenuiflorum* L. (Syn. *O. sanctum* L.) – these are the popularly cultivated species of basil due to their noteworthy medicinal and economical importance (Carovic-Stanko et al., 2010). The detailed description of 5 key species of basil was given by Linnaeus first in 1753. Later, Bentham in 1832 confirmed the identification of 40 species of *Ocimum* and clustered them into three sections viz. *Ocimum* (*Ocymodon* Benth.), *Gymnocymum* Benth. and *Hierocymum* Benth (Paton et al., 1999). Bentham again based on the calyx morphology, subdivided the *Ocimum* section into three subsections, i.e., *Ocimum*, *Hiantia* Benth and *Gratissima* including *Hemizgya* Benth. Bentham included *Hemizgya* as novel subsection under *Ocimum* section but later Briquet (1897) refused its inclusion for its exceptional taxonomic feature (fusion of anterior stamens). Paton (1992) identified 30 African *Ocimum* species. He included *Hemizgya* and *Hiantia* under section and subsection, respectively of the infra-generic classification of *Ocimum* provided by Bentham in 1848. This inclusion favored *Hiantia* to become a distinct genus (Paton et al., 1999). Pushpagadan (1974) devised a distinct infra-generic classification where he made 2 distinct groups viz. (i) *Basilicum* group (it contains annual herbs having ellipsoid, black, intensely mucilaginous seeds and basic chromosome number of  $x=12$ ); and (ii) *Sanctum* group (it contains perennial shrubs featured by brown globose, non or little mucilaginous seeds with a basic chromosome number of  $x=8$ ). According to his classification, *Basilicum* group has *Ocimum* section and subsection. Other 6 key cultivars and varieties like *basilicum* cv. ‘Genovese,’ var. *basilicum* cv. ‘Sweet Basil,’ var. *difforme* Benth, var. *purpurascens* Benth. cv. ‘Dark Opal’ and var. *thyrsiflorum* L. Benth. were included in *Basilicum* group, section *Ocimum* by Pushpagadan (1974). But this infra-generic classification is not in concurrence of International Code of Botanical Nomenclature (ICBN). Polyploidy, hybridization at inter and intra-specific level results in chemical and morphological inconsistency but the occurrence of chemotypes considerably don’t influence the variation in plant morphology. Despite having an array of methods according to the morphological features, geographic origin, karyotypic features, extent of crossability and chemical compositions are already in use to have a better understanding about the taxonomy and phylogenetic relationship within *Ocimum* genus, their identity is still in question (Shasany, 2016).

Basil species and cultivars also vary depending in the geographical source, morphological, and cytological features, chemical constituents of many Eugenols contained species are *O. gratissimum* L. ( $2n = 40$ ), *O. viridae* wild ( $2n = 40$ ), *O. suave* wild ( $2n = 64$ ) and *O. carnosum* ck ( $2n = 48$ ). While *O. micranthum* ( $2n = 48$ ) is rich in Elimicin and Methyl isoeugenol. *O. sanctum* ( $2n = 24,26$ ) also contains linalool or camphor, *O. basilicum* ( $2n = 48$ ) methyl chavicol, methyl cinnamate and Eugenol, *O. americanum* ( $2n = 72$ ) contains methyl chavicol and citral, *O. kilimandscharicum* ( $2n = 76$ ) camphor, *O. sanctum* ( $2n = 32$ ) contains eugenol.

### 3.7 VARIETIES AND CULTIVARS

Different varieties of *Ocimum* spp. having range of phenotypic features, as for example flower hues greatly vary among these 6 varieties of *Ocimum basilicum*, i.e., *O. basilicum* var. 'Pilosum' (White-Purple), *O. basilicum* var. 'basilicum' (Pinkish-White), *O. basilicum* var. 'glabratum' (Pinkish-White or White), *O. basilicum* var. 'Difforme' (White), *O. basilicum* var. 'Thyrsiflora' (White), *O. basilicum* var. 'Purpuracense' (Purple). Lamina surface is smooth in *O. basilicum* var. 'Glabratum' while smooth in rest 5 varieties. Lamina is moderately pubescent in *O. basilicum* var. 'Pilosum,' *O. basilicum* var. 'Difforme,' *O. basilicum* var. 'Thyrsiflora,' medium and sparse in *O. basilicum* var. 'Basilicum;' glabrous in *O. basilicum* var. 'Glabratum' and dense in *O. basilicum* var. 'Purpuracense.' Lamina shape is ovate-lanceolate in *O. basilicum* var. 'Pilosum,' *O. basilicum* var. 'Basilicum,' *O. basilicum* var. 'Difforme' and *O. basilicum* var. 'Purpuracense' and sub-ovate in *O. basilicum* var. 'Glabratum,' *O. basilicum* var. 'Thyrsiflora.' Lamina color is purple-green in *O. basilicum* var. 'Pilosum,' *O. basilicum* var. 'Basilicum;' purple and dark-green in *O. basilicum* var. 'Glabratum'; dark Green in *O. basilicum* var. 'Difforme,' *O. basilicum* var. 'Thyrsiflora' and purple in *O. basilicum* var. 'Purpuracense.' Stem pubescence is medium in *O. basilicum* var. 'Pilosum,' *O. basilicum* var. 'Basilicum;' dense in *O. basilicum* var. 'Difforme,' *O. basilicum* var. 'Purpuracense,' *O. basilicum* var. 'Thyrsiflora,' and dense or medium pubescent in *O. basilicum* var. 'Glabratum.' Stem color is purple green in *O. basilicum* var. 'Pilosum,' *O. basilicum* var. 'Basilicum,' and light green in *O. basilicum* var. 'Difforme,' *O. basilicum* var. 'Thyrsiflora;' Purple in *O. basilicum* var. 'Purpuracense' and light green or purple green in *O. basilicum* var. 'Glabratum.'

Among 50–150 species of basil few are culinary basil essentially the cultivars of *O. basilicum* but it's very challenging to ascertain the exact group where a basil resides. Crossbreed friendly nature of basil pose difficulties to draw boundaries between species. Basil cultivars differ in several ways. For example, the shape and size of the leaves, it may be large lettuce-like leaves (e.g., 'Mammoth basil') or tiny leaves (e.g., 'Lettuce leaf basil,' 'Dwarf bush basil') also. More practically, varying degree and quantity of essential oils found liable to the variation of fragrance of the basil. The most vital are 1,8-cineol, linalool, citral, methyl chavicol (estragole), eugenol and methyl cinnamate, although hardly any basil contains all of these in any significant amount (Rawat et al., 2016). Two varieties of Holy basil namely 'Cim-Ayu' and 'Cim-Angana' also contain 83% and 40% of Eugenol, respectively. While the former one only contains 7.47% of beta element.

Large number of cultivars, high polymorphism and frequent cross-pollination (resulting in new hybrids) at inter and intra-specific level causes taxonomic uncertainty. *Ocimum basilicum* has at least 60 varieties, which further complicates the taxonomy (Simon, 1999).

Most basil are cultivars of sweet basil viz.:

- Anise basil, Licorice basil or Persian basil (*O. basilicum* var. 'Licorice').
- Cinnamon basil (*O. basilicum* var. 'Cinnamon').
- Dark opal basil (*O. basilicum* var. 'dark Opal').
- Lettuce leaf basil (*O. basilicum* var. 'Crispum').
- Leaf basil (*O. basilicum* var. 'Crispum').
- Purple basil (*O. basilicum* var. 'Purpurescens').
- Rubin basil (*Ocimum basilicum* var. 'Rubin').
- Globe basil, dwarf basil, French basil (*O. basilicum* var. 'Minimum').
- Thai basil (*O. basilicum thyrsifolium*).

(Source: <https://web.archive.org/web/20150924161135/http://www.ars-grin.gov/~sbmljw/cgibin/taxon.pl?70463>).

There is also few Hybrids like 'African blue basil' (*Ocimum basilicum* x *O. kilimandscharicum*), Spice basil (*Ocimum basilicum* x *O. americanum*) (sometimes sold as 'Holy' or 'Lemon' basil) (<https://web.archive.org/web/20160913143509/https://npgsweb.arsgrin.gov/gringlobal/taxonomydetail.aspx?id=463843>; <http://www.theplantlist.org/tpl1.1/record/kew-136798>). Camphor basil, African basil (*O. kilimandscharicum*), Clove basil (*Ocimum gratissimum*) (Fandohan et al., 2008), Holy basil (*Ocimum tenuiflorum*), formerly known as *O. sanctum* are of similar species (Pessoa

et al., 2002). Several basil varieties grown in various parts of Asia exclusively contain clove-like flavor which is generally stronger than the Mediterranean basils, such as *tulsi*. Lemon basil has a strong lemony smell and flavor very different from other varieties because it contains 'citral' chemical widely used in Indonesia (familiar in *kemangi* name), served raw along with raw cabbage, green beans and cucumber as an accompaniment to fried fish or duck. Its flowers when broken up, are a zesty salad condiment.

Apart from these species and varieties of basil, some other cultivars are also existing. As for example *O. basilicum* 'lettuce leaf' (C.N. lettuce leaf Basil) (featured by large leaves Used in salads). *O. basilicum* 'mammoth' (C.N. Mammoth Basil) (featured by bordered leaves and intense Flavor), *O. basilicum* 'nufar' basil (C.N. Nufar basil) (fusarium wilt resistant Cultivar), *O. basilicum* 'spicy globe' (C.N. Spicy Globe basil) (characterized by its bushy form minute leaves and strong flavor), *O. basilicum* 'Greek yevani' (C.N. Greek yevani basil) (organically grown cultivar), *O. basilicum* 'Piccolo' (C.N. Finoverde basil) (featured by its Narrow leaves and less pungent smell), *O. basilicum* 'Boxwood' (C.N. boxwood basil) (featured by its dense growth, small foliage and Strong scent), *O. basilicum* 'Purple Ruffles' (C.N. Purple Ruffles basil) (characterized by its solid purple hue and spicy flavor), *O. basilicum* 'Magical Michael' (C.N. Magical Michael) (exported for its degree of uniformity and nice flavor), *O. basilicum* 'Red Rubin' (C.N. Red Rubin basil) (identified by its magenta color and flavor) *O. basilicum* 'Osmin purple' (C.N. Osmin purple basil) (Distinguished for its dark shiny purple colored leaves), *O. basilicum* (C.N. Cuban basil) (similar like sweet basil but with much smaller leaves) *O. basilicum* Var *Thyrsoflorum* (C.N. Thai basil or Ho-Ra-pain Thai) (featured for its unique scent) *O. basilicum* Var *Thyrsoflorum* 'Siam Queen' (C.N. Siam queen) (cultivar of Thai basil), *O. basilicum* 'Cinnamon' (C.N. Cinnamon basil/Mexican spice basil) (featured for its scent and purple blue Bloom), *O. basilicum* Licorice (C.N. Licorice basil or Persian basil or Anise basil) (characterized for its silvery leaves, spicy Licorice alike smell due to the presence of in anise and Anethole chemicals. *O. basilicum* var 'Citriodora 'Mrs. Burns Lemon' (C.N. Mrs. Burns Lemon) (featured by its aromatic lemon scent), etc.

*O. americanum* is commonly known as lemon basil contains citral and limonene and sweeter in taste. In Indonesia, it is popularly known as *kemangi*.

*O. X citriodorum* is known as Thai lemon basil featured by its distinct lemon balm-like odor. Its common cultivar is 'Lesbos' propagated by cuttings.

Except this *O. tenuifolium* (holy basil), *O. gratissimum* (clove basil), *O. minimum* (Greek basil), *O. basilicum X americanum* (spice basil) are used in Ayurveda. They were much preferred by the perfuming industry.

There is other few cultivate strains of basil like RRL-011 (it is a sweet-smelling strain, it has 320 kg/ha oil extraction capacity, linalool 40% and methyl chavicol 35% and enriched essential oil. It gives an herbage yield of 50 tn/ha), 'Vikarsudha' (this hybrid is 75–90 cm tall, photo insensitive or day neutral variety, round the year could be cultivated, yield capacity 3.73 tn of herb and 78% methyl chavicol enriched essential oil is extracted from this variety), 'Kusumohak' (it essential oil contains 46% of linalool and 38% of methyl chavicol; oil yielding capacity is 134 kg/ha), 'Cim-Saumya' (a short duration variety, could matured within 60–80 days and contains 62% of methyl chavicol and 24% of linalool).

The most commonly available species and intraspecific hybrids of Basils are as follows:

1. *O. basilicum* (commonly known as Sweet Basil): It is erect by habit, produce white flowers, bright green clove scented foliages (1 cm long) (Anon, 1980; Darrah, 1972, 1974, 1980; De Baggio & Bisinger, 1996; Marotti et al., 1996; Morales & Simon, 1997).
2. *O. basilicum var. Genovesa* (commonly known as Genovese basil): Erect habit, bears dark green foliages (approx. 2 inches long), and characteristically delayed bolting found. This Italian strain of basil used for pesto and garlic dishes.
3. *O. basilicum var minimum* (commonly known as Bush or Greek basil): It is a dwarf variety (height less than 1 cm) produce white blooms, leaves are pungent, popular varieties like 'Green bouquet,' 'Spices globe' and 'Fine green' are used for edging purpose and container growing.
4. *O. basilicum purpurascens* (commonly known as Purple basil): Popular varieties of this species are 'Opal,' 'Purple Ruffles' and 'Red Rubin.' Traditionally they are used as culinary ingredients. But also, sometimes grow as ornamental one. Shape of leaf and size almost identical like sweet basil but produce lavender like flowers.
5. *O. basilicum Crispum* (commonly known as Lettuce leaf basil): It possesses large, wide leaves, less flavored species, mostly used for salads or sauces. 'Mammoth,' 'Napoletano' and 'Green Ruffles' are its popular variety.



6. *O. basilicum odoratum* (commonly known as Scented basil): This flavored basil species used for fruit preservation in custards and sorbets.
7. *O. cannum* (commonly known as Holy basil): it is a clove fragrant species with minute leaves, produce white- and violet-colored blooms, commonly used for worshipping purpose.
8. *O. kilimandsharicum* (commonly known as Camphor basil): Identifying features of this species are its grey-green foliage and strong fragrance. Not useful for culinary purpose.
9. *O. micranthum* (commonly known as Peruvian basil): It produce purple-colored flowers, commercially grown for ornamental seed head.

### 3.8 SOIL AND CLIMATE

1. **Soil Condition:** Basil can grow in wide range of soils viz. loam, poor laterite, saline, and alkaline – moderately acidic soil. Soil pH should be 6–7 for *Ocimum sanctum* and 4.3–9.1 for *Ocimum basilicum*) with good drainage capacity for optimum vegetative growth. Dwarf growth other than the varietal specifications caused by root-rot disease originates from water logged conditions. Clayey soils are entirely unsuitable. In fact, the tolerance level for Cu and Zn is high in case of *O. basilicum* while it is susceptible to Co and Ni (Smitha et al., 2014).
2. **Climate:** Subtropical climate is best suited for basil cultivation. More clearly crop grows well in warm and humid climate, even at an altitude range from 900–1,800 m also. It is essentially a warm season crop grow optimally in areas where daytime temperatures are consistently above 21°C (70°F) and night time temperatures stay above 10°C (50°F). High rainfall, moderate relative humidity (RH), long days and moderate-high temperatures favor its growth and oil production. They are sensitive to frost and cold but can moderately be tolerant to drought. Semi shaded condition also favors its growth. It requires around 6–8 hours of sun every day and benefits from some shade in the afternoon (Smitha et al., 2014).

To increase the potency of phenolic activity and flavonoid and essential oil content of sweet basil, the major antioxidant and anticancerous

substances, the application of organic and bio-organic fertilizers is vital since the amount of fertilizers applied and the enhancement of phytoconstituents level are positively correlated (Taie et al., 2010). The growth parameters, pigments content, total phenolics, total flavonoids and antioxidant activity of methanolic plant extract were evaluated being used various doses of organic fertilizers (compost) with or without biofertilizers. He reported that use of equal amount of compost and sand (50:50) with biofertilizer causes the enhancement of fresh and dry weights, total phenolics, total flavonoids and pigment content as compared to the use of compost alone. Around 50% and 75% of compost treatments with bio-fertilizer resulted in fortified antioxidant and anticancer potential.

Generally, in case of *O. sanctum* during mid Feb, seeds of 200–300 g seeds/ha are used for raising seedlings and in Feb-March seedlings are transplanted in well prepared land. As a basal dose, FYM @ 10 tn/ha and ½ dose of full amount of N and full amount of P<sub>2</sub>O<sub>5</sub> and K<sub>2</sub>O is applied. The recommended dose of N.P.K. for *O. sanctum* is 120.60.60. Then on April 6–8 weeks old seedlings are transplanted at the spring of 40–50 × 30–50 cm. Irrigation should be given based on requirement. Weeding, hoeing, and earthing up operations could be continued during May–June. After 90–95 days of transplantation (during July–Aug), 1<sup>st</sup> harvest could be carried out while during Sep–Oct and again in Nov–Dec, 2<sup>nd</sup> and 3<sup>rd</sup> harvesting could be done but after every harvesting optimum nutrient level should be maintained otherwise next phase of harvesting may be hampered.

### 3.9 PROPAGATION

Seeds are the principle propagating materials for *Tulsi*. It is advisable to germinate the seeds in the nursery followed by transplanting to the field since direct sowing remain unsuccessful most of the time. Seed health is quite vital for quality oil yielding but high rate of cross-pollination causes the deteriorations of oil over generations. Hence, healthy, disease, and pest-free pedigree stock seeds (approximately 125 g seeds are needed for 1 hec of land) are needed to get healthy seedlings.

In general basil seeds should be sown indoors 6–8 weeks before planting outside. Sowing of seeds in a sterile seed mixture in seed trays or pots at a depth of 0.2–1.0 cm (0.08–0.4 in) followed by gentle watering is advantageous. The temperature should be between 15.5°C and 27°C (60–80°F). Optimum germination temperature is 21°C, which facilitates basil seed's germination up to 5 days (Smitha et al., 2014).

### 3.10 PLANTING, IRRIGATION, AND NUTRIENT MANAGEMENT

#### 3.10.1 PLANTING TIME

All types of basil especially popularly cultivated species viz. *Ocimum sanctum* and *Ocimum basilicum* could be grown from the middle of February to the end of September and during Kharif in North or South India plains. In the hilly part of North India, it can be grown during *kharif*.

#### 3.10.2 NURSERY

The appropriate bed size for *O. sanctum* is 15×4×9 ft. Before sowing the seeds, the seed bed soil should be prepared thoroughly using FYM@ 10 kg bed<sup>-1</sup>. Maximum 200–300 g seeds are sufficient for 1 hec of land. For minute size of seeds, they could be mixed with fine sand during sowing at a depth of 2 cm followed by spreading of a thin layer of mixture of FYM and soil over the seeds and irrigation with a sprinkler hose. The seeds usually germinate within 8–12 days and become ready for transplanting within 1 month and 2 weeks at 4–5 leaf stage. Around 15–20 days before of transplanting, spraying using urea solution@ 2% on nursery plants yields healthy seedlings for transplanting (Smitha et al., 2014).

On the other hand, the way of raising nursery seedlings of *Ocimum basilicum* is more or less same. Here, seed bed should be prepared using well rotten FYM and leaf mold at the rate of 1 kg/sq m followed by thorough mixing with the soil. Seeds at the rate 10–15 g/bed after mixing with sand or wood ashes are usually sown in raised seed beds of 10–15 cm height. Seedlings of 10–15 cm height (usually attain after 6 weeks) are considered to be ready for transplanting. Appropriate bed sizes are 1 m × 4 m, with irrigation channels. Line sowing at a distance of 6 cm or broadcasting method could be adopted. After sowing a thin mulching with fine soil or farm yard manure is mandatory followed by immediate watering. Water requirement of the juvenile seedlings should be investigated on regular basis. In plains of North India (NI) the seeds are sown in the nursery during April-May or August-September and in hills sowing is done in April. Regular weeding to keep the seed bed weed free is a vital operation. A spray of 2% urea solution is also useful for *O. basilicum* to get healthy and vigorous seedlings (Smitha et al., 2014).

For *O. basilicum* April–May/Aug–Sep is the appropriate time for raising nursery seedling. Seed rate is 125 g/ha, sown in 1 × 4 m in lines of 6 cm apart.

In the month of May-June in plowed and manured (40:40:40 N.P.K Kg/ha) land 6–8 weeks old seedlings are transplanted at a spacing of 40–60 cm. in this species also watering should be given below on the requirement. All essential intercultural operations could be carried out in July–August. For this species 1<sup>st</sup> harvesting could be done in Sep (after 90 days of planting) and the subsequent harvesting could be made from November onwards.

### **3.10.3 LAND PREPARATION**

The land should be plowed up to a fine tilth. As a basal dose 15 t ha<sup>-1</sup> of FYM along with recommended fertilizers (well-mixed) are preferred.

### **3.10.4 TRANSPLANTING**

Under Lucknow, New Delhi and Indore condition 45 days old seedlings at 4–5 leaf stage is transplanted at a spacing of 40×40, 40×50, and 50×30 cm, respectively to enhance the herbage and oil yielding. During transplantation 2 irrigation regimes should be maintained. First irrigation should be provided immediately after transplanting to minimize the hardening shock and second irrigation after 15–20 days usually aids to establish seedlings properly. At this stage gap filling and replacement of the weak, unhealthy plants should be executed so that uniform plant stand could be achieved (Smitha et al., 2014).

In most of the temperate climatic region 6–8 weeks old basil seedlings are usually transplanted in main field, about 15 days after the last frost date. Conventionally spacing of approximately 30 cm (12 inches) and 45 cm (18 inches) between rows are followed (Majkowska-Gadomska et al., 2017).

### **3.10.5 CROP NUTRITION**

Soil nutrients are vital for *Tulsi* since its mainly grown for its vegetative growth. Nutritional requirements are species-specific. For *Ocimum sanctum* well-decomposed FYM@10 t/ha should be applied prior to planting. For this species use of city waste compost, composted human excreta and any sort of fresh manures should be restricted as these may yield adverse impact on plant growth. Application of N<sub>2</sub>@ 120 kg, P<sub>2</sub>O<sub>5</sub> and K<sub>2</sub>O@ 60 kg ha<sup>-1</sup> has found optimum. As basal dose, full amount of P<sub>2</sub>O<sub>5</sub> and K<sub>2</sub>O and ½ dose

of  $N_2$  could be applied first while the remaining dose of  $N_2$  could again splitted in 2 doses, usually applied after 1<sup>st</sup> and 2<sup>nd</sup> cuttings. Micronutrients especially cobalt (Co) and manganese (Mn)@ 50 and 100 ppm, respectively could enhance the oil yielding capacity. According to Smitha et al. (2014), use of  $N_2$ @ 120 kg,  $P_2O_5$  and  $K_2O$ @ 105 kg ha<sup>-1</sup> each is effective for alkaline and saline soils at Lucknow condition. About 40:40:40 kg ha<sup>-1</sup> of N,  $P_2O_5$  and  $K_2O$  is good for economic yield while 120:100:100 kg ha<sup>-1</sup> significantly enhance the oil yield. Basil is resistant to Cu and Zn while vulnerable to Co and Ni. Several qualitative and quantitative parameters such as leaf greenness index, fresh and dry herbage yield, dry matter and total sugars content are ecotype based. Their habitats have huge influence on their fresh and dry herbage yields (Majkowska-Gadomska et al., 2015, 2017).

All plant parts of basil contain some nutritional and mineral content. Leaves of *Ocimum sanctum* contain 2.38% of protein, 3.20% of citrol, 68.05% of carbohydrate, 11.45% of fiber, 6.20% of moisture and 10.42% of ash content while 41204.1 and 800 ppm of Calcium and Zinc. Seeds of *Ocimum sanctum* don't contain any other nutritional content. Whereas whole plant contains Ca mineral (403 ppm) only. Stem of this species contain 9.25%, 2.75%, 2.20%, 18.30%, 88.30% and 20.15% of its dry weight of protein, lipid, carbohydrate, fiber, moisture, and ash (Narendhirakanna et al., 2005; Koche et al., 2011; Kashiz & Ullah, 2013). Except these nutrition compositions, seeds, leaves, stems, and whole plant also contain meagre amount of Fe (range 2.32–2,830 ppm) and Cu (range 0.01–4,785 ppm) (Shafqatullah et al., 2013; Barua et al., 2015; Vidhani et al., 2016; Wisdom et al., 2016; Koche et al., 2011). From whole plant extraction 4.8 ppm of Vit B1, 2.4 ppm of Vit B12, 2.7 ppm of Niacin, 450 ppm of Vit C had been found (Shafqatullah et al., 2013; Dachkove & Dhale, 2012; Gowrishankar et al., 2010). Dachkove & Dhale (2012) recorded total calorific value of 262.84 Kcal/100 g from *Ocimum sanctum* extraction.

### 3.10.6 IRRIGATION

Frequency of watering depends on moisture level of soil and season. During summer 3 times irrigation month<sup>-1</sup> is needed while during monsoon it could be totally withdrawn and during other season it could be given based on the need. About 12–15 irrigations are mandatory annually. Mulching can conserve soil moisture. However, irrigation must be withdrawn before harvesting. Before watering, testing of irrigational water could be done to prevent any sort of contamination (Smitha et al., 2014).

### 3.11 INTER-CULTURAL OPERATION

Weeds are one of the threats which compete for key resources (nutrients and light) with the target crop. Manual weeding is recommended for basil field generally. After 30 days of planting, 1<sup>st</sup> weeding should be done followed by 2<sup>nd</sup> weeding after 1 month of the first weeding. After two successive weeding operations, it could be discontinued since plants bushy plants could suppress the weed growth effectively. At an interval of 60 days, 1 hoeing and earthing up operation should be carried out. Mulching could also effectively inhibit growth of weeds. Application of chemical herbicides for weeds eradication is less encouraged unless there is a dire need. Excessive weeding may cause drying up of soil may be harmful for growing of Tulsi (Smitha et al., 2014).

Green and purple basil cultivation underneath kiwi plantations (as inter-crop) may be implemented since total yield with fresh and dry herb yield had been proved to be increased (Yaldez et al., 2015).

### 3.12 PINCHING

Pinching operation (at growing apex) facilitates the emergence of a greater number of shoots. Regular pinching helps to promote its vegetative growth and prevent seed production.

### 3.13 DISEASE AND PEST MANAGEMENT

#### 3.13.1 PESTS

Sacred Tulsi (*Ocimum sanctum*) is usually infested by the following insects, pests, and diseases:

1. **Leaf Rollers:** They adhere on the ventral surface of leaf and effectively made backward rolling of them and finally form web (Garibaldi et al., 2004).
2. **Tulsi Lace Wing (*Cochlochila bullita*):** Due to gregarious feeding of juvenile leaves by both adult and nymphs leaves get curled and lastly dried. In fact, after completion of feeding the target pest leaves their excreta and make the produce unusable (Ceuppens et al., 2015).
  - **Management:** Azadirachtin at the concentration of 10,000 ppm can be sprayed at the dose rate of 5 ml l<sup>-1</sup> to control this insect (Smitha et al., 2014).

3. **Leaf Rollers:** Here, the larvae cause folding of leaves along the midrib followed by webbing. They basically adhered at the ventral surface of leaf. Finally, infected leaves shed off (Smitha et al., 2014).
4. **Bug (*Monantha globulifera*):** It causes leaf curling.
  - **Management:** Azadirachtin at the concentration of 10,000 ppm can be sprayed at the dose rate of 5 ml l<sup>-1</sup> to reduce this insect menace (Smitha et al., 2014).

### 3.13.2 DISEASES

Basils are highly susceptible to powdery mildew (*Oidium* sp.), seedling blight (*Rhizoctonia solani*), and root-rot (*Rhizoctonia bataticola*) (Roberts et al., 2009) are very common. Powdery mildew could be restricted using sulfur in wettable form (4 g lit<sup>-1</sup> of water) spray and the advanced phyto-sanitary measures can restrict the latter two diseases. In fact, soil drenching using 1% Bavistin could be also effective (Smitha et al., 2014).

1. **Leaf Spot (*Corynespora cassicola*):** Minute water-soaked spots appear on the laminae first. Finally, those spots turn brown.
2. **Scab (*Elsinoearxii*):** Puckered leaves and distorted tender twigs are most common symptoms of this disease.
3. **Blight (*Alternaria* sp.):** Initially few chlorotic patches are formed on laminae but as the infection progresses those chlorotic patches start to enlarge and turn into purple color followed by total shedding (Roberts et al., 2009). The proneness of older leaves to this disease are more.
  - **Management:** Foliar spray of 1% Bordeaux mixture at fortnight interval can control this.
4. **Wilt (*Fusarium oxysporum*):** Owing to this disease the entire plant starts to show wilting symptoms, may occur at any phase of plant growth. Specially, during monsoon basil plants become more vulnerable to this disease.
  - **Management:** Dipping of seedlings in tefalon or agallol solution during planting time can restrict this disease (Smitha et al., 2014; Ceuppens et al., 2015).

### 3.14 HARVESTING AND YIELD

Basil leaves could be harvested any time by pinching method from apical portion of stem to facilitate emergence of new branching but definitely after attaining the height of 15–20 cm (6–8 inches):

1. **Harvesting of *Ocimum sanctum*:** To avoid any type of contamination during harvesting proper care should be adopted as a protective measure. Harvesting could be made during flowering season to get utmost quantum and quality of essential oil yield. First harvesting should be done only after 90–95 DAP (Days after Planting) after that at an interval of every 65–75 days. Bright sunny days are most suitable for carrying out harvesting operation to get optimum quantity and supreme quality oil. During monsoon season harvesting is little bit problematic. It should harvest 15–20 cm above the soil surface (Smitha et al., 2014).
2. **Harvesting of *Ocimum basilicum*:** Harvesting time and condition of the produce – these two are the key factors determine the quality of essential oil. Generally, dry and sunny days are more appropriate than the damp, rainy days for harvesting of basil. Manual harvesting using sickles is made 90–95 days after planting (DAP). Flowering season and hues of lower leaves (from green to yellow) are usually considered as basil's harvesting indices. Generally, 2 grades of essential oils are made, i.e., 'Herb' and 'Floral' oil while the former type is produced using 'whole plant' and latter one using apical portions of inflorescences. Definitely, floral types are more superior in quality with finer notes. To get supreme quality of 'Floral' oil, morning harvesting of fully bloomed flowers at an interval of 65–75 days are needed. Around 3–4 floral harvests during peak blooming season are sufficient for this purpose. For 'Herb' oil production, whole herb leaving the stump on the ground (for its regeneration purpose) is harvested followed by wilting to reduce moisture and bulkiness of the produce under field conditions (Smitha et al., 2014).
3. **Expected Yield of *Ocimum sanctum*:** Types, season, and its origin – these three factors affect the oil-yielding capacity of basil. Generally, 2–3 times harvesting per annum can yield 5 tons of fresh herbage. This quantity of produce can yield 10–23 kg ha<sup>-1</sup> of 'Herb' oil and 0.1–0.23% of basil essential oil (Smitha et al., 2014; Majkowska-Gadomska et al., 2017).



- 4. Expected yield of *Ocimum basilicum*:** Usually, this species yields 13–141 tons of whole herb and 3–4 tons of flowers ha<sup>-1</sup>. To get the yield of 30–35 kg ha<sup>-1</sup> of ‘floral’ oil and 18–22 kg ha<sup>-1</sup> of ‘herb’ oil 4–5 harvesting year<sup>-1</sup> is important. Around 0.4% and 0.10–0.25% of essential oils could be obtained from its inflorescences and whole plant, respectively (Smitha et al., 2014; Majkowska-Gadomska et al., 2015). ‘Cinnamon’ and Greek ‘Minette’ are two popular Poland varieties hugely acclaimed for their commercial fresh herbage yield (Taie et al., 2010).

‘Ohre,’ ‘Lettuce leaf,’ ‘Purple opal,’ ‘Dark green,’ ‘Mammolo Genovese,’ ‘Manes,’ and ‘Red Rubin’ – these are the common high yielding varieties of *Ocimum basilicum* used for essential oil extraction. Extraction of essential oils ranges from 7.4–8.2 ml/kg of a dry weight in ‘Ohre,’ 3.9–4.9 ml/kg dry weight in ‘Lettuce leaf,’ 4.1–5.0 ml/kg dry weight in ‘Purple opal,’ 4.5–5.9 ml/kg dry weight in ‘Dark green,’ 5.3–8.1 ml/kg dry weight in ‘Mammolo Genovese,’ 17.3–17.7 ml/kg dry weight in ‘Manes’ and 3.7–4 ml/kg dry weight in Red Rubin cultivars (Gupta et al., 2014; Pimenta et al., 2014).

### 3.15 PROCESSING TECHNIQUES

- 1. Processing of *Ocimum sanctum*:** Wilting of the harvested produce takes place within 4–5 hours significantly reduce the bulkiness and become easy to carry for further processing but prolonged delay could affect the quality and quantity of oils although up to 6–8 hours after harvesting any deterioration in oil’s quality and quantity has not been reported. Steam distillation is more superior to hydro distillation and hydro cum steam distillation. Clean, rust-free and odor-free distillation unit should be used. After decanning and distillation procedures, the oil is treated with anhydrous sodium sulfate/sodium chloride@ 20 g/liter to eliminate moisture. Then transferred in a sealed amber colored stainless steel made storing container. Containers should be placed in cool and dry place (Smitha et al., 2014).
- 2. Processing of *Ocimum basilicum*:** *Post-harvest* processing determines the quality of products especially produced from aromatic plant materials. Hydro-distillation or steam distillation process is

followed for oil extraction of sweet basil using juvenile inflorescences or whole plants. The latter procedure requires less time as compared to the former one for recovery of optimum quality essential oil. Hydro-distillation involves direct heating method, which consequently produces inferior-quality oil (Smitha et al., 2014). Hydro-distillation is suitable for smaller plantations while steam distillation used commercially. The decanning, filtering, and other storing-related procedures of distilled oil are the same as *O. sanctum*.

### 3.16 CHARACTERIZATION OF PHYTOCONSTITUENTS

*Tulsi* is the most well-known name in Ayurveda and as folk medicine too due to have wide range of nutrients and other biologically active compounds which make its chemical composition quite complex. The variations in chemical compositions may be for diversity between strains or for varying cultivation pattern, harvesting time, mode of processing and storage infrastructures which are yet to be understood.

*O. tenuiflorum* has essential oils basically reserved in green leaves responsible for the distinct aroma. Volatile oil of leaf chiefly comprises phenols, terpenes, and aldehydes. Besides its essential or fixed oils, plant also contains alkaloids, glycosides, tannins, and saponins. Significant amount of carotene and ascorbic acid contents are also available. Chemical properties of basil leaves depend on numerous worldwide studies, and hence geographic and edaphic factors influence different chemical ingredients. Variations in aroma of essential oil extracts from different varieties of *O. basilicum* is nothing but the differences in their chemical composition. In various parts of the world, basil cultivars are present in large diversity, indicating a diverse range of chemical composition. The essential oil of basil usually contains  $\alpha$ -terpineol, eucalyptol, eugenol, methyl eugenol, linalool,  $\beta$ -element, germacrene D,  $\alpha$ -bergamotene,  $\alpha$ -guanine, cubenol,  $\tau$ -cadinol, camphor, bornylacetate,  $\alpha$ -caryophyllene,  $\beta$ -caryophyllene, elixen,  $\beta$ -cadinene,  $\alpha$ -copaene,  $\alpha$ -bisabolol,  $\beta$ -farnesene, epibicyclosesquiphelandrene,  $\tau$ -muralol,  $\delta$ -gurjunene and  $\delta$ -cadinene (Hanif et al., 2011). Diversified categories of fatty acids are found in 3 *Ocimum* species are presented in Table 3.1. Cardiac glycosides, tannins, and saponins are found in aqueous extract of *O. basilicum* plants proven by phytochemical analysis.

**TABLE 3.1** Summary of Micro-Propagation Protocols of Basils

Species	Explant	Medium	Plant Growth Regulator(s)	Growth Response	References
<i>O. basilicum</i>	Apical, lateral or adventitious buds.	MS, Linsmaier	0–10 $\mu\text{M}$ BA + 5–50 $\mu\text{M}$ NAA	Bud induction	Kanebo Ltd. (1992)
<i>O. sanctum</i>		B5, Nitsch-Nitsch white	0–0.1 Mm Kin + 0–10 $\mu\text{M}$ 2,4-D	Bud multiplication	
<i>O. citriodorum</i>			0–0.1 $\mu\text{M}$ Zea + 0–0.1 $\mu\text{M}$ IAA	Plant regeneration	
<i>O. killimandscharicum</i>					
<i>O. basilicum</i>	Adventitious buds	MS	0.5 $\text{mgL}^{-1}$ BA + 0.3 $\text{mgL}^{-1}$ GA <sub>3</sub>	Shoot induction	Pattnaik et al. (1995)
<i>O. sanctum</i>			1.0 $\text{mgL}^{-1}$ BA + 0.5 $\text{mgL}^{-1}$ GA <sub>3</sub>	Shoot induction	
<i>O. americanum</i>			0.25 $\text{mgL}^{-1}$ BA + 0.5 $\text{mgL}^{-1}$ GA <sub>3</sub>	Shoot induction	
<i>O. gratissimum</i>			0.5 $\text{mgL}^{-1}$ BA + 0.3 $\text{mgL}^{-1}$ GA <sub>3</sub>	Shoot induction	
<i>O. basilicum</i>	Adventitious buds	MS ½ MS	1.0 $\text{mgL}^{-1}$ IBA/NAA	Root induction	Sahoo et al. (1997)
			1 $\text{mgL}^{-1}$ BA + 0.4 $\text{mgL}^{-1}$ GA <sub>3</sub>	Shoot induction	
			0.25 $\text{mgL}^{-1}$ BA	Shoot proliferation	
<i>O. sanctum</i>	Young inflorescence	MS	1 $\text{mgL}^{-1}$ IBA	<i>in vitro</i> flowering	Singh & Sehgal (1990)
			1 $\text{mgL}^{-1}$ BA + 0.05 $\text{mgL}^{-1}$ IAA	Shoot induction + proliferation	
				Root induction	
<i>O. basilicum</i>	Leaves, intermodal stem segments	MS, ½ MS	1.5 $\text{mgL}^{-1}$ BA	Shoot induction + proliferation	Makri & Kintzios (1999)
			0.5 $\text{mgL}^{-1}$ BA + 1 $\text{mgL}^{-1}$ IBA	Shoot induction + proliferation	
				Root induction	

Synergistic interactions between several active phytochemicals cause the variations and enrichment in nourishment and phyto-chemical properties of the entire herb. As a result, the inherent botanical and biochemical complexity, posing constraints to make the replica of all isolated compounds of basil extracts to get the utmost wholesome effects. Volatile oils extracted from leaf (Kelm et al., 2000) possesses urosolic acid (Shishodia et al., 2003), euginal (known as eugenol), eugenol (1-hydroxy-2-methoxy-4-allylbenzene), carvacrol (5-isopropyl-2-methylphenol), 2,3,4,5,6,6a,7,8,8a,10,11,12,13,14b-tetradecahydro-1H-picene-4a-carboxylic acid, limatrol, linalool (3,7-dimethylocta-1,6-dien-3-ol), caryophyllene (4,11,11-trimethyl-8-methylene-bicycloundec-4-ene), methyl carvicol (known as Estragol: 1-allyl-4-methoxybenzene) whereas fatty acids and sitosterol found to be present in seed extracted volatile oil. Additionally, meagre quantity of sugar (xylose and polysaccharides) and anthocyanin are found to exist in seed mucilage and green leaves, respectively but trace of any stimulants (especially caffeine) are unavailable. As a 'general vitalizer' *Tulsi* is quite popular since it boosts up physical endurance and energy level. Saponins, flavonoids, triterpenoids, and tannins (Jaggi et al., 2003) are also found available in stem and leaf extracts of 'holy basil.' Range of phenolic active constituents like Rosmarinic acid ((2R)-2-[[[(2E)-3-(3,4-Dihydroxyphenyl)-1-oxo-2-propenyl]]-oxy]-3-(3,4-dihydroxyphenyl), apigenin (5,7'-dihydroxy-2-[4-hydroxyphenyl]-4H-1-benzopyran-4-one), Propanoic acid, Isothymonin, and isothymusin (6,7-dimethoxy-5,8,4'-trihydroxyflavone) and Cirsimaritin (5,4'-dihydroxy-6,7-dimethoxyflavone) possess antioxidant and anti-inflammatory activities. Orientin (8-C-beta-glucopyranosyl-3,4,5,7-tetrahydroxyflav-2-en-3-one) and Vicenin (6-C-beta-D-xylopyranosyl-8-C-beta-D-glucopyranosyl apigenin) – these two water-soluble flavonoids aid to protect the radiation-induced chromosomal damage in human blood lymphocytes (Umadevi et al., 2000).

In food and fragrance industry essential oil (EOs) derived from basil using steam distillation method are very useful as flavoring agent. In fact, for oral usages also it could be also employed. Easy to crossbreed nature of this herb has created significant uncertainty in botanical nomenclature while innumerable number of varieties, cultivars, and chemotypes at interspecific level without possessing any prominent visual differences make its taxonomy complicated manifold times. Chemotaxonomy is a useful tool for the characterization of economically viable *Ocimum* species as variations in composition of volatile oil constituents are well-proven. Using principal component analysis (PCA) on the aromatic volatile oil, *Ocimum* could be

classified into five groups like: (i) citral-spathulenol group; (ii) linalool-rich group; (iii) methylchavicol-rich group; (iv) linalool-methylchavicol group; and (v) methyl(*E*)-cinnamate-rich group. Clustering according to the morphological features doesn't corroborate the grouping made based on volatile oil constituents (Vieira & Simon, 2005).

### 3.17 VALUE ADDITIONS

Wide range of herbs *viz.* garlic, juniper, oregano, mustard, pepper, rosemary, marjoram, paprika, parsley, sage, thyme, etc., after blending with basil leaves could be employed in variety of cuisines (example: stuffings, soups, stews, rice, fish, vegetables, chicken, meats, etc.). In cheese, oil, liquors, drinks, teas, and vinegars too it could be principal component. For example, delicious dessert item namely 'Purple Basil Vinegar' could be prepared using leaves of purple basil (due to striking hue). Additionally, cinnamon and lemon basil (based on personal taste) to make it more palatable may be added. Large or minute-sized uncooked leaves (may be chopped or minced or torn form) may be supplemented in variety of vegetarian dished and other cuisines (salads, rice, and pasta). After only completion of cooking, basil leaves should be added to capture its maximum flavor. Both fresh and desiccated form of basil could be used but definitely the latter form contains low flavors. Chilling process of basil preservation is more effective in terms of retention of flavor as compared to desiccated form but definitely the dried form possesses more shelf life than the chilled preserved one. Its diverse and plenteous uses could be proven by its presence in range of cuisines (like in meat, fish, sauce, stew, herbal tea, mocktail, liquors, and salad recipes). Basil, garlic, cheese, oil, and nuts are the ingredients of a universally popular dish known as 'Pesto' which is commercially prepared by domestic and international entrepreneurs. Addition of tomatoes could enhance its palate. Vinegar and oil could be medium for preserving garden-fresh basil leaves while frozen form is also available (Lupton et al., 2012).

Medicinal and aromatic plants are rich in phyto-constituents which have antimicrobial and antioxidative activities responsible for quenching the reactive oxygen species (ROS) and stop the spreading of pathogenic infections by certain physiological processes for wide range of flora and fauna (Burt, 2004). The chemical composition validates the synergistic form of various chemical compounds, among which most common are ethers, ketones, aldehydes, phenols, esters, terpenes, and alcohols. Their distinct aroma, taste,

and biological activity secured their position in the international market (Arumugan et al., 2016; Swamy & Sinniah, 2016; Stanojevic et al., 2017).

Very finite information about the origin of essential oil of basil is available. It is thought that Republic of Srpska was the actual place of origin (Grayer et al., 2002). Its chemotype is evaluated depending on some constituents (e.g., linalool, methyl cinnamate, methyl eugenol and eugenol) (Grayer et al., 2002). Different categories based on essential oil's chemical structure, composition, and aroma principally for diversity in geographic origin and existence of dominant components are accessible in world market. Principally two separate pathways, i.e., phenylpropanoids [methyl chavicol (estragole), eugenol, methyl eugenol and methyl cinnamate] via shikimic acid and Terpenoids [linalool and geraniol] via mevalonic acid pathway are there to synthesize basil essential oil. Common basil essential oil chemotypes are Egyptian, Bulgarian, European/French, Javanese, and Reunion while European type has the supreme quality for its premium fragrant note for the presence of linalool and methyl chavicol fetch high price in the market. Other components like 1,8-cineole, eugenol, geraniol, germacrene D, ocimene,  $\gamma$ -terpinenemay, sabinene,  $\beta$ -caryophyllene, thujone, and  $\alpha$ -terpineol are found in significant concentration. Terpenoids like camphor,  $\alpha$ -pinene, germacrene, linalool, ocimene, sesquiterpenes, and  $\alpha$ -terpineol are of huge biological as well as ecological significance influence the efficacy of antimicrobial activity. Sesquiterpenes are very strong antifungal secondary metabolites, among which germacrene is noticeable one. Linalool,  $\alpha$ -terpineol, monoterpenes, 1,8-cineol, etc., have significant antibacterial efficacy (Stanojevic et al., 2017).

Quality of basil essential oil is determined by its composition while its usefulness as a fresh material at pharmaceutical, food and chemical industries depend on its phytochemical storage (Jelacic et al., 2011). The inefficacy of synthetic drugs to manipulate the action of certain pathogens and also prohibitions on using antimicrobial synthetic drugs for their acute toxicity, potential environmental hazard and carcinogenic effect motivating researchers to search for novel molecules with antimicrobial character. In this backdrop, essential oils for controlling and suppressing the spoiling action of resistant pathogenic microorganisms could be a viable alternative (Mulyaningsih et al., 2010). Significant anti-inflammatory, antioxidant, anti-stress (Volpato et al., 2002; Nguefack et al., 2004; Divya et al., 2009; Nebedum et al., 2009; Sánchez et al., 2010; Hemalatha et al., 2011; Venuprasad & Khanum, 2012) and antimicrobial activity (Tagnolini et al., 2006; Jelacic et al., 1996; Sokovic & Griensven, 2006; Sokovic et al., 2010) of basil essential oil is

well established. Consequently, fruitful incorporation in medicine, especially in aromatherapy, and to treat cardiovascular diseases, diabetes, Alzheimer's disease, and cancer (Ali et al., 2015; Stanojevic et al., 2017) is found.

### **3.18 BIO-PROSPECTION**

#### **3.18.1 PHARMACOLOGICAL PROPERTIES**

##### *3.18.1.1 ANALGESIC AND ANTI-INFLAMMATORY ACTIVITY*

The analgesic activity of methanolic extract of *O. basilicum*'s leaves has been investigated by Choudhury et al. (2010) on animal model (Swiss Albino mice). The concentration of 200 mg kg<sup>-1</sup> has almost the identical efficacy of aspirin. About 50, 100, and 200 mg kg<sup>-1</sup> of basil (*O. basilicum*) essential oil could lower down the abdominal contraction of mice during acetic acid-induced writhing test (Choudhury et al., 2010). In fact, basil essential oil @ 50 mg/body weight could too enhance the latency of pain as proved in hot plate test. Prostaglandins, prostacyclins, and opioid receptor interactions are engaged with the biosynthesis of pain mediators. The peripheral and antinociceptive impacts of its essential oils had been found to associate with the inhibition process of pain intermediaries (Venancio et al., 2010).

To heal severe inflammation triggered by turpentine oil, *O. basilicum*' tincture (1:10) proved effective as compare with diclofenac in Wistar male rats. Its tincture significantly activates the circulating phagocytes and monocyte percentage and along with that reduce total leukocyte count but rendered mild inhibitory effect on NO synthesis (Benedec et al., 2007).

##### *3.18.1.2 ANTIDIABETIC*

Lowered level of glucose, glycosylated hemoglobin and urea along with higher level of glycogen, hemoglobin, and protein had been found after using ethanolic extracts of *O. sanctum* in case of streptozotocin-induced diabetic rats (Narendhirakannan et al., 2006). Its potency to elevate the insulin and peptide level had also been proved. The antidiabetic action of its leaf extracts by stimulating insulin secretion had been reported by Hannan et al. (2006). Grovel et al. (2005) had also endorsed the above findings after testing in animal model. However, *O. sanctum* L. extract has no impact on hyperinsulinemia. Extracts of *O. sanctum* decrease the

cortisol and glucose concentration in blood serum expressed antiperoxidative effect. Ghosap et al. (2004) narrated the same glucose-lowering mechanism of extracts of *O. sanctum*. It can also regulate corticosteroid-induced diabetic mellitus. Phosphofructokinase (PFK), glucokinase (GK) and hexokinase (HK) – these are three major enzymes control carbohydrate metabolism. *O. sanctum* has significant impact on aforementioned enzymes to balance glycogen content of insulin-dependent muscles (skeletal muscle and liver) and tissues (kidneys and brain) (Vats et al., 2004; Chattopadhyay, 1993). Dusted leaves of *O. sanctum* also cause effective reduction in fasting blood sugar, urogenic acid, and total amino acid levels (Rai et al., 1997).

#### 3.18.1.3 ANTI-HYPERLIPIDEMIC AND ANTI-ULCERATIVE ACTIVITY

Total cholesterol, LDL-cholesterol, and triglycerides level could be significantly reduced after the treatment using aqueous extract of *O. basilicum*. Suanarunsawat et al. (2016) reconfirmed the efficacy of basil extracts for lowering lipid level. They found that its aqueous extract reduced the triton induced lipid level in rat model but without enhancing HDL-cholesterol level. They concluded that Fenofibrate treatments for anti-hyperlipidemic effect could be compensated by *O. basilicum* extract treatment. Its extract possesses significant antioxidant property (Suanarunsawat et al., 2016). According to Suanarunsawat et al. (2009) ethanolic and aqueous extracts derived from whole plant of *O. basilicum* could cease the spreading of gastric and duodenal ulceration induced by cysteamine hydrochloride as proved in animal models. Patil et al. (2011) revealed that the lipoxigenase inhibiting, histamine antagonistic and anti-secretory impacts against alcohol, aspirin, indomethacin, serotonin, reserpine, and stress-induced ulceration were possible due to the antiulcer activity of *O. basilicum*'s fixed oil. Furthermore, the methanolic and aqueous extract derived from aerial parts of *O. basilicum* could minimize the aspirin led gastric ulcer issue while reduced quantity of acid and pepsin could also increase the gastric mucosal strength (Suanarunsawat et al., 2016).

#### 3.18.1.4 CARDIO-PROTECTIVE AND STIMULANT ACTIVITY

Better cardiac functions and histopathological improvements in myocardial infraction (MI) (usually induced by isoproterenol) could be achieved using ethanolic extracts prepared from aerial parts of basil. Range of doses markedly



reduce ST segment elevation (an interval between ventricular depolarization and ventricular repolarization) induced by isoproterenol. Suppression of left ventricular contractility, better myocardial necrosis and fibrosis and increase of left ventricular end-diastolic pressure could be achieved by its extracts. Basil extracts have cardioprotective effects by protecting the myocardium against isoproterenol-induced infarction due to its antioxidant activities further reported by Fathiazad et al. (2012) where the reduced elevation of malondialdehyde levels in myocardium and serum duo had found.

The cardiotonic and  $\beta$ -adrenergic effects are based on reduction and rise in membrane  $Mg^{+2}$  ATPase and  $Ca^{+2}$  and  $Na^{+}/K^{+}$  ATPase, respectively while aqueous and alcoholic extracts duo could produce both effects had been proved in frog model while reduced chronotropic and enhanced ionotropic actions could be obtained by using alcoholic extracts prepared from aerial parts of basil (Muralidharan & Dhananjayan, 2004).

#### 3.18.1.5 SEDATIVE, HYPNOTIC, AND ANTICONVULSANT ACTIVITY

Sedative, hypnotic, anticonvulsant, and local anesthetic actions of essential oil derived from aerial part of *O. basilicum* are dose-dependent since higher doses could cause motor impairment while convulsions and percent of colonic seizures could also be enhanced proved in mice model by Juliana et al. (2009). The dose rates of  $1.27 \text{ ml kg}^{-1}$ ,  $0.43 \text{ ml kg}^{-1}$ , and  $0.61 \text{ ml kg}^{-1}$  (considered as  $ED_{50}$  values of basil oil) could also work against strychnine, picrotoxin, and pentylene tetrazole induced convulsions. According to Juliana et al. (2009), pentobarbitone induced sleeping span in mice could be enhanced by using basil essential oil@  $>0.2 \text{ ml kg}^{-1}$ . *O. basilicum* oil doesn't have any local anesthetic effect proved by Ismail (2006) in frog model. Essential oils never affect the strychnine induced convulsion. Anticonvulsant properties of basil essential oil make interaction with GABAergic receptors and act as CNS depressant (Juliana et al., 2009). Satoh & Sugawara (2003) found through IBVA-EEG measurement and multi-channel skin thermometer tests that to minimize the arousal response inhalation administration of basil's essential oils are quite effective.

#### 3.18.1.6 STROKE INHIBITORY AND MEMORY RETENTION MECHANISMS

Antioxidant efficacy of flavonoids, tannins, and terpenoids for augmented retention and retrieved memory capacity is especially well-known; these

potencies are magnified in hydroalcoholic extract of green basil. On the other hand, the influential role of ethyl acetate extract prepared from leaves of *O. basilicum* on ischemia and reperfusion-induced motor dysfunctions and cerebral damage was noteworthy (Sarahroodi et al., 2012). Same authors (Sarahroodi et al., 2012) also corroborated the memory-preserving potential of basil extracts (effective dose rate is 400 mg kg<sup>-1</sup>) in mice models. Bora et al. (2011) concluded based on the output of their studies that pre-treatment using basil extracts could decrease lipid peroxidation rate and cerebral infarct size, attenuate motor coordination and impaired short-term memory, and restore glutathione content (GSH). Conclusively, significantly prevent the chances of stroke.

### 3.18.1.7 ANTIMICROBIAL ACTIVITY

Ranges of test using basil essential oil showed the antibacterial activity against multi-resistant ESKAPE pathogens (especially *Escherichia coli* strain [ATCC 25922]) and also on wide ranges of *E. coli* strains (60 clinical strains approximately) and its efficacy on extended spectrum of  $\beta$ -lactamase positive bacteria was noticeable but it is ineffective in nosocomial infections (Benedec et al., 2007). Methanolic, ethanolic, and aqueous extracts made from stem bark of *O. basilicum* exhibited the antimicrobial activities. The potential of ethanolic and methanolic extracts of basil as bacteriocides (Minimal Bactericidal Concentration [MBC] ranges between 2 and 20 mg ml<sup>-1</sup> and 2–12.5 mg ml<sup>-1</sup> for ethanol and methanol extracts, respectively) and inhibitor of bacterial growth (0.5–6.25 mg ml<sup>-1</sup> and 5–10 mg ml<sup>-1</sup> for ethanol and methanol extracts, respectively) are notable. The potential action of methanol, ethanol, and water extracts against *Candida albicans* again validate their antimicrobial potential (inhibition zones usually range from 8–20, 5–12, and 0–8 mm, respectively) (Khosro et al., 2012). According to Khosro et al. (2012) to get wide spectrum *in vitro* bacteriocidal impact hexane extract could be considered as best. Essential oils (EOs) derived from leaves and stems of *O. basilicum* have the potential to restrict the growth of food-borne pathogenic bacteria. The bacteriocidal effect against *Bacillus megaterium*, *B. cereus*, *B. subtilis*, *Escherichia coli*, *Staphylococcus dysenteriae*, *S. aureus*, *Listeria monocytogenes*, *Vibrio parahaemolyticus*, *Shigella boydii*, *V. mimicus* and *Salmonella typhi* of *O. basilicum* had been confirmed by Hossain et al. (2010). Hossain et al. (2008) reported the efficacy of 'Linalool' (a terpene alcohol, produce naturally in basil plants)

against wide range of bacterial strains (like *S. aureus*, *Fusarium solani*, *Botryo diploidiatheobromae*, *E. coli*, *B. subtilis*, *Pasteurella mulicida*, *Aspergillus niger*, *Rhizopus solani* and *Mucor mucedo*). Furthermore, Opalchenova & Obreshkova (2003) had also corroborated the inhibition potential of *O. basilicum*'s essential oil against *Staphylococcus*, *Pseudomonas*, and *Enterococcus*. Minimum Inhibitory Concentrations (MICs) of basil leaf-derived EOs range from 36–18 µg/mL for *B. cereus* while 18 µg/mL for *S. aureus* (Amir et al., 2011). Gel formulations of EOs and the synergistic effect of acetic acid and keratolytic medication is highly effective to solve acne problems. Acetic acid combination yielded better consequences as improvements up to 75% had been achieved. It's due to their combined antiseptic and keratolytic action (Matiz et al., 2012).

### 3.18.1.8 ANTIMYCOBACTERIAL AND ANTIVIRAL ACTIVITY

Crude methanolic extract of basil at 6.25 µg/ml found effective to inhibit up to 49% *Mycobacterium tuberculosis H37Rv-induced* tuberculosis (Siddiqui et al., 2012). It corroborates its use in ethnomedicine to heal tuberculosis. Several purified chemical components (linalool, apigenin, ursolic acid) and aqueous and ethanolic extracts of *O. basilicum* showed wide range of virucidal actions. Out of these compounds, urosolic acid found optimum against DNA viruses (like Enterovirus 71 and Herpes virus-1) and RNA viruses (like coxsackie virus B1 and adenoviruses-8) while linalool and apigenin demonstrated utmost efficacy against AVD-II and ADV-3, HSV-2, Hepatitis B antigen and Hepatitis B surface antigen prohibition, respectively (Chiang et al., 2005). Another study had been made by Erler et al. (2005) where they found the anti-HIV-1 activity of aqueous extract (ED<sub>50</sub>@16 µg/ml) of *O. basilicum*.

### 3.18.1.9 LARVICIDAL AND ANTIPARASITIC ACTIVITY

Methanolic extract of *O. basilicum* could potentially be utilized as bio-pesticide. The potency with 85% mortality of malarial vector ascertains the efficacy of *O. basilicum* extracts (Arthi & Murugan, 2010). Essential oils extracted from the dried foliage of species could successfully be used as mosquito repellent (especially against the adult females of *Culex pipiens*) (Sienkiewicz et al., 2013). Varied lethal dose rates (LC<sub>90</sub>@ 23.44, 21.17, and 18.56 ppm and LC<sub>50</sub>@ 14.01, 11.97, and 9.75 ppm) of basil's EOs could

be effective enough to kill *Culex tritaeniorhynchus*, *Aedes albopictus* and *Anopheles subpictus* at larvae stage (3<sup>rd</sup> stage) (Govindarajan et al., 2013).

The antiparasitic activity of *O. basilicum*'s essential oils could be demonstrated by interaction between *Giardia lamblia* parasite and peritoneal mouse macrophage. Basic components of basil essential oil, Linalool (300 µg/ml) exhibited anti-giardial activity being inhibited cysteine proteases (De Almeida et al., 2007). Hayam & Abeer (2003) found that the growth of *Trichomonas vaginalis* trophozoites was inhibited due to damage in their membrane system and also for extensive vacuolization of the cytoplasm caused by basil essential oil. They inferred 30, 20, and 10 µg/ml as minimal lethal concentrations of *O. basilicum* oil after 24, 48, and 96 hrs. of incubation (Hayam & Abeer, 2003).

#### 3.18.1.10 CHEMOPREVENTATIVE AND CHEMOMODULATORY ACTIVITY

Enhanced 0,6-methylguanine-DNA methyl transferase (MGMT) activity is an advantageous chemoprevention strategy, in fact modifications in MGMT activity by ethanolic and aqueous extract of *O. basilicum* results in its expression in human cancer cell lines and peripheral blood lymphocytes. It also increased glutathione S-transferase-pi (GSTP1) expression at lesser degree than MGMT (Niture et al., 2006). The noteworthy impact on hepatic system of hydroalcoholic extract of fresh leaves of *O. basilicum* had been investigated on 8–9 weeks old Swiss albino mice model. Basil leaf extract has anticarcinogenic potential being inhibited carcinogen-induced tumor at peri-initiation level. It ceases Phase I enzyme activity and augments essentially Phase II enzyme activity related with detoxification of xenobiotics. Significant reduction in lipid peroxidation activity and lactate dehydrogenase formation finally boosts up the antioxidant level (Dasgupta et al., 2004).

#### 3.18.1.11 ANTICANCER ACTIVITY

Kathirvel & Ravi (2012) found the anticancerous potential of EOs extracted from *O. basilicum* on human murine leukemia cell lines (P<sub>388</sub>) and mouth epidermal carcinoma (KB). Ranges of 0.019–4.962 mg ml<sup>-1</sup> are most effective concentrations for aforesaid purposes. The same authors later found that the IC<sub>50</sub> values of 90.5–96.3 µg ml<sup>-1</sup> of basil EOs could be the most effective to treat against HeLa (Human Cervical Cancer Cell Line), HEP-2 (Human Laryngeal Epithelial Carcinoma Cell Line) and NIH 3T3 mouse embryonic

fibroblasts. Fundamental principle of MTT (Methyl Thiazol Tetrazolium) assay is to determine the cellular metabolic activity as a marker of cell proliferation, viability, and cytotoxicity. According to Manosroi et al. (2006)  $IC_{50}$  value of  $0.0362 \text{ mg ml}^{-1}$  showed the utmost anti-proliferative potential (usually measured by MTT assay) for P<sub>388</sub> cell lines.

#### 3.18.1.12 CYTOPROTECTIVE AND IMMUNOMODULATORY ACTIVITY

Basil contains phenolic compounds including rosmarinic acid [RA] (Tada et al., 2006) a major polyphenolic compound found in Lamiaceae and Boraginaceae families. It is an ester of caffeic acid and 3,4-dihydroxyphenyl lactic acid. Its cytoprotective effects against aflatoxin, mycotoxin, and ochratoxin influence cytotoxicity and carcinogenicity in hepatoma-derived cell line (HepG2) of human. The potency of RA to prevent the programmed cell death, apoptosis by reducing DNA fragmentation, protein synthesis and inhibiting caspase-3 activation (Renzulli et al., 2004). The aqueous and ethanolic extracts prepared using basil leaves could enhance the immunomodulatory response by a marked increase in total antibody count. A significant increase observed in primary and secondary hemagglutination (HA) measurement in cyclophosphamide treated group as compared to control due to basil extract's capacity to inhibit white blood cell activity. In sheep red blood cells (SRBCs) (at the dose rate of  $400 \text{ mg kg}^{-1} \text{ day}^{-1}$ ) sensitized mice, basil treatments could enhance the antigen concentration by DTH (Delayed Type Hypersensitivity) reaction. The flavonoid content present in basil extracts aids to uplift the ratio of neutrophils adhesion to nylon fibers and also augment the phagocytic action to achieve immunostimulant effect (Neelam & Nilofer, 2010).

#### 3.18.1.13 ANTIOXIDANT ACTIVITY

*In vitro* antioxidant activities of *O. basilicum*'s ethanolic, carbon tetrachloride, and chloroform extracts could be effectively measured by DPPH, hydroxyl, and nitric oxide radical scavenging assays. Among the aforementioned extracts, ethanolic extracts are most significant for having highest antioxidant activity (Khosro et al., 2012). Around 3% concentrated extract of basil evinced noteworthy impacts on skin wrinkles, scaliness, roughness, its moisture volume, smoothness, and prominent enhancement in energy for its antioxidant activity. Hence, the obtained output could revalidate the anti-aging impacts using topical application procedures of basil's extract-made

formulations (Rahul & Akhtar, 2011). Significant nitric oxide and superoxide radical scavenging potential proved the antioxidant potential of ethanolic extracts derived using basil (*O. basilicum*) leaves (Meera et al., 2009). Niture et al. (2006) found the increased level of O<sub>6</sub>-methylguanine-DNA methyl transferase and glutathione S-transferase-P1 liable to antioxidant effects of aqueous and ethanolic extracts from *O. basilicum* in human cells. Furthermore, the antioxidant enzyme response could be elevated using the appropriate doses (200 and 400 mg/kg body weight) of hydroalcoholic extract of fresh basil leaves being increased the hepatic glutathione reductase, superoxide dismutase and catalase activities. According to Dasgupta et al. (2004), suppression, and production of lipid peroxidation activity and lactate dehydrogenase, respectively could be taken place due to enhanced antioxidant level. EOs derived from aerial parts of basil effectively inhibit linoleic acid oxidation and bleaching of  $\beta$ -carotene in linoleic acid system due to their antioxidant potential (measured by DPPH assay) (Hussain et al., 2008). According to Yesilogu & Sit (2012) antioxidant activities may be for significant lipid peroxidation inhibition, metal chelating activities and radical scavenging properties of water, acetone, and ethanolic extracts obtained principally from leaves and flowers of basil. Ethyl acetate n-butanol and aqueous extracts of basil leaves showed prominent free radical scavenging activity also exerted the potential antioxidant activity may be for phenolics and flavonoids contents present in the extract (Kaurinovic et al., 2011).

#### 3.18.1.14 EFFECT ON FERTILITY AND TESTICULAR TOXICITY

The cadmium induced testicular toxicity could be healed by major progression on immunohistochemical, histological, and morphometrical changes using aqueous *O. basilicum* extracts proved to contain antioxidant properties (Sakar & Nooh, 2013). Hydro-alcoholic extracts prepared from the leaves of basil species had been proved to act as anti-implantation, anti-ovulatory, and abortifacient agent in adult female cyclic Wistar rats' model. The screened doses to have this effect were 364 mg/kg and 624 mg kg<sup>-1</sup> of body weight (Bilal et al., 2013). A prolonged diestrus phase and changes in estrus cycle using basil extract could affect the normal ovulation which endorses its female contraceptive potential while decreased ovarian weight and notable increase in ovarian tissue cholesterol level in treated rats revalidate its anti-implantation and abortifacient effect (Bilal et al., 2013) while presence of large corpora lutea in ovarian parenchyma was also evident based on histological report.

### 3.18.1.15 ACUTE AND SUB-CHRONIC TOXICITY OF BASIL

The use of hydro-alcoholic extracts of *O. basilicum* is how far safe to use had been studied by Rakesh et al. (2012). For their study, they used Wister rat model. They reported no adverse effect on blood serum parameters when the dose rate is at sub-chronic level but LD<sub>50</sub> dose (>5 mg kg<sup>-1</sup> of body weight) of the same could be toxic. Reduced hematocrit, lower number of platelets and red blood cells (RBC) count, etc., was evident by hematological outputs.

### 3.18.1.16 WOUND HEALING ACTIVITY

Conventional wound healing especially, dexamethasone-depressed healing was studied by Udupa et al. (2006) using ethanolic extract derived from *O. sanctum*'s leaf resulted significant development of wound breaking strength, rapid wound epithelialization and wound contraction with enhanced granulation tissue (dry and wet) weight and its breaking strength. Shetty et al. (2006) also evaluated the efficacy of aqueous extract of *O. sanctum* L. in all wound healing models (i.e., wound breaking strength in the incision wound model and percent wound concentration in excision wound model).

## 3.19 PROCESSING TECHNIQUES IN PHARMACEUTICALS

Basil, the most widespread tropical and ethnomedicinally significant herbal plant. It has varied ranges of uses. Despite the use of whole plant, leaves, and inflorescences are the imperative useful parts of basil. Fresh basil leaves are mostly used in culinary purpose as they are the cheapest and richest source of vitamin K, manganese (Mn), iron (Fe), vitamin A, ascorbic acid, omega-3-fatty acids, Mg, and Ca. Their involvement is not merely restricted in food industry and as folk medicine but its essential oil extracts could be use in several formulations to treat cuts, wounds, and skin infections. Apart from its fresh use, various processed forms counting whole desiccated plant parts, frozen or grounded leaves, etc., are also popularly used. Owing to its usefulness, whole plants or chopped leaves are preserved in frozen manner or in alternative traditional manner (i.e., preserve in salt or in form of oil concentrates) with the motive of preserving for extended periods beyond the fresh shelf life (Meyers, 2003).

Dehydration is another viable way to have this multifaceted herb perpetually. Inverted hanging method is the most traditional method of drying of

cleaned bundles of *Tulsi* whereas press drying method could be too adopted for effective drying of leaves to prevent oxidation and discoloration. Commercially forced air dehydration is generally used. To minimize the occurrence of dark spots on leaf surface caused for prolonged exposure to open air basil leaves should be dried immediately after harvest. Optimum drying temperature is below 40°C could cease the evaporational loss of volatile compounds (Putievsky & Galambosi, 1999). Protection from high temperature and humidity could enhance the longevity of dried basil (Meyers, 2003).

According to Srivastava (1980); and Putievsky & Galambosi (1999), extracted basil's essential oils are of two types of generally *viz.* i. Herbal oil and ii. Superior-quality floral oil. The former one produced from leaves (0.1–0.25%) while the latter one from flowers (0.4%). The quantity of yielded oil is more from the whole plants as compared to flowers only. About 12–13 kg ha<sup>-1</sup> of floral oil could be obtained during peak flowering season while 18–22 kg ha<sup>-1</sup> from fresh yield of whole plants in India circumstances (Srivastava, 1980). In Israel, to yield 120–140 kg ha<sup>-1</sup> of essential oil, 75 tons ha<sup>-1</sup> yield of whole plant at 50% flowering condition is needed (Putievsky & Galambosi, 1999). Conventional distillation process is used for basil too takes around an hour while fresh leaf materials are used (Wijesekera, 1986; Denny, 1995).

Healing of many diseases and disorders could be made by basil herb, a well-known repository of medicinal compounds. Wide range of therapeutic activities of different phytomolecules are yet to be explored. Vast research works on chemical extracts and EO components of *Ocimum* sp. have secured many patents. To evaluate the full metabolic efficiency of basil, Rastogi et al. (2015) worked on whole nuclear and chloroplastic genome sequencing. Among numerous medicinal herbs, full genome sequencing followed by analyzing was first done in basil. Based on the revealed data, two libraries (both long and short reads) were of Illumina HiSeq2000, other two were of 454 GS FLX and Mate-pair library of SOLiD 5500XL, respectively. This data was obtained from the combined sequence reads of 4 libraries of 3 NGS platforms (Rastogi et al., 2015). This result elicited the smallest size of the saturated draft genome (386 Mb) along with a plastid genome (1,42,245 bp) among entire Lamiaceae members. Employing paired-end and mate-pair sequence libraries, Upadhyay et al. (2015) investigated the draft genome of *O. tenuiflorum* L (Krishna Tulsi). Consequently, they found the draft genome of 374 Mb size. About 22,776 and 9,059 scaffolds and super-scaffolds, respectively were formed from 107,785 contigs. Path analysis proved the abundance of phenylpropanoids in *O. sanctum*. With aid of SSR molecular markers 136 number of homologous proteins were identified



from 5 plant genomes. According to Shasany (2016), the comparative study (using phylogenetic tree) on available genes and chemical constituents proved *Salvia miltiorrhiza* as closest neighbor of *O. sanctum*. These elicit further possibility of discovering novel bio-active molecules which will be helpful to understand the medicinal properties of available secondary metabolites synthesized *in-situ*. The therapeutic potential of basil is for the biosynthesis of phenylpropanoids and terpenoids. Information generated through molecular study may aid to identify many explicit metabolites' from other related species and their successive DNA annotation could furnish new insight about the therapeutical values as well as functions also.

Eugenol is the main component of Tree basil (*O. gratissimum*) and white basil oil. Its low concentration will deteriorate the qualitative value of the extracted oil. Lal et al. (2003) found low eugenol yield in rainy season basil crop. In this backdrop, a new cultivar of *O. sanctum* namely 'CIM-AYU' had been developed at CSIR-IMAP, Lucknow. It contains high percentage of eugenol (83% of oil) and EOs along with significant herbage yield. Even during monsoon also, the amount of EO production remains high (approximately >47% in comparison with other existing strains [<5%]) in this cultivar (Lal et al., 2003). 'CIM-Angna' (dark purple colored variety, rich in eugenol [40%],  $\beta$ -elemene [14%], germacrene-D [16%] and  $\beta$ -caryphyllene [9%]) and 'CIM-Kanchan' (contains methy eugenol [70%],  $\beta$ -elemene [7.6%] and  $\beta$ -caryphyllene [15%]) – these are two varieties of *O. sanctum* released by CSIR-CIMAP (Lal et al., 2008; Kothari et al., 2004). They are more advanced strains as compared to other existing control varieties.

## **3.20 POTENTIAL BIOMOLECULES AND THERAPEUTIC APPLICATIONS**

### **3.20.1 PRE-CLINICAL STUDIES (ANIMAL MODELS)**

Among several pre-clinical studies on therapeutic potential of *O. sanctum*, verified on *in vitro* animal models, made during last two decades, only few noteworthy outputs have been depicted here.

### **3.20.2 METABOLIC DISORDERS**

In an investigation range of doses (300 mg/d to 6 g/d) using varied form of 'Tulsi' leaves (whole plant, leaf juice, leaf dust and ethanolic and aqueous extract) were applied on animal model by Singletary (2018) to observe the impact of infusions on various blood quality parameters. Significant improvement in

lipid profiles, low BP (Blood Pressure) in case of obese and diabetic patient and noticeable blood glucose reduction in both fasting and postprandial had been found by the author. Collaterally, in obese participants, low Body Mass Index (BMI) and hemoglobin A1C (HbA1c) were found. Improvement in lipid profiles of several participants were proved through randomized, double-blind, and placebo-controlled trial without having any adverse events.

Viseshakul et al. (1985) made another study using seeds of different *Ocimum cannum* (or *O. americanum* L.), known as 'Hairy Basil' to determine its efficacy on diabetic patient. In his experiment, insulin-dependent ( $n = 2$ ) and non-insulin dependent ( $n = 14$ ) Thai diabetic patients were involved. They were treated being consumed 30 grams of dried seeds after meals in divided doses for 1 month. After 1 month treatment blood sugar concentration was determined comparing the baseline values. To reduce PP glucose levels and increase glucose tolerance, consumption of basil seeds @  $24 \text{ g day}^{-1}$  is most effective, in fact, it provides ample dietary fiber also (Viseshakul et al., 1985). This dose was also found optimum for both non-insulin-dependent and insulin-dependent diabetic patients.

*O. cannum* seeds have some influential impact on obesity related issues. Leelahagul et al. (1992) experimented on 5 overweight and obese participants. They were administered for their regular total calories intake (TCI) (i.e., 30% fat, 50% carbohydrate and 20% protein of total TCI). One month after, 4 g/day of swollen basil seeds were provided for 3 months to consume. As a consequence, some effects they found on metabolic parameters and body composition. They found 2.3 and 2.4% decrease in overall body weight and BMI level as compare with baseline values but any changes in sugar and serum lipid levels as well as in body fat. Any undesirable impact on renal, hematological, and electrolyte parameters had not been detected.

Consumption of high-fiber seeds of *O. basilicum* at the rate of 10 g/day for 3 months could be an effective measure for nonalcoholic fatty liver patients. Akbarian et al. (2016) endorsed this view through their experiments where noticeable outcomes on anthropometric measures was obtained by parallel, randomized, and single-blind trial of patients ( $n = 18$ ). This effect is very much dose dependent otherwise any significant impact on percent body fat, lean body mass and BMI will be not found on the given subjects.

### **3.20.3 NEUROCOGNITION**

To evaluate Tulsi's neurocognition effect four clinical trials were made by Jamshidi & Cohen (2017) out of which two were randomized, double-blind,

placebo-controlled designs. The ethanolic extracts using whole plant or leaves of 'Tulsi' at the doses varied from 300 mg/d to 6 g/d were provided while alike consequences with meagre changes like reduced level of stress, anxiety, sexual problems, depression, and improved working memory and cognitive attention was found without any adverse events. The positive correlation between inhalation of sweet basil's (*O. basilicum*) essential oil and mental activities motivated researchers to investigate the actual scenario. Satoh & Sugawara (2003) made an inhalation trial experiment using basil's essential oil-loaded inhalers to assess its impact on brain. Based on the changes in sensory perception and mental work parameters the mature volunteers were evaluated and observed an increase in fingertip skin temperature and in electrical impulses (A waves) of brain which revalidate the preceding statement. This outcome demonstrates the capacity of fragrance to trigger neurophysiological stimuli which consequently elevate the alert state.

#### **3.20.4 IMMUNOMODULATION AND INFLAMMATION**

Increase in natural killer and T-helper cells count boost the immune system, which in turn help to combat against viral infections. Singletary (2018) used varied dosages (300 mg/d to 10 g/d) of ethanolic or aqueous extracts of Tulsi leaves to verify its impact as immunomodulators. The durations were 1 year and 4 weeks. Relief from asthmatic symptoms without any antagonistic effect were obtained after a randomized, double-blind, placebo-controlled trial of this experiment. The author suggested the higher circulating levels of selected cytokines and interferons may have some influential impact.

#### **3.20.5 ORAL HEALTH AND HEALING**

Phytoconstituents of *O. basilicum*'s extracts are highly useful for wide range of oral ailments. An assessment was made by Patel & Venkatakrishna-Bhatt (1988) on efficiency of basil extracts to improve oral cavity health. Around 50 participants from Brazil and India were employed in this investigation. They were treated by basil's extracts @ 250 mg day<sup>-1</sup> for 21 days duration. Before and after the treatment, 'Plaque Index' (PI) barring 3<sup>rd</sup> molars was evaluated by them. The consequence elicited notable reduction (12%) in PI along with some improvements in purulent discharges and gingival bleeding after the specified duration of treatment. Overall, reduction in total number of oral bacteria was evident.

To determine the efficacy of 0.2% Listerine, Chlorhexidine, and 4% of *Tulsi* extract to reduce the salivary *Streptococcus* mutants' levels as mouth rinses were made by Agarwal & Nagesh (2011) in India. The experiment was conducted based on randomized, crossover, Latin square Y statistical design where 45 school children were the participants. The effectiveness of all three rinses were found at par. Mean reductions in salivary *S* mutants counting of 53%, 45%, and 43% for chlorhexidine, Listerine, and Tulsi, respectively, were found along with a negative score of bitter taste of Tulsi rinse may be for its higher 4% concentration. Gupta et al. (2014) also conducted a triple-blind, randomized, parallel-design, and controlled trial employing 4% ethanolic extract of holy basil (*O. sanctum*) (prepared from dried, powdered leaves), 0.12% chlorhexidine, and saline as control to evaluate the potency of these mouth rinses in decreasing plaque and gingival inflammation. Here also, the elicited outcomes proved the same effect both treatments.

Water extract of holy basil could also diminish the plaque regrowth as compared to water (control treatment) proved by a 4-day treatment trial (a single-blind, randomized, parallel-design study) among 30 mature volunteers (Hosmane et al., 2014). The clinical efficacy was similar with 0.2% chlorhexidine. The usefulness of *O. gratissimum* extracts were also noticeable to inhibit the *de novo* dental plaque development and gingival inflammation. Its impact was better than 0.12% chlorhexidine digluconate (CLX) solution (Pereira et al., 2014). Basil extract's rinses (3 times per day) could also remove the existing plaque proved in brushed teeth and rinsed teeth. Reduction of PI by 43 and 64% while gingival bleeding by 63 and 77% were found by Pereira et al. (2014) after rinsing using basil extracts and CLX. This result proves almost the equal efficacy of both. Regular rinsing by basil (10% v/v EO) and CLX (0.12%) could compensate daily brushing. According to Mohammad et al. (2014), to abbreviate the duration of jaw immobilization operation (up to 32%), intake of 2.5 g of *Tulsi* (*O. sanctum*) leaves' (4 times per day) alcoholic extract are very useful. Based on the radiological evidence and outputs of bite force tensile strength, authors endorsed the healing potential of Tulsi extracts as compared to placebo control group.

### **3.20.6 SKIN HEALTH**

The importance of basil extract made facial skin cream for skin smoothness, moisture, and wrinkle prevalence is less popular. Balambal et al. (1985),

used basil-based formulations for acne treatments of some Indians. The treatment for 'Control' group consisted of oral tetracycline (500 mg, twice a day) and facial sulfur lotion (twice a day) while for 'Treatment' group fresh leaf juice of *O. basilicum* were used (it was applied on acne lesions followed by leaving overnight). After continuous use of both formulations for 30 days, better results (comedones, papules, pustules, and cysts) were obtained in treated group. Hence, the authors corroborated the usage of basil leaf extract for acne treatment. Around 3% concentrated ethanol extract of basil leaves and blooms, for a single-blind study (Rasul & Akhtar, 2011), were used to prepare a facial skin cream. As control they used base formulation without basil. Both the creams were applied on subjects for 3 months duration on separate cheeks and to evaluate the efficacy different biophysical measurements had been conducted. Basil based formulation lowered down the roughness and wrinkling nature of skin with increased moisture content. Several authors (Orafidiya et al., 2002; Martin & Ernst, 2003), further assessed the potency of 16 strains of *O. gratissimum*'s extracts to heal acne problems. The subjects were the students of Nigeria. The best-standardized dose of *O. gratissimum*'s essential oil was blended with base formulation for preparing test concoctions and instructed for topical application on face (2 times per day) for 1 month. Comparatively better consequences were obtained in terms of lesser lesion counts in case of basil oil treated participants than a reference drug product (10% benzoyl peroxide lotion) in reducing the number of papules and pustules. Minimal adverse impacts were noted with some higher degree of doses producing skin irritation.

### **3.20.7 SAFETY**

In general, adverse impacts of Tulsi in human trials are least which facilitates its incorporation in Ayurvedic medicine as it's a natural drug. It doesn't possess any oral toxicity too (Kumar et al., 2010). Toxicological experiments in animals of the essential oil and of alcoholic extracts demonstrated negative toxic impact on oral administration in fact at maximum doses too (Singh & Majumder, 1994; Raina et al., 2015) but excessive consumption may lead to adverse effect due to the high contents of estragole (Barfi et al., 2016). The reproductive behavior influenced by dietary Tulsi had been also tested in animal models (Kantak & Gogate, 1992; Sethi et al., 2010) although the relevance of the doses examined to human intakes is not known (Singletary, 2018).

### **3.20.8 PATENTS**

Intellectual Property Rights (IPRs) are now more pronounced in fact, after the foundation of World Trade Organization (WTO) in 1995. IPR basically deals with trades and commerce (both international and domestic) and policy-making issues. It protects biological resources of a country (counting medicinal and aromatic plants) and also indigenous invention. Some medicinal flora-based traditional and advanced invention on medicines and cosmetics are now under IPR systems (James, 2016). The available granted patents of 'Tulsi' has been enlisted in Table 3.5.

### **3.21 CONCLUSION**

The significance of Ayurveda in human life are acknowledged in modern era also. But the resurrection of interest to pay more attention on plant derived benefits for health issues is quite prominent now-a-days. The uses of Tulsi as traditional and natural medicine have attracted its investments both nationally and internationally. Tulsi contains diversified phytochemical constituents which contribute its significant nutritional and pharmacological characteristics. The natural benefits obtained from basil are basically due to the synergistic interactions made among active biological substances. Hence, replicases containing individual compounds were found impossible. For the complex chemical properties of its phytochemicals, it seems tough to utilize its benefits in wholesome. As a natural vitalizer, Tulsi has gained fame without any other adjuvants. Despite startling achievements in modern medical sciences, their inefficacy for effective restriction on innumerable diseases (may be due to fast lifestyle or personal stresses, etc.) is plaguing our society. In this backdrop, the use of herbal medicines would be a comprehensive approach to healing array of ailments. Basil is one of the major medicinal plants utilized as folk medicine endorsed by WHO (World Health Organization). Inclusion of its advanced formulations in modern medical therapies can efficiently address several health issues. Therapeutic properties of basil are known since time immemorial but its potential to treat several stress-related degenerative endemic diseases are enough noteworthy. Conclusively, advance research investigations could further enhance Basil's health-promoting qualities (Tables 3.2–3.5).

**TABLE 3.2** Chemical Composition of Basil Essential Oil**Chemical Composition of Essential Oils of Ocimum basilicum L. (Marwat et al., 2011).**

<b>Compound</b>	<b>m.f.</b>	<b>m.w.</b>	<b>Part</b>
<b>Monoterpenes</b>			
<b>Monoterpene hydrocarbons</b>			
$\alpha$ -Phellandrene	$C_{10}H_{16}$	136	Aerial parts
$\alpha$ -Pinene	$C_{10}H_{16}$	136	Aerial parts
$\alpha$ -Terpinene	$C_{10}H_{16}$	136	Inflorescence, leaves
$\alpha$ -Terpinolene	$C_{10}H_{16}$	136	Leaves
$\alpha$ -Myrcene	$C_{10}H_{16}$	136	Leaves
$\beta$ -Phellandrene	$C_{10}H_{16}$	136	Aerial parts
$\beta$ -Pinene	$C_{10}H_{16}$	136	Inflor., leaves
Camphene	$C_{10}H_{16}$	136	Inflor., leaves
<i>cis</i> - $\beta$ -Ocimene.0	$C_{10}H_{16}$	136	Aerial parts
<i>cis</i> -Ocimene	$C_{10}H_{16}$	136	Leaves
$\delta$ -3-Carene	$C_{10}H_{16}$	136	Leaves
$\beta$ -Ocimene	$C_{10}H_{16}$	136	Leaves
(E)- $\beta$ -Ocimene	$C_{10}H_{16}$	136	Aerial parts
Limonene	$C_{10}H_{16}$	136	Aerial parts
Myrcene	$C_{10}H_{16}$	136	Aerial parts
<i>p</i> -Cymene	$C_{10}H_{14}$	134	Aerial parts
Sabinene	$C_{10}H_{16}$	136	Aerial parts
Terpinolene	$C_{10}H_{16}$	136	Inflor., leaves
Thujene	$C_{10}H_{16}$	136	Leaves
$\gamma$ -Terpinene	$C_{10}H_{16}$	136	Aerial parts
<b>Oxygenated monoterpene</b>			
$\alpha$ -Citral	$C_{10}H_{16}O$	152	Leaves
$\alpha$ -Fenchyl acetate	$C_{12}H_{20}O_2$	196	Aerial parts
$\alpha$ -Terpineol	$C_{10}H_{18}O$	154	Aerial parts
Borneol	$C_{10}H_{18}O$	154	Aerial parts
Bornyl acetate	$C_{12}H_{20}O_2$	196	Aerial parts
Camphor	$C_{10}H_{16}O$	152	Aerial parts
Carvacrol	$C_{10}H_{14}O$	150	Aerial parts
Carvone	$C_{10}H_{14}O$	150	Aerial parts
1,8-Cineole	$C_{10}H_{18}O$	154	Aerial parts
<i>cis</i> -Linalool oxide	$C_{10}H_{18}O_2$	170	Aerial parts
<i>cis</i> -Rose oxide	$C_{10}H_{18}O$	154	Aerial parts
Citronellol	$C_{10}H_{20}O$	156	Aerial parts

TABLE 3.2 (Continued)

Compound	m.f.	m.w.	Part
Endo-Fenchol	$C_{10}H_{18}O$	154	Aerial parts
Estragol	$C_{10}H_{12}O_2$	174	Aerial parts
Eugenol	$C_{10}H_{12}O_2$	174	Leaves
Exo-2-hydroxycineole-acetate	$C_{12}H_{20}O_3$	212	Leaves
Fenchone	$C_{10}H_{16}O$	152	Aerial parts
Geranial	$C_{10}H_{16}O$	152	Aerial parts
Geraniol	$C_{10}H_{18}O$	154	Aerial parts
Geranyl acetate	$C_{12}H_{20}O_2$	196	Aerial parts
Hotrienol	$C_{10}H_{16}O$	152	Leaves
<i>iso</i> -Neomenthol	$C_{10}H_{20}O$	156	Aerial parts
<i>iso</i> -Pinocamphone	$C_{10}H_{16}O$	152	Aerial parts
<i>trans</i> -Pinocamphone	$C_{10}H_{16}O$	152	Aerial parts
L-Camphor	$C_{10}H_{16}O$	152	Leaves
L-Carvone	$C_{10}H_{14}O$	150	Leaves
Lavandulol	$C_{10}H_{18}O$	154	Leaves
Linalool	$C_{10}H_{18}O$	154	Aerial parts
Linalool <i>cis</i> -furanoid	–	–	Leaves
Linalool <i>trans</i> -furenoid	–	–	Leaves
Linalyl acetate	$C_{12}H_{20}O_2$	196	Leaves
Menthol	$C_{10}H_{20}O$	156	Aerial parts
Menthone	$C_{10}H_{18}O$	154	Aerial parts
Methyl chavicol	$C_{10}H_{12}O$	148	Aerial parts
Myrtenal	$C_{10}H_{12}O$	148	Leaves
Myrtenol	$C_{10}H_{16}O$	152	Aerial parts
Neral	$C_{10}H_{14}O$	152	Aerial parts
Nerol	$C_{10}H_{18}O$	154	Leaves
Ocimene oxide	$C_{10}H_{16}O$	152	Leaves
Pinocarvone	$C_{10}H_{14}O$	150	Aerial parts
P-menth-1,8-dien-4-ol	$C_{10}H_{16}O$	152	Leaves
Piperitone	$C_{10}H_{16}O$	152	Aerial parts
Pulegone	$C_{10}H_{12}O_2$	174	Aerial parts
Terpinen-4-ol	$C_{10}H_{18}O$	154	Aerial parts
Terpinylformate	$C_{11}H_{18}O_2$	182	Leaves
<i>trans</i> -Linalool oxide	$C_{10}H_{18}O_2$	170	Aerial parts
<i>trans</i> -Myroxide	$C_{10}H_{16}O$	152	Aerial parts
<i>trans</i> -Sabinene hydrate	$C_{10}H_{18}O$	154	Leaves



TABLE 3.2 (Continued)

Compound	m.f.	m.w.	Part
<i>trans-p</i> -Menth-2-en-1-ol	C <sub>10</sub> H <sub>18</sub> O	154	Leaves
Thymol	C <sub>10</sub> H <sub>16</sub> O	152	Leaves
Verbenone	C <sub>10</sub> H <sub>14</sub> O	150	Leaves
( <i>Z</i> )-Sabinene hydrate	C <sub>10</sub> H <sub>18</sub> O	154	Inflor., leaves
Sesquimonoterpenes			
Sesquiterpene hydrocarbons			
Cyclohexane, 2,4-diisopropenyl-1-methyl-1-vinyl	C <sub>15</sub> H <sub>24</sub>	204	Aerial parts
1,4,7-Cycloundecatriene, 1,5,9,9-tetramethyl	C <sub>15</sub> H <sub>24</sub>	204	Aerial parts
$\alpha$ -Acoradiene	C <sub>15</sub> H <sub>24</sub>	204	Aerial parts
$\alpha$ -Amorphene	C <sub>15</sub> H <sub>24</sub>	204	Aerial parts
	C <sub>15</sub> H <sub>24</sub>	204	
$\alpha$ -Bulnesene			Essential oil
	C <sub>15</sub> H <sub>24</sub>	204	
$\alpha$ -Cadinene			Inflor., leaves
$\alpha$ -Cedrene	C <sub>15</sub> H <sub>24</sub>	204	Inflor., leaves
	C <sub>15</sub> H <sub>24</sub>	204	
$\alpha$ -Copaene			Inflor., leaves
	C <sub>15</sub> H <sub>24</sub>	204	
$\alpha$ -Cubebene			Aerial parts
$\alpha$ -Guaiene	C <sub>15</sub> H <sub>24</sub>	204	Aerial parts
	C <sub>15</sub> H <sub>24</sub>	204	
$\alpha$ -Gurjunene			Aerial parts
$\gamma$ -Gurjunene	C <sub>15</sub> H <sub>24</sub>	204	Aerial parts
$\alpha$ -7-epi-Selinene	C <sub>15</sub> H <sub>24</sub>	204	Aerial parts
	C <sub>15</sub> H <sub>24</sub>	204	
$\alpha$ -Humulene			Aerial parts
Aromadendrene	C <sub>15</sub> H <sub>24</sub>	204	Inflor., leaves
	C <sub>15</sub> H <sub>24</sub>	204	
$\alpha$ -( <i>Z</i> )-Bergamotene	C <sub>15</sub> H <sub>24</sub>	204	Inflor., leaves
$\alpha$ -Zingiberene	C <sub>15</sub> H <sub>24</sub>	204	Inflor., leaves
$\beta$ -Acoradiene			Aerial parts
$\beta$ -Bourbonene	C <sub>15</sub> H <sub>24</sub>	204	Aerial parts
$\beta$ -Caryophyllene	C <sub>15</sub> H <sub>24</sub>	204	Aerial parts
	C <sub>15</sub> H <sub>24</sub>	204	
$\beta$ -Cedrene	C <sub>15</sub> H <sub>24</sub>	204	Aerial parts

TABLE 3.2 (Continued)

Compound	m.f.	m.w.	Part
$\beta$ -Copaene			Aerial parts
$\beta$ -Cubebene	$C_{15}H_{24}$	204	Aerial parts
	$C_{15}H_{24}$	204	
$\beta$ -Elemene	$C_{15}H_{24}$	204	Leaves
$\beta$ -Guaiene			Aerial parts
$\beta$ -Ocimene	$C_{15}H_{24}$	204	Aerial parts
	$C_{15}H_{24}$	204	
$\beta$ -Selinene	$C_{15}H_{24}$	204	Aerial parts
Bicycloelemene			Aerial parts
Bicyclogermacrene	$C_{15}H_{24}$	204	Aerial parts
Cadinene	$C_{15}H_{24}$	204	Aerial parts
Cadina-3,5-diene	$C_{15}H_{24}$	204	Aerial parts
<i>cis</i> -Calamene	$C_{15}H_{24}$	204	Aerial parts
<i>cis</i> -Muurola-4(14),5-diene	$C_{15}H_{24}$	204	Aerial parts
	$C_{15}H_{24}$	204	
(E)- $\beta$ -Farnesene			Inflor., leaves
(E)-Caryophyllene	$C_{15}H_{24}$	204	Inflor., leaves
1-Epibicyclosesqui-phellandrene	$C_{14}H_{22}O$	204	Roots, seeds
Epsilon-muurolene	$C_{15}H_{24}$	204	Leaves
Dehydroaromadendrene	$C_{15}H_{22}$	204	Leaves
Germacrene-A	$C_{15}H_{24}$	204	Aerial parts
	$C_{15}H_{24}$	204	
Germacrene-B			Leaves
Germacrene-D	$C_{15}H_{24}$	204	Aerial parts
Guaia-1(10),11-diene	$C_{15}H_{24}$	204	Aerial parts
Iso-caryophyllene	$C_{15}H_{24}$	204	Aerial parts
Isoledene	$C_{15}H_{24}$	204	Aerial parts
Longifolene	$C_{15}H_{24}$	204	Aerial parts
	$C_{15}H_{24}$	204	
$\delta$ -Selinene			Leaves
St $\alpha$ -ylangene	$C_{15}H_{24}$	204	Leaves
	$C_{15}H_{24}$	204	
<i>trans</i> - $\alpha$ -Bisabolene			Aerial parts
<i>trans</i> - $\alpha$ -Bergamotene	$C_{15}H_{24}$	204	Aerial parts
	$C_{15}H_2$	204	
<i>trans</i> - $\beta$ -Farnesene			Inflor., leaves

TABLE 3.2 (Continued)

Compound	m.f.	m.w.	Part
<i>trans</i> - $\beta$ -Ocimene	C <sub>15</sub> H <sub>24</sub>	204	Aerial parts
<i>trans</i> -Caryophyllene	C <sub>15</sub> H <sub>24</sub>	204	Aerial parts
Valencene	C <sub>15</sub> H <sub>24</sub>	204	Leaves
$\gamma$ -Cadinene	C <sub>15</sub> H <sub>24</sub>	204	Inflor., leaves
$\gamma$ -Terpin	C <sub>15</sub> H <sub>24</sub>	204	Aerial parts
	C <sub>15</sub> H <sub>24</sub>	204	
$\delta$ -Cadinene	C <sub>15</sub> H <sub>24</sub>	204	Inflor., leaves
$\gamma$ -Muurolene			Aerial parts
(Z)-Calamenene	C <sub>15</sub> H <sub>24</sub>	204	Inflor., leaves
Oxygenated sesquiterpenes			
$\alpha$ -Cadinol	C <sub>15</sub> H <sub>26</sub> O	222	Aerial parts
$\alpha$ -Humulene oxide	C <sub>15</sub> H <sub>24</sub> O	220	Leaves
Alloaromadendrene	C <sub>15</sub> H <sub>24</sub> O	220	Inflor., leaves
	C <sub>15</sub> H <sub>26</sub> O	222	
$\beta$ -Basibolol	C <sub>15</sub> H <sub>26</sub> O	222	Inflor., leaves
$\beta$ -Basibolol isomer			Leaves
$\beta$ -Eudesmol	C <sub>15</sub> H <sub>26</sub> O	222	Aerial parts
	C <sub>15</sub> H <sub>26</sub> O	222	
Cubenol			Oil
Caryophyllene oxide	C <sub>15</sub> H <sub>24</sub> O	220	Aerial parts
	C <sub>15</sub> H <sub>26</sub> O	222	
1,10-di-epi-cubenol			Aerial parts
Dihydroactinidiolide	C <sub>11</sub> H <sub>16</sub> O <sub>2</sub>	180	Leaves
Isospathulenol	C <sub>15</sub> H <sub>24</sub> O	220	Leaves
Muurolol	C <sub>15</sub> H <sub>26</sub> O	222	Aerial parts
Spathulenol	C <sub>15</sub> H <sub>24</sub> O	220	Aerial parts
T-cadinol	C <sub>15</sub> H <sub>26</sub> O	222	Roots, seeds
Viridiflorol	C <sub>15</sub> H <sub>26</sub> O	222	Aerial parts
	C <sub>15</sub> H <sub>26</sub> O	222	
(Z)-Nerolidol			Inflor., leaves
Triterpene			
	C <sub>30</sub> H <sub>48</sub> O <sub>4</sub>		
Alphitollic acid		472	Roots, seeds
Betulin	C <sub>30</sub> H <sub>50</sub> O <sub>2</sub>	442	Roots, seeds
Betulinic acid	C <sub>30</sub> H <sub>48</sub> O <sub>3</sub>	456	Roots, seeds
3-Epimaslinic acid			Root

TABLE 3.2 (Continued)

Compound	m.f.	m.w.	Part
Euscaphic acids	$C_{30}H_{48}O_5$	488	Root
Oleonolic acid	$C_{30}H_{48}O_3$	456	Rts,Sds,Lf,Fl.
Pomolic acid	$C_{30}H_{48}O_4$	472	Roots, Seeds
	$C_{30}H_{48}O_3$	456	
Ursolic acid			Rts,Sds,Lf,Fl.
	$C_{37}H_{52}O_4$	460	
Basilol			Leaves, Flower
Ocimol	$C_{39}H_{56}O_6$	620	Leaves, Flower
Aliphatic alcohol			
	$C_6H_{12}O$	100	
Cyclohexanol			Leaves
Hexanol	$C_6H_{14}O$	102	Leaves
Octanol	$C_8H_{18}O$	130	Leaves
3-Octanol	$C_8H_{18}O$	130	Leaves
1-Octen-3-ol	$C_8H_{16}O$	128	Leaves
1-Penten-3-ol	$C_5H_{10}O$	86	Leaves
	$C_5H_{10}O$	86	Leaves
(Z)-2-pentenol			
(Z)-3-hexanol	$C_6H_{14}O$	102	Leaves
Aliphatic aldehyde			
		98	Leaves
(E)-3-hexenal	$C_6H_{10}O$		
(E,Z)-2,4-heptadienal	$C_7H_{10}O$	110	Leaves
Hexanal	$C_6H_{12}O$	100	Leaves
Aliphatic ester			
	$C_8H_{14}O_2$	142	
(Z)-3-hexenyl acetate			Leaves
Aliphatic ketones			
	$C_{13}H_{20}O$	192	
$\beta$ -Ionone			Leaves
<i>cis</i> -Jasmone	$C_{11}H_{16}O$	164	Leaves
	$C_4H_8O_2$	88	Leaves
	$C_8H_{14}O$	126	Leaves
6-Methyl-5-heptenone			
6-Methyl-(E,E)-3,5-heptadien-2-one	$C_8H_{14}O$	126	Leaves
<i>trans</i> - $\beta$ -Ionone-5,6-epoxide			Leaves

TABLE 3.2 (Continued)

Compound	m.f.	m.w.	Part
Aromatic Compounds			
4-Allylphenol	$C_9H_{10}O$	134	Leaves
Anethole	$C_{10}H_{12}O$	148	Leaves
Anisaldehyde	$C_8H_8O_2$	136	Leaves
Benzyl alcohol	$C_7H_8O$	108	Leaves
Cuminaldehyde	$C_{10}H_{12}O$	148	Leaves
Estragole	$C_{10}H_{12}O$	148	Leaves
Ethyl cinnamate	$C_{11}H_{12}O_2$	176	Leaves
Methyl benzoate	$C_8H_8O_2$	136	Leaves
Methyl cinnamate	$C_{10}H_{10}O_2$	162	Leaves
Methyl eugenol	$C_{11}H_{14}O_2$	178	Leaves
Methyl salicylate	$C_8H_8O_3$	152	Leaves
<i>p</i> -Methoxycinnamaldehyde	$C_{10}H_{10}O_2$	162	Leaves
Phenethyl alcohol	$C_8H_{10}O$	122	Leaves
Phenyl acetaldehyde	$C_8H_8O$	120	Leaves
Safrole	$C_{10}H_{10}O_2$	162	Leaves
Benzaldehyde	$C_7H_6O$	106	Leaves
<i>cis</i> -hex-3-enyl acetate	$C_8H_{14}O_2$	142	Leaves
Flavonoids			
Quercetin	$C_{15}H_{10}O_7$	302	Leaves
Quercetin-3-O-diglycoside			Leaves
Quercetin-3-O-B-D-Galactoside	$C_{21}H_{20}O_{12}$	466	Whole plant
Quercetin-3-O-B-D-glucoside	$C_{21}H_{22}O_{12}$	468	Whole plant
Quercetin-3-O-B-D-glucoside-2''-gallate	$C_{21}H_{22}O_{11}$	452	Whole plant
Quercetin-3-O-(2''-O-galloyl)-rutinoside	$C_{27}H_{30}O_{16}$	610	Whole plant
Quercetin-3-O-a-L-rhamnoside	$C_{21}H_{20}O_{11}$	448	Whole plant
Isoquercetrin	$C_{21}H_{20}O_{12}$	468	Leaves
Kaempferol	$C_{15}H_{10}O_6$	286	Leaves
Kaempferol-3-O-rutinoside	$C_{22}H_{30}O_{15}$	534	Leaves
Kaempferol-3-O-B-D-glucoside	$C_{21}H_{22}O_{11}$	450	Whole plant
Rutin	$C_{22}H_{30}O_{16}$	550	Leaves
3,5-Pyridinedicarboxylic acid, 2,6-dimethyldiethyl ester	$C_{13}H_{17}NO_4$	251	Aerial parts
Monosaccharide			
L-Arabinose	$C_5H_{10}O_5$	150	Seeds
L-Rhamnose	$C_6H_{12}O_5$	154	Seeds

TABLE 3.2 (Continued)

Compound	m.f.	m.w.	Part
D-Xylose	C <sub>5</sub> H <sub>10</sub> O <sub>5</sub>	150	Seeds
Coumarin			
Coumarin	C <sub>10</sub> H <sub>8</sub> O <sub>4</sub>	192	Whole plant
Aesculetin	C <sub>9</sub> H <sub>6</sub> O <sub>4</sub>	178	Leaves
<i>p</i> -Coumaric acid	C <sub>9</sub> H <sub>8</sub> O <sub>3</sub>	164	Leaves
Cinnamates			
(1). 4'-carbomethoxy-2'-hydroxy phenyl ferulate	–	–	Essential oil
(2). (E)-3'-hydroxy-4'-(1''-hydroxyethyl)-phenyl-4-methoxycinnamate	–	–	Essential oil
Caffeic acid	C <sub>9</sub> H <sub>8</sub> O <sub>4</sub>	180	Leaves
Caftaric acid (caffeoyl-tartaric acid)	C <sub>13</sub> H <sub>12</sub> O <sub>9</sub>	312	Leaves
Polyphenols			
Rosmarinic acid	C <sub>18</sub> H <sub>16</sub> O <sub>8</sub>	360	Whole plant
chicoric acid (dicafeoyltartaric acid)	C <sub>22</sub> H <sub>18</sub> O <sub>12</sub>	474	Leaves
Phenylpropene			
Estragole	C <sub>10</sub> H <sub>12</sub> O	148	Aerial parts
Glycoside			
Esculin	C <sub>9</sub> H <sub>8</sub> O <sub>6</sub>	212	Leaves
Syringin	C <sub>17</sub> H <sub>24</sub> O <sub>9</sub>	372	Whole plant
Steroids:			
Basilimoside	C <sub>36</sub> H <sub>60</sub> O <sub>6</sub>	588	Aerial parts
Daucosterol	C <sub>35</sub> H <sub>60</sub> O <sub>6</sub>	576	Whole plant
B-Sitosterol	C <sub>29</sub> H <sub>50</sub> O	414	Leaves, flower
Stigmasterol	C <sub>29</sub> H <sub>48</sub> O	412	
Stigmasterol-3-O-B-D-glucoside	C <sub>35</sub> H <sub>58</sub> O <sub>6</sub>	574	Whole plant
Miscellaneous compounds			
Dihydroactinidiolide			
2,6-Dimethylpyrazine	C <sub>6</sub> H <sub>8</sub> N <sub>2</sub>	94	Leaves
Myristicin	C <sub>11</sub> H <sub>12</sub> O <sub>3</sub>	192	Leaves
γ-Butyrolactone	C <sub>4</sub> H <sub>6</sub> O <sub>2</sub>	86	Leaves
Cyclohexene	C <sub>6</sub> H <sub>10</sub>	82	Aerial parts
2-Pentanone, 4-hydroxy-4-methyl	C <sub>6</sub> H <sub>12</sub> O <sub>2</sub>	116	Aerial parts

**TABLE 3.3** Antimicrobial Activity of Basil Essential Oils

<b>Biological activities of various chemical constituents of <i>Ocimum basilicum</i></b>	
<b>Target Causal Organisms</b>	<b>Effective Bio-constituents</b>
<b>Antibacterial activities</b>	
<i>Staphylococcus aureus</i> , <i>Salmonella enteritidis</i> , <i>Escherichia coli</i>	Essential Oil (EO)
<i>Bacillus cereus</i>	EO
<i>Pseudomonas aeruginosa</i> , <i>Listeria monocytogenes</i> , <i>Shigella</i> sp., <i>Staphylococcus aureus</i>	Methanol-based extract of different plant parts
Different strains of <i>Escherichia coli</i>	Methanol-based extract of different plant parts
<i>Haemophilus influenzae</i> , <i>Pneumococci</i>	EO
<i>Staphylococcus aureus</i>	EO
<i>Staphylococcus</i> , <i>Enterococcus</i> <i>Pseudomonas</i>	Linalool, methyl chavikol, methyl cinnamat, linolen
<i>Escherichia coli</i> , <i>Pseudomonas aeruginosa</i> , <i>Salmonella typhi</i> , <i>Staphylococcus aureus</i> .	Various plant part's extracts
<i>Staphylococcus aureus</i> , <i>Escherichia coli</i> , <i>Bacillus subtilis</i> , <i>Pasteurella multocida</i> , Pathogenic fungi like <i>Aspergillus niger</i> , <i>Mucor mucedo</i> , <i>Fusarium solani</i> , <i>Micrococcus</i> , Gram (+) & (-) bacteria	EO
<i>Giardia lamblia</i>	Linalool
<i>Pseudomonas aernuginosa</i>	Rosmarinic acid
<i>Acinetobacter</i> , <i>Bacillus</i> , <i>Escherichia</i> , <i>Staphylococcus</i>	Ethanol-based extract of different plant parts
<i>Acinetobacter</i> , <i>Bacillus</i> , <i>Escherichia</i> , <i>Micrococcus</i> , <i>Staphylococcus</i>	Methanol-based extract of different plant parts
<i>Acinetobacter</i> , <i>Bacillus</i> , <i>Brucella</i> , <i>Escherichia</i> , <i>Micrococcus</i> , <i>Staphylococcus</i>	Hexane based extract of different plant parts
<i>Bacillus cereus</i> , <i>B. subtilis</i> , <i>B. megaterium</i> , <i>Escherichia coli</i> , <i>Staphylococcus aureus</i> , <i>Listeria monocytogenes</i> , <i>Shigella boydii</i> , <i>S. dysenteriae</i> , <i>Vibrio mimicus</i> , <i>V. parahaemolyticus</i> , <i>Salmonella typhi</i> , <i>S. dysenteria</i>	EOs and Methanol-based extract of different plant parts
<b>Antifungal activity</b>	
<i>Sclerotiniasclerotiorum</i> (Lib.), <i>Rhizopus stolonifer</i> (Ehrens. exFr.) Vuill, <i>Mucor</i> sp. (Fisher)	Linalool and eugenol

**TABLE 3.3** (Continued)

<i>Alternaria alternata</i> (Fries : Fries) von Keissler <i>Fulvia fulva</i> (Cooke) Ciferri <i>Fusarium solani</i> var. <i>coeruleum</i> , <i>Glomerella cingulata</i> (Stonem.) Spauld. Et Schren	EO
<b>Target Causal Organisms</b>	<b>Effective Bio-constituents</b>
<i>Fusarium oxysporum</i> f. sp. <i>vasinfectum</i> and <i>Rhizopus nigricans</i>	Cineol, Linalool, methylchavicol, and eugenol
Isolates of <i>Candida albicans</i>	Methanol and hexane-based extract of different plant parts
<i>Candida albicans</i> , <i>Penicillium notatum</i> , <i>Microsporeum gyseum</i>	EO
Yeast and mould	EO
<i>Aureobasidium pullulans</i> , <i>Debaryomyceshanseni</i> , <i>Penicillium simplicissimum</i> , <i>P. citrinum</i> , <i>P. expansum</i> , <i>P. aurantiogriseum</i>	EO
<b>Antiseptic activity</b>	
<i>Proteus vulgaris</i> , <i>Bacillus substilis</i> , <i>Salmonella paratyph</i>	EO
<b>Antiviral activity</b>	
Herpes viruses, Adenoviruses, hepatitis B virus and coxsackie virus B1 and enterovirus 71	Apigenin, linalool
<b>Insecticidal activity</b>	
<i>Spodoptera littoralis</i>	Different plant extracts
<i>Tribolium castaneum</i> , <i>Sitophilus oryzae</i> , <i>Stagobiom paniceum</i> , <i>Bruchus chinensis</i>	Ocimene, cineole, linalool, methyl cinnamate, methyl chavicol
<i>Ceratitis capitata</i> , <i>Bactrocera dorsalis</i> , <i>B. cucurbitae</i>	Basil oil and <i>trans</i> -anethole, estragole, linalool
<b>Repellant activity</b>	
<i>Culex pipiens</i> (Mosquitoes)	EO
<b>Trypanocidal activity</b>	
Epimastigotes and trypomastigotes forms	EO (eugenol and linalool)

\*Source: Marwat et al., (2011).



**TABLE 3.4** Pharmacological Activities of Secondary Metabolites from *Ocimum sanctum*

Pharmacological Activities	Compounds/Plant Part	Class of compound	Dose(s)	Results
Anticancer	2-(Hydroxymethyl)-5,5,9-trimethylcyclo [7.2.0.03,6] undecan-2-ol (Lf)	Sesquiterpenoid	–	IC <sub>50</sub> 30 ± 0.5 µM against MCF-7 cell line.
	Luteolin (Lf and Ap)	Flavonoid	50 µM	IC <sub>50</sub> (78 ± 6 µM) for androgen-independent carcinoma of prostate (LNCaP) and IC <sub>50</sub> (53 ± 4 µM) for androgen-dependent carcinoma of prostate (PC-3 and DU-145) cells at 72 h.
	Orientin (Lf and Ap)	Flavonoid	50 µM	IC <sub>50</sub> (124 ± 7 µM) for androgen-independent carcinoma of prostate (LNCaP) and IC <sub>50</sub> (104 ± 7 µM) for androgen-dependent carcinoma of prostate (PC-3 and DU-145) cells at 72 h.
	Vicenin-2 (Apigenin 6,8-diglucoside (Lf and Ap)	Flavonoid	–	IC <sub>50</sub> (44 ± 3 µM) for androgen-independent carcinoma of prostate (LNCaP) and IC <sub>50</sub> (25 ± 3 µM) for androgen-dependent (PC-3, DU-145) cells at 72 h.
Antioxidant	Rosmarinic acid (Lf and St)	Phenolic acid	10 µM	Better antioxidant than vitamin E in liposome oxidation model.
	Isothymusin (Lf and St)	Flavonoid	10 µM	Strong antioxidant activity (50% more active than positive control TBHQ and BHT) in liposome oxidation model.
	Isothymonin (Lf and St)	Flavonoid	10 µM	Better antioxidant activity than positive control TBHQ and BHT using liposome oxidation model.
	Cirsimaritin (Lf and St)	Flavonoid	10 µM	Poor antioxidant using liposome oxidation model.
	Cirsilineol (Lf and St)	Flavonoid	10 µM	Good antioxidant activity using liposome oxidation model.
	Eugenol (Lf)	Phenyl propanoid	10 µM	Better antioxidant activity than positive controls TBHQ and BHT using liposome oxidation model.
Anti-inflammatory	Apigenin (Lf, Ap, and St)	Flavonoid	1,000 µM	Showed 65% COX-1 enzyme inhibition activity, compared to ibuprofen, naproxen, and aspirin with 33%, 58%, and 46% at 10, 10, and 1,000 µM concentration, respectively.

**TABLE 3.4** (Continued)

Pharmacological Activities	Compounds/Plant Part	Class of compound	Dose(s)	Results
	Rosmarinic acid (Lf and St)	Phenolic acid	1,000 $\mu$ M	Showed 58% COX-1 enzyme inhibition activity, compared to ibuprofen, naproxen, and aspirin with 33%, 58%, and 46% at 10, 10, and 1,000 $\mu$ M concentration, respectively.
	Isothymusin (Lf and St)	Flavonoid	1,000 $\mu$ M	Inactive against COX-1 and COX-2 enzyme
	Isothymonin (Lf and St)	Flavonoid	1,000 $\mu$ M	Showed 37% COX-1 enzyme inhibition activity, compared to standard ibuprofen, naproxen, and aspirin with 33%, 58%, and 46% COX-1 inhibitory activity at 10, 10, and 1,000 $\mu$ M concentration, respectively.
	Cirsimaritin (Lf and St)	Flavonoid	1,000 $\mu$ M	Showed 50% COX-1 enzyme inhibition activity, compared to standard ibuprofen, naproxen, and aspirin with 33%, 58%, and 46% at 10, 10, and 1,000 $\mu$ M concentration, respectively.
	Cirsilineol (Lf and St)	Flavonoid	1,000 $\mu$ M	Showed 37% COX-1 enzyme inhibition activity, compared to standard ibuprofen, naproxen, and aspirin with 33%, 58%, and 46% at 10, 10, and 1,000 $\mu$ M concentration, respectively.
	4',5-Dihydroxy-3',7,8-trimethoxy flavone (Lf)	Flavonoid	1,000 $\mu$ M	Showed 37% COX-1 enzyme inhibition activity, compared to standard ibuprofen, naproxen, and aspirin with 33%, 58%, and 46% at 10, 10, and 1,000 $\mu$ M concentration, respectively.
	Eugenol (Lf)	Phenyl propanoid	1,000 $\mu$ M	Showed 97% COX-1 enzyme inhibition compared to ibuprofen, naproxen, and aspirin with 33%, 58% and 46% at 10, 10, and 1,000 $\mu$ M, respectively.
Radiation protection	Orientin (Lf and Ap)	Flavonoid	50 $\mu$ g/kg (i.p.)	Pre-treatment of vicenin protected fetal against irradiation-induced genomic damage and reduced the delayed chromosomal abnormalities and tumorigenesis in pregnant Swiss albino mice.

TABLE 3.4 (Continued)

Pharmacological Activities	Compounds/Plant Part	Class of compound	Dose(s)	Results
			6.5, 12.5, 15, 17.5 and 20 $\mu$ M	Pre-treatment significantly ( $p < 0.05-0.001$ ) reduced the micronucleus counts to 51–67% of RT with dose modification factor (DMF) of 2.62 at 17.5 $\mu$ M in cultured human peripheral lymphocytes using micronucleus test.
	Vicenin (Lf)	Flavonoid	50 $\mu$ g/kg (i.p.)	Pre-treatment showed maximum survival 60% from the 30 days of administration with DMF of 1.30.
			50 $\mu$ g/kg (i.p.)	Pre-treatment of vicenin protected fetal against irradiation-induced genomic damage and reduced the delayed chromosomal abnormalities and tumorigenesis in pregnant Swiss albino mice.
			6.5, 12.5, 15, 17.5 and 20 $\mu$ M	Pre-treatment significantly ( $p < 0.05-0.001$ ) reduced the micronucleus counts to 51–67% of RT with DMF of 2.48 at 17.5 $\mu$ M in cultured human peripheral lymphocytes using micronucleus test.
			50 $\mu$ g/kg (i.p.)	Pre-treatment showed significant ( $p < 0.05$ ) protection to bone marrow chromosomes. Showed maximum survival 67% from the 30 days of administration with DMF of 1.37.
Antidiabetic	16-Hydroxy-4,4,10,13-tetramethyl-17-(4-methyl-pentyl)-hexadecahydro-cyclopenta[a]-phenanthren-3-one (Ap)	Triterpenoid	–	Isolated from antidiabetic activity-guided fraction
Antistress	Apigenin-7-O- $\beta$ -D-glucuronic acid (Lf)	Flavonoid	40 mg/kg body weight	Ineffective in Sprague-Dawley rats

**TABLE 3.4** (Continued)

Pharmacological Activities	Compounds/Plant Part	Class of compound	Dose(s)	Results
	Ociglycoside-I (4-Allyl-1-O-β-D-glucopyranosyl-2-hydroxybenzene/or hydroxychavicol glucoside) (Lf)	Phenyl propanoid	40 mg/kg body weight	Pre-treatment significantly ( $p < 0.05$ ) reduced the increase in corticosterone levels and ( $p < 0.01$ ) reduced the acute stress-induced increase in CK levels. Less effective on plasma glucose level in acute stress induced Sprague-Dawley rats.
	7-Hydroxy-3-(2-hydroxyethyl)-4-methyl-2H-1-benzopyran-2-one (ocimarin) (Lf)	Coumarin	40 mg/kg body weight	Ineffective in acute stress male Sprague-Dawley rats
	1-O-(β-D-glucopyranosyl)-(2S,3S,4R,8Z)-2-[(2'R)-2'-hydroxydocosanoylamino]-8(Z)-octadecene-1,3,4-triol (Lf)	Cerebroside	40 mg/kg body weight	Inactive
	1-O-(β-D-glucopyranosyl)-(2S,3S,4R,8Z)-2-[(2'R)-2'-hydroxytetrasanoylamino]-8(Z)-octadecene-1,3,4-triol (Lf)	Cerebroside	40 mg/kg body weight	Pretreatment showed antistress activity and reduced significantly ( $p < 0.05$ ) the increased corticosterone levels and effective ( $p < 0.01$ ) reducing the creatine kinase levels in Sprague-Dawley rats.
	(2S)-1-O-hexadecanoyl-2-O-docosanoyl-3-O-[6-deoxy-6-amino-α-D-glucopyranoside] glycerol (Ocimumoside A) (Lf)	Cerebroside	40 mg/kg body weight	Pretreatment showed significant ( $p < 0.05$ ) anti stress effects by normalizing hyperglycemia, plasma corticosterone, plasma creatine kinase and adrenal hypertrophy in Sprague-Dawley rats. Ginseng crude powder root, Panax quinquefolium (100 mg/kg body weight) was used as standard.
	(2S)-1-O-Octadecanoyl-2-O-tetradecanoyl-3-O-[α-D-galactopyranosyl-(1"→6')-O-β-D-galactopyranosyl] glycerol (Ocimumoside B) (Lf)	Cerebroside	40 mg/kg body weight	Pretreatment showed antistress activity and reduced significantly ( $p < 0.05$ ) the increased corticosterone levels without affecting plasma glucose level in Sprague-Dawley rats.
Lieshmanicidal	Apigenin ((Lf, Ap, and St)	Flavonoid	–	IC <sub>50</sub> 358.7 μg/ml against L. major
	Luteolin (Lf and Ap)	Flavonoid	–	IC <sub>50</sub> 73.9 μg/ml against L. major

TABLE 3.4 (Continued)

Pharmacological Activities	Compounds/Plant Part	Class of compound	Dose(s)	Results
	4',5-Dihydroxy-7,8-dimethoxy flavone (Lf)	Flavonoid	–	IC <sub>50</sub> > 25 µg/ml against L. major
	4',5-Dihydroxy-3',7,8-trimethoxy flavone (Lf)	Flavonoid	–	IC <sub>50</sub> > 25 µg/ml against L. major
	Ferulaldehyde (Lf)	Phenyl propanoid	–	IC <sub>50</sub> 0.9 µg/ml against L. major
	Bieugenol (Lf)	Phenyl propanoid	–	IC <sub>50</sub> 13.6 µg/ml against L. major
	Dehydrodieugenol B (Lf)	Phenyl propanoid	–	IC <sub>50</sub> 16.9 µg/ml against L. major
	6-Allyl-3',8-dimethoxy-flavon-3,4'-diol (tulsinol A) (Lf)	Neolignan	–	IC <sub>50</sub> > 25 µg/ml against L. major
	6-Allyl-3-(4-allyl-2-methoxyphenoxy)-3',8-dimethoxyflavan-4'-ol (tulsinol B) (Lf)	Neolignan	–	IC <sub>50</sub> 43.9 µg/ml against L. major
	5-Allyl-3-(4-allyl-2-methoxyphenoxy)-2-(4-hydroxy-3-methoxyphenyl)-7-methoxy-2,3-dihydrobenzofuran (tulsinol C) (Lf)	Neolignan	–	IC <sub>50</sub> 9.1 µg/ml against L. major
	1,2-Bis(4-allyl-2-methoxyphenoxy)-3-(4-hydroxy-3-methoxyphenyl)-3-methoxypropane (tulsinol D) (Lf)	Neolignan	–	Not done
	1-(4-Hydroxy-3-methoxyphenyl)-1,2,3-tris(4-allyl-2-methoxyphenoxy)propane (tulsinol E) (Lf)	Neolignan	–	IC <sub>50</sub> 47.1 µg/ml against L. major
	1-Allyl-4-(5-allyl-2-hydroxy-3-methoxyphenoxy)-3-(4-allyl-2-methoxyphenoxy)-5-methoxybenzene (tulsinol F) (Lf)	Neolignan	–	IC <sub>50</sub> 23.8 µg/ml against L. major

**TABLE 3.4** (Continued)

Pharmacological Activities	Compounds/Plant Part	Class of compound	Dose(s)	Results
	3-(5-Allyl-2-hydroxy-3-methoxyphenyl)-1-(4-hydroxy-3-methoxyphenoxy)-prop-1-ene (tulsinol G) (Lf)	Neolignan	–	IC <sub>50</sub> 89.7 µg/ml against <i>L. major</i>
	β-Caryophyllene epoxide (Lf)	Sesquiterpenoid	–	IC <sub>50</sub> > 25 µg/ml against <i>L. major</i>
	Ursolic acid	Triterpenoid	–	IC <sub>50</sub> 2.2 µg/ml against <i>L. major</i> using amphotericin B (IC <sub>50</sub> 0.04 µg/ml) as positive control
	Oleanolic acid	Triterpenoid	–	IC <sub>50</sub> 17.1 µg/ml against <i>L. major</i>
	β-Sitosterol glucopyranoside (Lf)	Steroid	–	–
	Stigmasterol (Lf)	Steroid	–	IC <sub>50</sub> > 25 µg/ml against <i>L. major</i>
Antimicrobial	Orientin (Lf and Ap)	Flavonoid	400 mg/ml	Active against <i>S. aureus</i> , <i>S. cohnii</i> and <i>K. pneumonia</i> with maximum zone inhibition (18.04, 17.13, and 16.11 mm).
	Vicenin (Lf)	Flavonoid	400 mg/ml	Effective against <i>E. coli</i> and <i>Proteus</i> with maximum ZOI (18.84 and 17.16 mm).
Mosquitocidal	Eugenol (Lf)	Phenyl propanoid	100–250 ppm	LD <sub>100</sub> (200 µg/ml) against fourth instar <i>Aedes aegyptii</i> larvae.
	(E)-6-Hydroxy-4,6-dimethyl-3-heptene-2-one (Lf and St)	Acetone oligomer	–	LD <sub>100</sub> (6.25 µg/ml) against fourth-instar <i>Aedes aegyptii</i> larvae in 24 h.
	1,3-dilinolenoyl-2-palmitin (Lf and St)	Triglyceride	–	Inactive against <i>Aedes aegyptii</i> larvae.

*Abbreviations:* Ap: areal part; Lf: leaf; Rt: root; St: stem; and Tw: twig.

*Source:* Singh & Chowdhury (2018).

**TABLE 3.5** Patents on Ayurvedic Medicines/Herbal Extracts

Sl. No.	Patent No.	Title	Main Herbs
1.	1048/MUM/2003	Ayurvedic immuno modulator composition for treatment of acquired immunodeficiency syndrome	Tulsi or Krishna Tulsi (Holy Basil),
2.	1049/MUM/2003	Ayurvedic antiretroviral composition for treatment of acquired immunodeficiency syndrome.	Tulsi ( <i>Ocimum sanctum</i> )
3.	553/KOL/2003	A process for preparing nutrient-fortified Ayurvedic sweets like Sandesh and Rosogolla containing at least one herb.	Tulsi ( <i>Osimum sanctum</i> ) leaves

## KEYWORDS

- **basil**
- **biomolecules**
- **essential oil**
- **medicinal plants**
- **nutraceuticals**
- **oral health**
- **phytomolecules**
- **therapeutic applications**

## REFERENCES

- Agarwal, C., Sharma, N. L., & Gaurav, S. S., (2013). An analysis of basil (*Ocimum* sp.) to study the morphological variability. *Indian Journal of Fundamental and Applied Life Sciences*, 3, 521–525.
- Agarwal, P., & Nagesh, L., (2011). Comparative evaluation of efficacy of 0.2% chlorhexidine, Listerine, and Tulsi extract mouth rinses on salivary *Streptococcus mutans* count of high school children RCT. *Contemporary Clinical Trials*, 32(6), 802–808.
- Ahmed, M., Ahamed, R. N., Aladakatti, R. H., & Ghosesawar, M. G., (2002). Reversible antifertility effect of benzene extract of *Ocimum sanctum* leaves on sperm parameters and fructose content in rats. *Journal of Basic Clinical Physiology and Pharmacology*, 13, 51–59.

- Akbarian, S. A., Asgary, S., Feizi, A., Iraj, B., & Askari, G., (2016). Comparative study on the effect of *Plantago psyllium* and *Ocimum basilicum* seeds on anthropometric measures in non-alcoholic fatty liver patients. *International Journal of Preventive Medicine*, 7, 114.
- Albuquerque, U., (1996). *Taxonomy and Ethnobotany of the Genus Ocimum* (pp. 48–68). Federal University Pernambuco, Mexico.
- Ali, B., Al-Wabel, N. A., Shams, S., Ahamad, A., Khan, S. A., & Anwar, F., (2015). Essential oils used in aromatherapy: A systemic review. *Asian Pacific Journal of Tropical Biomedicine*, 5(8), 601–611.
- Amir, M. D. M., Jalal, S., Peyman, M., & Jalil, D. S., (2011). Antimicrobial activity of essential oil extract of *Ocimum basilicum* L. leaves on a variety of pathogenic bacteria. *Journal of Medicinal Plants Research*, 5(15), 3453–3456.
- Anbarasu, K., & Vijayalakshmi, G., (2007). Improved shelf life of protein-rich tofu using *Ocimum sanctum* (Tulsi) extracts to benefit Indian rural population. *Journal of Food Science*, 72, 300–305.
- Arthi, N., & Murugan, K., (2010). Larvicidal and repellent activity of *Vetiveria zizanioides* L, *Ocimum basilicum* Linn and the microbial pesticide spinosad against malarial vector, *Anopheles stephensi* Liston (Insecta: Diptera: Culicidae). *Journal of Biopesticides*, 3, 199–204.
- Arumugam, G., Swamy, M. K., & Sinniah, U. R., (2016). *Plectranthus amboinicus* (Lour.) Spreng: Botanical, phytochemical, pharmacological and nutritional significance. *Molecules*, 21(4), 369.
- Asami, D. K., Hong, Y., Barrett, D. M., & Mitchell, A. E., (2003). Comparison of the total phenolic and ascorbic acid content of freeze-dried and air-dried marionberry, strawberry, and corn grown using conventional, organic, and sustainable agricultural practices. *Journal of Agriculture Food Chemistry*, 51(5), 1237–1241.
- Balambal, R., Thiruvengadam, K. V., Kameswarant, L., Janaki, V. R., & Thambiah, A. S., (1985). *Ocimumbasilicum* in acne vulgaris-a controlled comparison with a standard regime. *The Journal of the Association Physicians of India*, 33(8), 507, 508.
- Barfi, A., Nazem, H., Saeidi, I., Peyrovi, M., Afsharzadeh, M., Barfi, B., & Salavati, H., (2016). In-syringe reversed dispersive liquid-liquid microextraction for the evaluation of three important bioactive compounds of basil, tarragon and fennel in human plasma and urine samples. *Journal of Pharmaceutical and Biomedical Analysis*, 121, 123–134.
- Beatović, D., Krstić-Milošević, D., Trifunović, S., Šiljegović, J., Glamočlija, J., Ristić, M., & Jelačić, S., (2015). Chemical composition, antioxidant, and antimicrobial activities of the essential oils of twelve *Ocimum basilicum* L. cultivars grown in Serbia. *Records of Natural Products*, 9, 62–75.
- Benedec, D., Pârnu, A. E., Oniga, I., Toiu, A., & Tiperciuc, B., (2007). Effects of *Ocimum basilicum* L. extract on experimental acute inflammation. *Revista Medico-Chirurgicola a Societatii de Medici si Naturalisti Din Lasi*, 111(4), 1065–1069.
- Bentham, G., (1832). *Ocimum*. In: *Labiatarum Genera and Species* (pp. 1–19). London, Ridgeway.
- Bentham, G., (1848). *Ocimum*. In: Candolle, A. P. De., (ed.), *Prodromus Systematis Naturalis* (Vol. 12, pp. 31–44). Paris.
- Bilal, A., Jahan, N., Ahmed, A., Bilal, S. N., & Habib, S., (2013). Antifertility activity of hydroalcoholic extract of *Ocimum basilicum* Linn leaves on female Wistar rats. *Journal of Reproduction and Contraception*, 24(1), 5–54.



- Bilal, A., Jahan, N., Ahmed, A., Bilal, S. N., Habib, S., & Hajra, S., (2012). Phytochemical and pharmacological studies on *Ocimum basilicum* L.: A review. *International Journal of Current Research Review*, 4(23), 73–83.
- Bora, K. S., Arora, S., & Shri, R., (2011). Role of *Ocimum basilicum* L. in prevention of ischemia and reperfusion-induced cerebral damage, and motor dysfunctions in mice brain. *Journal of Ethnopharmacology*, 137(3), 1360–1365.
- Briquet, J., (1897). *Ocimum*. In: Engler, A., & Prantle K. A. E., (eds.), *Die Natürlichen Pflanzenfamilien* (pp. 369–372). Engelmann W, Leipzig.
- Burt, S., (2004). Essential oils: Their antibacterial properties and potential application in foods: A review. *International Journal of Food Microbiology*, 94(3), 223–253.
- Carovic-Stanko, K., Liber, Z., Besendorfer, V., Javornik, B., Bohanec, B., Kolak, I., & Satovic, Z., (2010). Genetic relations among basil taxa (*Ocimum* L.) based on molecular markers, nuclear DNA content, and chromosome number. *Plant Systematics and Evolution*, 285, 13–22.
- Ceuppens, S., Delbeke, S., De Coninck, D., Boussemaere, J., Boon, N., & Uyttendaele, M., (2015). Characterization of the bacterial community naturally present on commercially grown basil leaves: Evaluation of sample preparation prior to culture-independent techniques. *International Journal of Environmental Research and Public Health*, 12(8), 10171–10197.
- Chalchat, J. C., & Özcan, M. M., (2008). Comparative essential oil composition of flowers, leaves and stems of basil (*Ocimum basilicum* L.) used as herb. *Food Chemistry*, 110, 501–503.
- Chattopadhyay, R. R., (1993). Hypoglycemic effect of *Ocimum sanctum* leaf extract in normal and streptozotocin diabetic rats. *Indian Journal of Experimental Biology*, 31, 891–893.
- Chiang, L. C., Ng, L. T., Cheng, P. W., Chiang, W., & Lin, C. C., (2005). Antiviral activities of extracts and selected pure constituents of *Ocimum basilicum*. *Clinical Physiology and Pharmacology*, 32(10), 811–816.
- Choudhury, G. B., Prabhat, K. J., Nayak, B. S., Panda, S. K., & Tripathy, S. K., (2010). Phytochemical investigation and evaluation of analgesic activity of leafy extracts of various *Ocimum* (Tulsi) species. *The Indian Pharmacist*, 8(12), 67–70.
- Darrah, H. H., (1972). The basils in folklore and biological science. *The Herbalist*, 38, 3–10.
- Darrah, H. H., (1974). Investigations of the cultivars of basils (*Ocimum*). *Economic Botany*, 28, 63–67.
- Darrah, H. H., (1980). *The Cultivated Basils* (p. 82). Buckeye Printing Company, MO.
- Dasgupta, T., Rao, A. R., & Yadava, P. K., (2004). Chemomodulatory efficacy of basil leaf (*Ocimum basilicum*) on drug metabolizing and antioxidant enzymes and on carcinogen-induced skin and fore stomach papillomagenesis. *Phytomedicine*, 11(2, 3), 139–1351.
- De Almeida, I., Alviano, D. S., Vieira, D. P., Alves, P. B., Blank, A. F., & Lopes, A. H., (2007). Antigiardial activity of *Ocimum basilicum* essential oil. *Parasitological Research*, 101(2), 443–445.
- Denny, E. F. K., (1995). *Field Distillation for Herbaceous Oils*. Denny Mckenzie Associates, Lilydale, Tasmania, Australia.
- Divya, N. V., Jaleel, A. C., Gopi, R., Gomathinayagam, M., & Panneerselvam, R., (2009). Antioxidant potential of *Ocimum sanctum* under growth regulator treatments. *Eurasia Journal of Bioscience*, 3, 1–9.

- Eldin, H. M. E., & Badawy, A. F., (2013). *In vitro* anti-trichomonas vaginalis activity of *Pistacia lentiscus* mastic and *Ocimum basilicum* essential oil. *Journal of Parasitic Diseases*, 39(3), 465–473.
- Erler, F., Ulug, I., & Yalcinkaya, B., (2006). Repellent activity of five essential oils against *Culex pipiens*. *Fitoterapia*, 77(7, 8), 491–494.
- Fandohan, P., Gnonlonfin, B., Laleye, A., Gbenou, J. D., Darboux, R., & Moudachirou, M., (2008). Toxicity and gastric tolerance of essential oils from *Cymbopogon citratus*, *Ocimum gratissimum* and *Ocimum basilicum* in Wistar rats. *Food and Chemical Toxicology*, 46(7), 2493–2497. doi: 10.1016/j.fct.2008.04.006.
- Fathiazad, F., Matlobi, A., Khorrami, A., Hamedeyazdan, S., Soraya, H., & Hammami, M., (2012). Phytochemical screening and evaluation of cardioprotective activity of ethanolic extract of *Ocimum basilicum* L. (basil) against isoproterenol induced myocardial infarction in rats. *DARU Journal of Pharmaceutical Sciences*, 20, 87.
- Garibaldi, A., Minuto, A., Minuto, G., & Gullino, M. L., (2004). First report of downy mildew on Basil (*Ocimum basilicum*) in Italy. *Plant Disease*, 88, 312–312.
- Ghosap, S., & Kar, A., (2004). Hypoglycemic effects of some plant extracts are possibly mediated through inhibition in corticosteroid concentration. *Pharmazie*, 59, 876–878.
- Ghosh, G. R., (1995). Tulasi (genus *Ocimum*). *New Approaches to Medicine and Health (NAMAH)*, 3, 23–29.
- Govindarajan, M., Sivakumar, R., Rajeswary, M., & Yogalakshmi, K., (2013). Chemical composition and larvicidal activity of essential oil from *Ocimum basilicum* (L.) against *Culex tritaeniorhynchus*, *Aedes albopictus* and *Anopheles subpictus* (Diptera: Culicidae). *Experimental Parasitology*, 134(1), 7–11.
- Grayer, R. J., Kite, G. C., Veitch, N. C., Eckert, M. R., Marin, P. D., & Senanayake, P., (2002). Leaf flavonoid glycosides as chemosystematic characters in *Ocimum*. *Biochemical Systematics and Ecology*, 30, 327–342.
- Grieve, M. A., (1931). *A Modern Herbal* (Vol. 1). Dover Publications, New York. ISBN: 0486227987.
- Grieve, M., & Marshall, M., (1982). *A Modern Herbal: The Medicinal, Culinary, Cosmetic and Economic Properties, Cultivation and Folk-lore of Herbs, Grasses, Fungi, Shrubs, and Trees with All Their Modern Scientific Uses* (Vol. 2). Dover Publications, New York, ISBN: 0486227995.
- Grover, J. K., Vats, V., & Yadav, S. S., (2005). *Pterocarpus marsupium* extract (Vijayasar) prevented the alteration in metabolic patterns induced in the normal rat by feeding an adequate diet containing fructose as sole carbohydrate. *Diabetes Obesity and Metabolism*, 7, 414–420.
- Gupta, D., Bhaskar, D., & Gupta, R., (2014). A randomized controlled clinical trial of *Ocimum sanctum* and chlorhexidine mouthwash on dental plaque and gingival inflammation. *Journal of Ayurveda Integrative Medicine*, 5, 109–116.
- Gutierrez, B., Ryan, C., & Bourke, P., (2008). The antimicrobial efficacy of plant essential oil combinations and interactions with food ingredients. *International Journal of Food Microbiology*, 124, 91–97.
- Hanif, M. A., Al-Maskari, M. Y., Al-Maskari, A., Al-Shukaili, A., Al-Maskari, A. Y., & Al-Sabahi, J. N., (2011). Essential oil composition, antimicrobial and antioxidant activities of unexplored Omani basil. *Journal of Medicinal Plants Research*, 5, 751–757.

- Hannan, J. M., Marenah, L., Ali, L., Rokeya, B., Flatt, P. R., & Abdel-Wahab, Y. H., (2006). *Ocimum sanctum* leaf extracts stimulate insulin secretion from perfused pancreas, isolated islets and clonal pancreatic beta-cells. *Journal of Endocrinology*, 189, 127–136.
- Hemalatha, R., Babu, N. K., Karthik, M., Ramesh, R., Dinesh, K. B., & Kumar, U. P., (2011). Immunomodulatory activity and Th<sub>1</sub>/Th<sub>2</sub> cytokine response of *Ocimum sanctum* in myelo-suppressed Swiss albino mice. *Trends in Medical Research*, 6(1), 23–31.
- Hiltunen, R., & Holm, Y., (1999). *Basil: Industrial Profiles*. Harwood Academic Publisher, New Jersey.
- Hosamane, M., Acharya, A., & Vij, C., (2014). Evaluation of holy basil mouthwash as an adjunctive plaque control agent in a four-day plaque regrowth model. *Journal of Clinical and Experimental Dentistry*, 6, 491–496.
- Hossain, M. A., Kabir, M. J., Salehuddin, S. M., Rahman, S. M., Das, A. K., Singha, S. K., Alam, M. K., & Rahman, A., (2010). Antibacterial properties of essential oils and methanol extracts of sweet basil *Ocimum basilicum* occurring in Bangladesh. *Pharmaceutical Biology*, 48(5), 504–511.
- Hosseini-Parvar, S. H., Matia-Merino, L., & Golding, M., (2015). Effect of basil seed gum (BSG) on textural, rheological, and microstructural properties of model processed cheese. *Food Hydrocolloids*, 44, 557–567.
- Hussain, A. I., Anwar, F., Sherazi, S. T. H., & Przybylski, R., (2008). Chemical composition, antioxidant, and antimicrobial activities of basil (*Ocimum basilicum*) essential oils depends on seasonal variations. *Food Chemistry*, 108, 986–995.
- Ismail, M., (2006). Central properties and chemical composition of *Ocimum basilicum* essential oil. *Pharmaceutical Biology*, 44(8), 619–626.
- Jaggi, R. K., Madaan, R., & Singh, B., (2003). Anticonvulsant potential of holy basil, *Ocimum sanctum* Linn, and its cultures. *Indian Journal of Experimental Biology*, 41, 1329–1333.
- James, T. C., (2016). IPR issues related to medicinal and aromatic plants (Herbs & their allied products). *Journal of Traditional and Folk Practices*, 2–4(1), 7–17.
- Jamshidi, N., & Cohen, M. M., (2017). The clinical efficacy and safety of Tulsi in humans: A systematic review of the literature. *Evidence-Based Complementary and Alternative Medicine*, 2017, 9217567.
- Javanmardi, J., Khalighi, A., Kashi, A., Bais, H. P., & Vivanco, J. M., (2002). Chemical characterization of basil (*Ocimum basilicum* L.) found in local accessions and used in traditional medicines in Iran. *Journal of Agricultural and Food Chemistry*, 50, 5878–5883.
- Jelacic, S. C., Beatovic, D. V., Prodanovic, S. A., Tasic, S. R., Moravecic, Đ. Z., Vujošević, A. M., & Vuckovic, S. M., (2011). Chemical composition of the essential oil of basil (*Ocimum basilicum* L. Lamiaceae). *HemijksaIndustrija*, 65(4), 465–471.
- Kantak, N. M., & Gogate, M. G., (1992). Effect of short-term administration of Tulsi (*Ocimum sanctum* Linn.) on reproductive behavior of adult male rats. *Indian Journal of Physiology and Pharmacology*, 36(2), 109–111.
- Kathirvel, P., & Ravi, S., (2012). Chemical composition of the essential oil from basil (*Ocimum basilicum* Linn.) and its *in vitro* cytotoxicity against HeLa and HEp-2 human cancer cell lines and NIH 3T3 mouse embryonic fibroblasts. *Natural Product Research*, 26(12), 1112–1118.
- Kaurinovic, B., Popovic, M., Vlasisavljevic, S., & Trivic, S., (2011). Antioxidant capacity of *Ocimum basilicum* L and *Origanum vulgare* L extracts. *Molecules*, 16(9), 7401–7414.

- Kelm, M. A., Nair, M. G., Strasburg, G. M., & DeWitt, D. L., (2000). Antioxidant and cyclooxygenase inhibitory phenolic compounds from *Ocimum sanctum* Linn. *Phytomedicine*, 7, 7–13.
- Khosro, I., Pahlaviani, M. R., Massiha, A., Bidarigh, S., Giahi, M., & Muradov, P. Z., (2012). Analysis of the phytochemical contents and anti-microbial activity of *Ocimum basilicum* L. *International Journal of Molecular and Clinical Microbiology*, 2(1), 141–147.
- Kirtikar, K. R., & Basu, B. D., (2003). *Indian Medicinal Plants with Illustrations* (2<sup>nd</sup> edn., Vol. 8, pp. 2701–2705). Uttaranchal, Oriental Enterprises.
- Kividompolo, M., & Hyotylainen, T., (2007). Comprehensive two-dimensional liquid chromatography in analysis of *Lamiaceae* herbs: Characterization and quantification of antioxidant phenolic acids. *Journal of Chromatography*, 1145, 155–164.
- Klimánková, E., Holadová, K., Hajšlová, J., Cajka, T., Poustka, J., & Koudela, M., (2008). Aroma profiles of five basil (*Ocimum basilicum* L.) cultivars grown under conventional and organic conditions. *Food Chemistry*, 107, 464–472.
- Kothari, S. K., Bhattacharya, A. K., Singh, C. P., Singh, K., Rao, B. R. R., Syamasundar, K. V., et al., (2004). Registration of a new chemotype Kanchan of sacred basil/holy basil, *Ocimum tenuiflorum* syn. *O. sanctum* rich in methyl eugenol. *Journal of Medicinal and Aromatic Plant Sciences*, 26(2), 336–340.
- Kumar, A., Shukla, R., Singh, P., & Dubey, N., (2010). Chemical composition, antifungal and anti-aflatoxicogenic activities of *Ocimum sanctum* L. essential oil and its safety assessment as plant-based antimicrobial. *Food and Chemical Toxicology*, 48, 539–543.
- Lal, R. K., Khanuja, S. P. S., Agnihotri, A. K., Misra, H. O., Shasany, A. K., Naqvi, A. A., Dhawan, O. P., et al., (2003). High yielding eugenol rich oil producing variety of *Ocimum sanctum* – CIM-Ayu. *Journal of Medicinal and Aromatic Plant Science*, 25, 746, 747.
- Lal, R. K., Khanuja, S. P. S., Shasany, A. K., Ahmad, R., Chandra, R., Naqvi, A. A., Mishra, H. O., et al., (2008). Registration of a high yielding dark purple pigmented variety ‘CIM-Angana’ of Shayam Tulsi (*Ocimum sanctum* L.). *Journal of Medicinal and Aromatic Plant Sciences*, 30(1), 92–94.
- Leelahagul, P., Putadechakum, S., & Tanphaichitr, V., (1992). The effects of soluble dietary fiber from the Thai herb, sweet basil seed, on human body composition. *Asia Pacific Journal of Clinical Nutrition*, 1, 169–174.
- Lupton, D., Khan, M. M., Al-Yahyai, A. R., & Hanif, M. A., (2012). Basil: A natural source of antioxidants and nutraceuticals. In: Ambrose, D. C. P., et al., (eds.), *Leafy Medicinal Herbs: Botany, Chemistry, Postharvest Technology and Uses* (pp. 27–41).
- Lupton, D., Khan, M. M., Yahyai, R. A. A., & Hanif, M. A., (2019). Medicinal plants of South Asia: Novel sources for drug discovery. In: Basil: A natural source of antioxidants and nutraceuticals. *The Lancet*, 27–41.
- Majkowska-Gadomska, J., Dziedzic, A., Dobrowolski, A., & Mikulewicz, E., (2015). The effect of sowing time on the yield and nutritional value of Basil (*Ocimum basilicum* L.) herbage. *Acta Agrophysica*, 22(2), 165–172.
- Majkowska-Gadomska, J., Kulczycka, A., Dobrowolski, A., & Mikulewicz, E., (2017). Yield and nutritional value of basil grown in a greenhouse. *Acta Agrophysica*, 24(3), 455–464.
- Manosroi, J., Dhumtanom, P., & Manosroi, A., (2006). Anti-proliferative activity of essential oil extracted from Thai medicinal plants on KB and P<sub>388</sub> cell lines. *Cancer Letters*, 235(1), 114–120.

- Marotti, M., Piccaglia, R., & Giovanelli, E., (1996). Differences in essential oil composition of basil (*Ocimum basilicum* L.) Italian cultivars related to morphological characteristics. *Journal of Agriculture and Food Chemistry*, 44, 3926–3929.
- Martin, K. W., & Ernst, E., (2003). Herbal medicines for treatment of bacterial infections: A review of controlled clinical trials. *Journal of Antimicrobial Chemotherapy*, 51(2), 241–246.
- Martins, A. P., Salgueiro, L. R., Vila, R., Tomi, F., Canigual, S., Casanova, J., Proenca Da, C. A., & Adzet, T., (1999). Composition of the essential oils of *O. canum*, *O. gratissimum* and *O. minimum*. *Planta Medica*, 65, 187–189.
- Marwat, S. K., Ur-Rehman, F., Khan, M. S., Ghulam, S., Anwar, N., Mustafa, G., & Usman, K., (2011). Phytochemical constituents and pharmacological activities of sweet basil-*Ocimum basilicum* L. (*Lamiaceae*). *Asian Journal of Chemistry*, 23(9), 3773–3782.
- Matiz, G., Osorio, M. R., Camacho, F., Atencia, M., & Herazo, J., (2012). Effectiveness of antimicrobial formulations for acne based on orange (*Citrus sinensis*) and sweet basil (*Ocimum basilicum*L) essential oils. *Biomedica*, 32(1), 125–133.
- Meera, R., Devi, P., Kameswari, B., Madhumitha, B., & Merlin, N. J., (2009). Antioxidant and hepatoprotective activities of *Ocimum basilicum* Linn. and *Trigonella foenum-graecum* Linn against H<sub>2</sub>O<sub>2</sub> and CCL<sub>4</sub> induced hepatotoxicity in goat liver. *Indian Journal of Experimental Biology*, 47(7), 584–590.
- Meyers, M., (2003). *Basil: An Herb Society of America Guide*. The Herb Society of America, Kirtland, Ohio. Retrieved from: [https://www.herbsociety.org/file\\_download/inline/c2cd2efa-f150-4aac-9c7b-f10a0ccaf889](https://www.herbsociety.org/file_download/inline/c2cd2efa-f150-4aac-9c7b-f10a0ccaf889) (accessed on 30 September 2023).
- Meyers, M., (2003). *Basil: Herb Society of America Guide* (pp. 1–45). The Herb Society of America, Ohio.
- Mohammad, S., Pal, U. S., Pradhan, R., & Singh, N., (2014). Herbal remedies for mandibular fracture healing. *National Journal of Maxillofacial Surgery*, 5(1), 35–38.
- Morales, M. R., & Simon, J. E., (1996). New basil selections with compact inflorescence for the ornamental market. In: Janick, J., (ed.), *Progress in New Crops* (pp. 543–546). ASHS Press, Alexandria.
- Mukherjee, R., Dasha, P. K., & Ramb, G. C., (2005). Immunotherapeutic potential of *Ocimum sanctum* (L.) in bovine subclinical mastitis. *Research of Veterinary Science*, 79, 37–43.
- Mulyaningsih, S., Sporer, F., Zimmermann, S., Reichling, J., & Wink, M., (2010). Synergistic properties of the terpenoids aromadendrene and 1,8-cineole from the essential oil of *Eucalyptus globulus* against antibiotic-susceptible and antibiotic-resistant pathogens. *Phytomedicine*, 17(13), 1061–1066.
- Muralidharan, A., & Dhananjayan, R., (2004). Cardiac stimulant activity of *Ocimum basilicum* Linn extracts. *Indian Journal of Pharmacology*, 36, 163–166.
- Narendhirakannan, R. T., Subramanian, S., & Kandaswamy, M., (2006). Biochemical evaluation of antidiabetogenic properties of some commonly used Indian plants on streptozotocin-induced diabetes in experimental rats. *Clinical and Experimental Pharmacology Physiology*, 33, 1150–1157.
- Nebedum, J., Ajeigbe, K., Nwobodo, E., Uba, C., Adesanya, O., Fadera, O., & Ofusori, D., (2009). Comparative study of the ethanolic extracts of four Nigerian plants against some pathogenic microorganisms. *Research Journal of Medicinal Plants*, 3(1), 23–28.
- Neelam, L. D., & Nilofer, S. N., (2010). Preliminary immunomodulatory activity of aqueous and ethanolic leaves extracts of *Ocimum basilicum* Linn in mice. *International Journal of PharmatTech Research*, 2(2), 1342–1349.

- Nguefack, J., Budde, B. B., & Jakobsen, M., (2004). Five essential oils from aromatic plants of Cameroon: Their antibacterial activity and ability permeabilize the cytoplasmic membrane of *Listeria innocua* examined by flow cytometry. *Letters in Applied Microbiology*, 39(5), 395–400.
- Niture, S. K., Rao, U. S., & Srivenugopal, K. S., (2006). Chemo-preventative strategies targeting the MGMT repair protein: Augmented expression in human lymphocytes and tumor cells by ethanolic and aqueous extracts of several Indian medicinal plants. *International Journal of Oncology*, 29(5), 1269–1278.
- Nurzynska-Wierdak, R., Borowski, B., Dzida, K., Zawislak, G., & Kowalski, R., (2013). Essential oil composition of sweet basil cultivars as affected by nitrogen and potassium fertilization. *Turkish Journal of Agriculture and Forestry*, 37, 427–436.
- Oliviera, J. S., Porto, L. A., Estevam, C. S., Siqueira, R. S., Barreto, P. B., Niculau, E. S., Blank, A. F., et al., (2009). Phytochemical screening and anticonvulsant property of *Ocimum basilicum* leaf essential oil. *Latin American and Caribbean Journal of Medicinal and Aromatic Plants*, 8(3), 195–202.
- Onayemi, O., Orafidiya, L., Agbani, B., Oyedele, A., & Babalola, O., (2002). Preliminary clinical tests on topical applications of *Ocimum gratissimum* Linn essential oil for the treatment of acne vulgaris. *Clinical Drug Investigation*, 22, 313–319.
- Opalchenova, G., & Obreshkova, D., (2003). Comparative studies on the activity of basil-an essential oil from *Ocimum basilicum* L. against multidrug resistant clinical isolates of the genera *Staphylococcus*, *Enterococcus* and *Pseudomonas* by using different test methods. *Journal of Microbiological Methods*, 54(1), 105–110.
- Patel, V., & Venkatakrisshna-Bhatt, H., (1988). Folklore therapeutic indigenous plants in periodontal disorders in India (review, experimental and clinical approach). *International Journal of Clinical Pharmacology Therapy and Toxicology*, 26, 176–184.
- Patil, R., Patil, R., Ahirwar, B., & Ahirwar, D., (2011). Isolation and characterization of antidiabetic actions of essential oil extracted from *Ocimum sanctum* L. leaves in rats fed with high cholesterol diet. *Journal of Applied Biomedicine*, 7, 45–53.
- Paton, A., (1992). A synopsis of *Ocimum* L. (Labiatae) in Africa. *Kew Bulletin*, 47, 403–435.
- Paton, A., Harley, M. R., & Harley, M. M., (1999). *Ocimum*: An overview of classification and relationship. In: Hiltunen, R., & Holm, Y., (eds.), *Basil: The Genus Ocimum* (pp. 1–38). Hardwood, Amsterdam.
- Pattanayak, P., Behera, P., Das, D., & Panda, S. K., (2010). *Ocimum sanctum* Linn. A reservoir plant for therapeutic applications: An overview. *Pharmacognosy Reviews*, 4, 95. doi: 10.4103/0973-7847.65323.
- Pereira, S. L., De Oliveira, J. W., Angelo, K. K., Da Costa, A. M., & Costa, F., (2011). Clinical effect of a mouth rinse containing *Ocimum gratissimum* on plaque and gingivitis control. *The Journal of Contemporary Dental Practice*, 12(5), 350–355.
- Pessoa, L. M., Morais, S. M., Bevilaqua, C. M., & Luciano, J. H., (2002). Anthelmintic activity of essential oil of *Ocimum gratissimum* Linn. and eugenol against *Haemonchus contortus*. *Veterinary Parasitology*, 109(1, 2), 59–63. doi: 10.1016/S0304-4017(02)00253-4.
- Pushpangadan, P., & Bradu, B. L., (1995). Basil. In: Chadha, K. L., & Gupta, R., (eds.), *Advances in Horticulture, Medicinal and Aromatic Plants, Planta Med.* (Vol. 11, pp. 627–657). Malhotra Publishing House, New Delhi, India.
- Pushpangadan, P., (1974). *Studies on Reproduction and Hybridization of Ocimum Species with View to Improving Their Quality*. Ph.D. thesis, Aligarh Muslim University, Aligarh, India.

- Putievsky, E., & Bertalan, G., (1999). Production systems of sweet basil. In: *Basil: The genus Ocimum* (pp. 39–65).
- Rai, V., Iyer, U., & Mani, U. V., (1997). Effect of Tulasi (*Ocimum sanctum*) leaf power supplementation on blood sugar levels, serum lipids and tissue lipids in diabetic rats. *Plant Foods and Human Nutrition*, 50, 9–16.
- Raina, P., Chandrasekaran, C., Deepak, M., Agarwal, A., & Ruchika, K., (2015). Evaluation of subacute toxicity of methanolic/aqueous preparation of aerial parts of *O. sanctum* in Wistar rats: Clinical, haematological, biochemical, and histopathological studies. *Journal of Ethnopharmacology*, 175, 509–517.
- Rasekh, H. R., Hosseinzadeh, L., Mehri, S., Kamli-Nejad, M., Aslani, M., & Tanbakoosazan, F., (2012). Safety assessment of *Ocimum basilicum* hydroalcoholic extract in Wistar rats: Acute and subchronic toxicity studies. *Iran Journal of Basic Medical Science*, 15(1), 645–653.
- Rastogi, S., Kalra, A., Gupta, V., Khan, F., Lal, R. K., Tripathi, A. K., Parameswaran, S., et al., (2015). Unravelling the genome of Holy basil: An ‘incomparable’ ‘elixir of life’ of traditional Indian medicine. *BMC Genomics*, 16(1), 413. doi: 10.1186/s12864-015-1640-z.
- Rasul, A., & Akhtar, N., (2011). Formulation and *in vivo* evaluation for anti-aging effects of an emulsion containing basil extract using non-invasive biophysical techniques. *DARU Journal of Pharmaceutical Sciences*, 19(5), 344–350.
- Rawat, R., Negi, K. S., Mehta, P. S., Tiwari, V., Verma, S. K., & Bisht, I. S., (2016). Study of six varieties of sweet basil (*Ocimum basilicum* L.) and their morphological variations. *Journal of Non-Timber Forest Products*, 23(1), 1–4.
- Renzulli, C., Galvano, F., Pierdomenico, L., Speroni, E., & Guerra, M. C., (2004). Effects of rosmarinic acid against aflatoxin B<sub>1</sub> and ochratoxin-A-induced cell damage in a human hepatoma cell line (Hep G2). *Journal of Applied Toxicology*, 24(4), 289–296.
- Robbins, S. R. J., & Gteenthalgh, P., (1979). *The Markets for Selected Herbs for Essential Oils* (p. 120). Tropical proceedings, Institute. London.
- Roberts, P. D., Raid, R. N., Harmon, P. F., Jordan, S. A., & Palmateer, A. J., (2009). First report of downy mildew caused by a *Peronospora* sp. on basil in Florida and the United States. *Plant Disease*, 93, 199.
- Sakar, S. A., & Nooh, H. Z., (2013). Effect of *Ocimum basilicum* extract on cadmium-induced testicular histomorphometric and immunohistochemical alterations in albino rats. *Anatomy and Cell Biology*, 46(2), 122–130.
- Samson, J., Sheeladevia, R., & Ravindrana, R., (2007). Oxidative stress in brain and antioxidant activity of *Ocimum sanctum* in noise exposure. *NeuroToxicology*, 28(3), 679–685. doi: 10.1016/j.neuro.2007.02.011.
- Sánchez, E., García, S., & Heredia, N., (2010). Extracts of edible and medicinal plants damage membranes of *Vibrio cholerae*. *Applied and Environmental Microbiology*, 76(20), 6888–6894.
- Sarahroodi, S., Esmaeili, S., Mikaili, P., Hemmati, Z., & Saberi, Y., (2012). The effects of green *Ocimum basilicum* hydroalcoholic extract on retention and retrieval of memory in mice. *Ancient Science of Life*, 31(4), 185–189.
- Satoh, T., & Sugawara, Y., (2003). Effects on humans elicited by inhaling the fragrance of essential oils: Sensory test, multi-channel thermometric study and forehead surface potential wave measurement on basil and peppermint. *Analytical Sciences*, 19(1), 139–146.
- Seidler-Łożykowska, K., & Król, D., (2008). The content of essential oil in ten sweet basil (*Ocimum basilicum* L.) cultivars and its composition. *Herbal Polonica Journal*, 54, 7–12.

- Sembulingama, K., Sembulingama, P., & Namasivayamb, A., (2005). Effect of noise stress. *Journal of Ethnopharmacology*, 96, 477–482.
- Shasany, A. K., (2016). The holy basil (*Ocimum sanctum* L.) and its genome. *Indian Journal of History of Science*, 51(2), 343–350. doi: 10.16943/ijhs/2016/v51i2.2/48446.
- Shetty, S., Udupa, S., Udupa, L., & Somayaji, N., (2006). Wound healing activity of *Ocimum sanctum* Linn with supportive role of antioxidant enzymes. *Indian J. Physiology and Pharmacology*, 50, 163–168.
- Shishodia, S., Majumdar, S., Banerjee, S., & Aggarwal, B. B., (2003). Urosolic acid inhibits nuclear factor-kappaB activation induced by carcinogenic agents through suppression of I-kappa-B-alpha kinase and p65 phosphorylation: Correlation with down-regulation of cyclooxygenase 2, matrix metalloproteinase 9, and cyclin D<sub>1</sub>. *Cancer Research*, 63, 4375–4383.
- Siddiqui, B. S., Bhatti, H. A., Begum, S., & Perwaiz, S., (2012). Evaluation of the antimycobacterium activity of the constituents from *Ocimum basilicum* against *Mycobacterium tuberculosis*. *Journal of Ethnopharmacology*, 144(1), 220–222.
- Sienkiewicz, M., Lysakowska, M., Pastuszka, M., Bienias, W., & Kowalczyk, E., (2013). The potential of use basil and rosemary essential oils as effective antibacterial agents. *Molecules*, 18(8), 9334–9351.
- Simon, J. E., Morales, M. R., Phippen, W. B., Vieira, R. F., & Hao, Z., (1999). Basil: A source of aroma compounds and a popular culinary and ornamental herb. In: Janick, J., (ed.), *Perspectives on New Crops and New Uses* (pp. 499–505). ASHS Press, Alexandria, Virginia.
- Singh, D., & Chaudhuri, P. K., (2018). A review on phytochemical and pharmacological properties of Holy basil (*Ocimum sanctum* L.). *Industrial Crops and Products*, 118, 367–382. <https://doi.org/10.1016/j.indcrop.2018.03.048>.
- Singh, S., & Majumdar, D., (1994). Toxicological studies of the fixed oil of *Ocimum sanctum* Linn. (Tulsi). *New Botanist*, 21, 139–146.
- Singletary, K., (2018). Basil: A brief summary of potential health benefits. *Nutrition Today*, 53, 92–97. doi: 10.1097/NT.0000000000000267.
- Smitha, G. R., Thania, S. V., & Manivel, P., (2014). *Cultivation of Ocimum* (pp. 7–26). Extension Bulletin, ICAR–Directorate of Medicinal and Aromatic Plant Research. Anand Press.
- Sokovic, M., & Van, G. L. J. L. D., (2006). Antimicrobial activity of essential oils and their components against the three major pathogens of the cultivated button mushroom, *Agaricus bisporus*. *European Journal of Plant Pathology*, 116(3), 211–224.
- Sokovic, M., Glamoclija, J., Marin, P. D., Brkic, D., & Van, G. L. J. L. D., (2010). Antibacterial effects of the essential oils of commonly consumed medicinal herbs using an *in vitro* model. *Molecules*, 15, 7532–7546.
- Srivastava, A. K., (1980). *French Basil and Its Cultivation in India*. Farm Bulletin No. 16. Central Institute Medicinal and Aromatic Plants, Lucknow, India.
- Stanojevic, L. P., Marjanovic-Balaban, Z. R., Kalaba, V. D., Stanojevic, J. S., Cvetkovic, D. J., & Cakic, M. D. (2017). Chemical composition, antioxidant and antimicrobial activity of basil (*Ocimum basilicum* L.) essential oil. *Journal of Essential Oil Bearing Plants*, 20(6), 1557–1569.
- Suanarunsawat, T., Anantasomboon, G., & Piewbang, C., (2016). Anti-diabetic and anti-oxidative component (bioactivity-guided fractionation) from *Ocimum sanctum* L. (*Lamiaceae*) aerial part. *Asian Pacific Journal of Tropical Biomedicine*, 4, 278–282.



- Suanarunsawat, T., Ayuthaya, W. D. N., Songsak, T., & Rattanamahaphoom, J., (2009). Antilipidemic activity of fixed oil extracted from *Ocimum sanctum* L. leaves in diabetic rats. *Experimental and Therapeutic Medicine*, 11, 832–840.
- Svecova, E., & Neugebauerova, J., (2010). A study of 34 cultivars of basil (*Ocimum* L.) and their morphological, economic, and biochemical characteristics, using standardized descriptors. *Acta Universitatis Sapientiae Alimentaria*, 3, 118–135.
- Švecová, E., (2006). *The Study of Ornamental Species and Varieties of Ocimum L. and Their Content Matters*. Diploma Thesis, Faculty of Horticulture in Lednice, Mendel University, Brno, Czech Republic.
- Swamy, M. K., & Sinniah, U. R., (2016). Patchouli (*Pogostemon cablin* Benth.): Botany, agrotechnology and biotechnological aspects. *Industrial Crops and Products*, 87, 161–176.
- Tada, K. M., Suireshi, M. P., & Mohammad, I. P., (2006). Chemopreventative strategies using extracts of several Indian medicinal plants targeting the expression in human lymphocytes. *International Journal of Oncology*, 29, 1269–1278.
- Tagnolini, M., Barocelli, E., Ballabeni, V., Bruni, R., Bianchi, A., Chiavarini, M., & Impicciatore, M., (2006). Comparative screening of plant essential oils: Phenylpropanoid moiety as basic core for antiplatelet activity. *Life Science*, 78(13), 1419–1432.
- Taie, H. A. A., Salama, Z. A. R., & Radwan, S., (2010). Potential activity of basil plants as a source of antioxidants and anticancer agents as affected by organic and bio-organic fertilization. *Notulae Botanicae Horti Agrobotanici Cluj-Napoca*, 38(1), 119–127.
- Tilebeni, H. G., (2011). Review to basil medicinal plant. *International Journal of Agronomy and Plant Production*, 2, 5–9.
- Tohti, I., Tursun, M., Umar, A., Turdi, S., Imin, H., & Moore, N., (2006). Aqueous extracts of *Ocimum basilicum* L. (sweet basil) decrease platelet aggregation induced by ADP and thrombin *in vitro* and rats arteriovenous shunt thrombosis *in vivo*. *Thrombosis Research*, 118, 733–739.
- Udupa, S. L., Shetty, S., Udupa, A. L., & Somayaji, S. N., (2006). Effect of *Ocimum sanctum* Linn. On normal and dexamethasone suppressed wound healing. *Indian Journal of Experimental Biology*, 44, 49–54.
- Uma, D. P., Ganasoundari, A., Vrinda, B., Srinivasan, K. K., & Unnikrishnan, M. K., (2000). Radiation protection by the *Ocimum* flavonoids orientin and vicenin: Mechanisms of action. *Radiation Research*, 154, 455–460.
- Uneric, S. C., Anaso, H. U., & Anyasoro, J. C., (1998). Insecticidal potentials of *Ocimum basilicum* leaf-extract. *Bioresearch Technology*, 64, 237–239.
- Upadhyay, A. K., Chacko, A. R., Gandhimathi, A., & Ghosh, P., (2015). Genome sequencing of herb Tulsi (*Ocimum tenuiflorum*) unravels key genes behind its strong medicinal properties. *BMC Plant Biology*, 15, 212. doi: 10.1186/s12870-015-0562-x.
- Vats, V., Yadav, S. P., & Grover, J. K., (2004). Ethanolic extract of *Ocimum sanctum* leaves partially attenuates streptozotocin-induced alterations in glycogen content and carbohydrate metabolism in rats. *Journal of Ethnopharmacology*, 90, 155–160.
- Venâncio, A. M., Onofre, A. S., Lira, A. F., Alves, P. B., Blank, A. F., Antonioli, A. R., Marchioro, M., et al., (2010). Chemical composition, acute toxicity, and antinociceptive activity of the essential oil of a plant breeding cultivar of basil (*Ocimum basilicum* L). *Planta Medica*, 77(8), 825–829.
- Venu, P. M. P., & Khanum, F., (2012). Antifatigue activity of ethanolic extract of *Ocimum sanctum* in rats. *Research Journal of Medicinal Plants*, 6(1), 37–46.

- Vieira, R. F., & Simon, J. E., (2000). Chemical characterization of basil (*Ocimum* spp.) found in the markets and used in the traditional medicine in Brazil. *Economic Botany*, 54, 207–216.
- Vieira, R. F., & Simon, J. E., (2005). Chemical characterization of basil (*Ocimum* spp.) based on volatile oils. *Flavor and Fragrance Journal*, 20, 1–8. doi: 10.1002/ffj.1513.
- Viseshakul, D., Premvatana, P., Chularojmontri, V., Kewsiri, D., & Tinnarat, P., (1985). Improved glucose tolerance induced by long term dietary supplementation with hairy basal seeds (*Ocimum canum*) in diabetics. *Journal of the Medical Association of Thailand*, 68(8), 408–411.
- Volpato, G. T., Damasceno, D. C., Calderon, I. M. P., & Rudge, M. V. C., (2002). Review of Brazilian plants with proven hypoglycemic effect in the control of diabetes mellitus. *Revista Brasileira de Plantas Mediciniais*, 4(2), 35–45.
- Waldstein, A., (2006). Mexican migrant ethnopharmacology, pharmacopoeia, classification of medicines and explanations of efficacy. *Journal of Ethnopharmacology*, 108, 99–310.
- Wijesekera, R. O. B., (1986). *Practical Manual on the Essential Oils Industry*. United Nations Industrial Development Organization, Vienna.
- Yaldiz, G., Gul, F., & Kulak, M., (2015). Herb yield and chemical composition of basil (*Ocimum basilicum* L.) essential oil in relation to the different harvest period and cultivation conditions. *African Journal of Traditional Complementary and Alternative Medicine*, 12(6), 71–76.
- Yanishieva, N. V., Marinova, E., & Pokorny, J., (2006). Natural antioxidant from herbs and spices. *European Journal of Lipid Science and Technology*, 108, 776–793.
- Yeşiloglu, Y., & Sit, L., (2012). Antioxidant properties of various solvent extracts from purple basil. *Spectrochimica Acta a Molecular and Biomolecular Spectroscopy*, 95, 100–106.
- Złotek, U., Michalak-Majewska, M., & Szymanowska, U., (2016). Effect of jasmonic acid elicitation on the yield, chemical composition, and antioxidant and anti-inflammatory properties of essential oil of lettuce leaf basil (*Ocimum basilicum* L.). *Food Chemistry*, 213, 1–7.

## CHAPTER 4

---

# *Dioscorea* spp.: Medicinal Plant with Pharmaceutical Uses

RAZA WARIS,<sup>1,2</sup> PRIYANKA AGNIHOTRI,<sup>2</sup> DEBASHIS MANDAL,<sup>3</sup> and AMRITESH C. SHUKLA<sup>1</sup>

<sup>1</sup>*Department of Botany, University of Lucknow, Lucknow, Uttar Pradesh, India*

<sup>2</sup>*Plant Diversity, Systematics and Herbarium Division, CSIR–National Botanical Research Institute, Lucknow, Uttar Pradesh, India*

<sup>3</sup>*Department of Horticulture, Aromatic and Medicinal Plants, Mizoram University, Aizawl, Mizoram, India*

---

### ABSTRACT

*Dioscorea* L. nested in the family Dioscoreaceae, having a wide distribution in Southeast Asia, Africa, Australia, and tropical America, with over 682 species worldwide. In India, there are 42 taxa in the genus (41 species and one variety) distributed mainly in Western Ghats and northeast India. The genus is characterized by having climber habit with tubers and possessing reticulate venation rarely found in monocots. *Dioscorea* is well known for its nutritional and therapeutic properties, and it is extensively in the pharmaceutical and nutraceutical industries. Several *Dioscorea* species exhibit biologically active compounds with antiarthritic, anti-inflammatory, and antifertility properties, making them useful in the treatment of medical ailments. One of the most crucial ingredients of *Dioscorea* is diosgenin. It is worth noting that *Dioscorea* species produce almost half of global steroid drug production. However, Several *Dioscorea* species are on the brink of

extinction due to unrelenting exploitation of the plant for its therapeutic effects mixed with habitat loss, as many of them are included in the IUCN red list.

## 4.1 INTRODUCTION

The largest percentage (70%) of the world's population relies on the conventional healthcare system to treat different diseases (World Health Organization). It is well known that this form of herbal medicinal system has limited side effects (Firenzuoli & Gori, 2007), and in comparison to other traditional pharmaceutical system, it is quite inexpensive, thus being the preferred system in developing countries for most patients. This has resulted in over exploitation of pharmaceutical medicinal plants, herbal medicines, cosmetics, and other natural products that have seen a significant increase in popularity in recent years (Batugal et al., 2004).

Medicinal plants with a wide range of medicinal applications include a wealth of phytochemicals. *Dioscorea* is a peculiar belonging to the family Dioscoreacea, comprising ca. 682 species that have become significant in traditional medicine worldwide. In the making of sex hormones, cardiotonic glucosides, fertility regulation compounds, corticosteroids, and anabolic agents, aglycons of their steroid saponins, such as diosgenin, have gained recognition as precursors (Jasem et al., 2014). It is used in the cure of leprosy and tumors, as well as in the treatment of sore throat and struma. In traditional Indian medicine, it has wide application in piles, ulcers, pain, and inflammation (Kumar et al., 2017). Its medical benefits have been documented in both historical and contemporary literature its tubers have therapeutic advantages such as purgative, anthelmintic, diuretic, rejuvenating tonic, and aphrodisiac, and it's also possible to use it to treat hematological disorders, diabetic disorders, worm infestation, hemorrhoids, and skin disorders (Abhyankar & Upadhyay, 2011). In both Indian and Chinese traditional medicine, it is frequently used to treat gastric cancer, rectum carcinoma, and goiter (Das et al., 2008). Similarly, anti-hyperlipidemic, antitumor, antioxidant, analgesic, anti-inflammatory, and antihyperglycemic extracts are tested (Wang et al., 2012; Mbiantcha et al., 2011). Apart from syphilis in Java and Brazil, it is regarded as a treatment against dysentery and diarrhea. Interestingly, in addition to hepatic fibrosis, it is used in China against dog bites, snake bites, and food poisoning by protecting the liver (Hans, 1996). Remedial capacity against conjunctivitis,

leukoderma, dyspepsia, urinary discharge, jaundice, diabetes, asthma, and bronchitis is also reported (Sharma et al., 2017). *Dioscorea* has emerged as a promising complementary and alternative source of conventional medicine in the recent past, drawing primary attention to impressive scientific developments in modern biomolecule exploration.

## 4.2 BOTANICAL TAXONOMIAL CLASSIFICATION

The herb, *Dioscorea*, is a member of the family Dioscoreaceae. The taxonomic classification of the plant is as described below:

- **Kingdom:** Plantae.
- **Phylum:** Tracheophyta.
- **Order:** Dioscoreales.
- **Class:** Spermatopsida, Mangolipsida, Monocotyledons.
- **Family:** Dioscoreaceae.
- **Genus:** *Dioscorea* L.
- **Species:** *deltodea*, *bulbifera*, *alata*.

The systematic status of the genus has been fascinating to study. The genus for the first time was published by Linnaeus in *Species plantarum*. In *Philosophica Botanica*, he listed *Dioscorea* in the family Sarmantaceae. Later on, de Jussieu, in 1789, put *Dioscorea* along with *Smilax* in section II of the order Asparagi. Finally, Brown, in 1810, placed the genus under Dioscoreaceae and separated it from Smilaceae. Both *Dioscorea* and *Smilax* belong to the same genus and can be differentiated on the basis of the inferior ovary, the capsular fruit, and the large albumen cavity found in *Dioscorea*. Knuth, in 1924, on the basis of his studies, divided the genus *Dioscorea* into four subgenera which were further divided into 60 sections. Later on, several workers like Matuda (1954), Burkill (1960), and Ayenshu (1972) provided different treatments to the genus. Hooker, in his flora of British India, recorded 150 species of *Dioscorea* from the Indian subcontinent. Prain & Burkill (1939) conducted research in many places of the world and concluded with the occurrence of 50 species from India of the genus. Karthikeyan (1989) reported 33 species and 24 Varieties belonging to *Dioscorea* from the Indian subcontinent. In traditional medicinal systems, *Dioscorea* species have been used under the name of yam, Tarun, Garh, Gun, Kin, Singli, Mingli, Gethi, etc. (Table 4.1).

**TABLE 4.1** Vernacular Names of *Dioscorea* Species

Sl. No.	Language	Vernacular Names
1.	English	Water yam, white yam
2.	Hindi	Ratalu, khamalu, kada kanda
3.	Marathi	Chinem, khanphal
4.	Kannada	Dandaanu, hennu genasu
5.	Malayalam	Kacil, Kavattu
6.	Sanskrit	Alukam, dandalu, kandaka
7.	Tamil	Kappan, kavali, pindaka
8.	Telugu	Dukka pendalam, nelavupandalum

### 4.3 GEOGRAPHICAL SOURCE

The plant is mostly distributed in the tropical and subtropical regions of West Africa, Central America, the Caribbean, the Pacific islands, and Southeast Asia tropical and subtropical climates (Caddick et al., 2002). The genus has 50 species in India (Karthikeyan et al., 1989), widely distributed from tropical to sub-temperate zones of Jammu and Kashmir to Arunachal Pradesh, including U.P., M.P., Assam Meghalaya, Manipur, and Nagaland at altitudes of 100–3,500 m. asl. (Table 4.2).

### 4.4 MORPHOLOGY

The Dioscoreaceae family includes the genus *Dioscorea*, or simply the Yam Family. *Dioscorea* L. is either annual or semi-perennials, or perennials. Cultivated species are annuals that are characterized by tubers, stalked or not, elongated to globose, bearing superficial rootlets (sometimes armed). Stem climbing, twining to left or right, with or without recurved prickles, and axillary bulbils are often present. The flowers are basically dioecious. Male flowers are borne singly or in clusters on spikes; spikes aggregated along leafless axes, axes axillary and terminal, or in axillary fascicles; stamens 6 or 3 alternating with staminodes; female flowers with bifid stigma and inferior 3-celled ovary, narrowly ellipsoid, locules each with 2 ovules, style short, stout; stigmatic ridges 3. These flowers consist of a three-sepal calyx and a three-petal corolla, regularly arranged and almost identical in size and appearance (Onwuemw, 1978). Fruits are mostly capsules, broadly 3-winged, shortly stipitate and dehiscent from the apex, sometimes reflexed.

**TABLE 4.2** *Dioscorea* Species: Geological Distribution and Pharmacological Potential

Sl. No.	Name of Taxa	Altitude in Meters	Flowering and Fruiting	Indian Distribution	Worldwide Distribution	Parts Used	Medicinal Application	References
1.	<i>D. alata</i> L.	142–2,272	Aug–Nov	AS, UK, KL, SK	Brazil, China, Nigeria, Thailand	Tuber, leaves, Bulb	Piles, leprosy, kill stomach worms, reduce weakness	Jadhav, Mahadkar, & Valvi (2011)
2.	<i>D. belophylla</i> (Prain) Voigt and Haines	575–1,398	Sep–Dec	MP, AS, KL, SK	Bhutan, Cambodia, Indonesia, Myanmar, Thailand, Vietnam	Tuber	Headache, dysentery, malaria, jaundice, mumps	Srivastava & Nyishi (2010)
3.	<i>D. bulbifera</i> L.	143–2,671	July–Dec	AS, MP, KL, UP, UK, WB	Africa, Pacific Island, Myanmar, Sri Lanka, Tanzania	Tuber	Reduce menopausal problems, and labor pain, prevent miscarriage, reduce body heat, throat pain, skin infection, diabetes, muscular pain, sexual vigor, and wormicide.	Nayak et al. (2004); Patil & Patil (2005); Bhogaonkar & Kadam (2006); Mehta & Bhatt (2007)
4.	<i>D. deltoidea</i> Wall. Ex Gries	122–3,352	July–Nov	AP, J&K, HP, UK, SK, PB	AFG, China, Bhutan, Nepal, Thailand, Vietnam	Tuber	Useful as a uterine sedative, hemostatic, diuretic, and expectorant and eliminates worms from the body.	Humayun (2007)
5.	<i>D. pentaphylla</i> L.	144–2,266	Aug–Nov	MP, UK, SK, WB	Australia, Bangladesh, China, Japan, Nepal, Taiwan	Tuber	Improve body immunity, stomach pain, swelling, abdominal pain, digestive tract, and skin infection.	Edison et al. (2006); Choudhary et al. (2008); Kamble et al. (2010)

Each capsule contains a small seed having wings with numerous species that vary in appearance (Onwueme, 1978). The seeds are light and smooth, and the wings assist with dispersion. Two seeds in each cell, compact, with a broad membranous wing; 2 laminated, compressed, fleshy, or hard albumen; embryo between the blades; suborbicular cotyledons. A distinctive feature of the genus is that, unlike other herbaceous vines such as smilax and morning glories, all leaf veins originate from the leaf base. The main mechanism of propagation is vegetative reproduction.

This is a result of the formation of aerial tubers are formed in the axils of leaves or bulbils. These differ in shape and size, which are roundish. In addition, vast underground tubers are formed, some reaching more than 6 inches in diameter (Figure 4.1).



**FIGURE 4.1** Morphological picture of *Dioscorea deltoidei*.

## 4.5 PHYTOCHEMISTRY

### 4.5.1 CHEMICAL CONSTITUENTS PRESENT IN DIOSCOREA SPECIES

The presence of saponins, tannins, flavonoids, sterols, polyphenols, glycosides (Ghose, 2015), and steroidal saponins (Tapondjou, Jenett-Siems, Bottger, & Melzig, 2013) is shown by *D. bulbifera* in the phytochemical study. Depending on the geographical location, parts of the plants, and the extractions solvents used, the phytochemicals vary. Saponins are the most common secondary metabolites and had 100 steroidal saponins synthesized from aglycone components such as stigmastanol, furostanol, cholesterol, ergostanol, and glycosides of pregnanol were extracted from various *Disocorea* species. Clrodane diterpenes, phenolics, cyanidins, quinones,



diarylheptanoids, and nitrogen-containing compounds were analyzed in *Dioscorea* tubers in addition to such steroids (Kumar et al., 2017). Steroidal saponins primarily consist of furostane, a sixth open ring pentacyclic ring system; spirostane, a hexacyclic ring system; and a tetracyclic ring system, peganane. Glucose and rhamnose constitute the majority of the sugar component in various proportions and couplings. Glucosides consist of an aglycon (diosgenin), and multiple glycosyl moieties are steroidal saponins. Pentose (arabinose, xylose, etc.), hexose (glucose, galactose, etc., and 6-deoxyhexose) are the most popular sugars contained in saponins (rhamnose, etc.). The saponins in this plant species are steroid saponins that are water soluble and water insoluble. *Dioscorea* species are well known to possess steroidal saponins, which have been used as marker compounds for botanical product quality control. Diosgenin (3- $\beta$ -hydroxy-5-spirostene), as stated by Jesus et al. (2016), is the primary furostanol saponin is a promising bioactive component identified in a range of plants, including *Dioscorea* species with a variety of therapeutic activities, including hypolipidemic, antioxidant, anti-inflammatory, hypoglycemic, and antiproliferative (Abhyankar & Upadhyay, 2011).

The rhizomes of *Dioscorea* contain 75% starch. Due to their bitter taste, they are non-edible. The key constituent of *Dioscorea* is diosgenin, a structurally cholesterol-like steroidal saponin that is employed in the production of steroidal hormones and drugs. It is metabolized and removed by bile in the liver (Caven & Dvornik, 1979). Owing to its structural resemblance to estrogen precursors, diosgenin's estrogenic and anti-inflammatory effect has been hypothesized. According to Asha & Nair (2005), the key species exploited in India for the production of diosgenin from rhizomes is *D. deltoidea* Wall. ex Griseb. Tubers are also rich in phenolic compounds and glycosides. Diosgenin is the saponin-dioscin hydrolytic product (Kokate et al., 2008). L-rhamnose and one molecule of D-glucose are made from Dioscin. The flavonoid constituents cyaniding-3-glucoside and procyanidin dimmers B-1 and B-3 were reported in *Dioscorea alata* L. (Ozo et al., 1985). A study shows that *Dioscorea* also includes dioscorins that exhibit activities of carbonic anhydrase and trypsin inhibition (Hour et al., 2000). The presence of saponins, alkaloids, flavonoids, tannins, and phenols in *Dioscorea belophylla* is documented in other studies (Poornima et al., 2007). In *Dioscorea*, bitter components were described as furanoid norditerpenes cyanogens by Bhndari & Kawabata (2005). In 2008, Yoon et al. also documented Allantoin in rhizomes of *Dioscorea*. Allantoin is present in plants as a nitrogen storage form or as a result of the ammonia detoxification process in plant tissues

(Fujihara & Yamaguchi, 1978). Allantoin inhibits the activity responsible for its antidiabetic action of  $\alpha$ -amylase and  $\alpha$ -glucosidase. It has activities that are antioxidant, anti-hyperglycemic, and anti-dyslipidemic. Allantoin could be an excellent standard molecule for the quality control of *Dioscorea* tubers due to their pharmacological significance. Each of these factors makes them sound pharmacological agents and a reliable source of isolation and novel chemical formulation to combat a variety of disorders.

#### 4.5.2 DIOSGENIN AS A RAW MATERIAL FOR STEROID

For the commercial development of 16-dehydropregnenolone acetate (16-DPA), which is a potent intermediate steroid drug obtained from diosgenin, there is a three-step procedure with an average performance of 60%. The steps are: diosgenin 3 acetolysis (isomerization) to pseudodiosgenin diacetate 4, Diosone 5 pseudodiosgenin diacetate 4 oxidation, Dioscone 5 hydrolytic degradation to 16-DPA 1 (Prithish Chowdhary, 2011) (Table 4.3).

**TABLE 4.3** Steroidal Compounds of *Dioscorea* Species

Sl. No.	Class	Compounds	References
1.	Steroidal saponins	Dioscoreanoside A-K, Dioscoreanoside B-K, Dioscin	Liu et al. (2009)
2.	Steroidal sapogenin	Spirostane Glycosides, Cholestane Glycosides Diosbulbin A-D, Diosbulbins A-C, Diosgenin, Sinodiosgenin	Das (2008); Komori (1997)
3.	Diterpenoids	Diosbulbin A-O, Diosbulbin P, 8-Epidiosbulbin E	Tang et al. (2014); Kuetze et al. (2012)
4.	Flavonoids derivatives	Quercetin-3-O- $\beta$ -D-glucopyranoside, Quercetin-3-O- $\beta$ -D-galactopyranoside, Myricetin-3-O- $\beta$ -D-galactopyranoside, Myricetin-3-O- $\beta$ -D-glucopyranoside, 3,5-dimethoxy-kaempferol, 3,5,3'-trimethoxyquercetin, Caryatin, Hyperoside, Kaempferol, Kaempferol-3-O- $\beta$ -D-galactopyranoside, Kaempferol-3-O- $\beta$ -D-glucopyranoside, Kaempferol-3,5-dimethyl ether, Quercetin-3-O-galactopyranoside, Myricetin, Isoquercitrin, Lutein, Quercetin-3-O- $\beta$ -D-glucopyranoside, 7-bis-(4-hydroxyphenyl)-4E, 6E-heptadien-3-one, 5,3,4-trihydroxy-7,7-dimethoxyflavone.	Gao et al. (2002); Liu et al. (2002)
5.	Carotenoids	Neoxanthin, Auroxanthin, Violaxanthin, Cryptoxanthin	Khare (2016)

**TABLE 4.3** (Continued)

Sl. No.	Class	Compounds	References
6.	Phytosterols	Daucosterol, $\beta$ -sitosterol, 3-O- $\beta$ -D-glucopyranosyl-b-sitosterol, Stigmasterol	Liu et al. (2010); Teponno et al. (2006); Gao et al. (2002)
7.	Fatty acids	Palmitic acid, Succinic acid, Shikimic acid, Tetracosanoic acid, 1-(tetracosanoyl)-glycerol, Trans-tetracosanylferulate, Mono-arachidin, C22 $\omega$ -hydroxy fatty acid, 3-hydroxy-5-methoxybenzoic acid, Batatasin III, Behenic acid, Ethyl ester of undecanoic acid, Z-1,9-dodecadiene (CH), n-Hexadecanoic acid, Ethyl ester of Eicosanoic acid.	Kamori (1997); Teponno et al. (2006); Tang et al. (2014)
8.	Tannins	Catechin, Protocatechuic acid, (+) Epicatechin, (-) Epicatechin	Gao et al. (2002); Tang et al. (2014)
9.	Volatile oils	Vanillic acid, Isovanillic acid	Gao et al. (2002); Gupta (1989)
9.	Glycoside derivatives	Dihydrodioscorine a) Methyl-O- $\alpha$ -D-fructofuranoside, Butyl-O- $\alpha$ -D-fructofuranoside, EthylO- $\beta$ -D-fructopyranoside, Butyl-O- $\beta$ -D-fructopyranoside, 3-phenyl-2-propenyl-O- $\beta$ -D-glucopyranoside, 2-(4-methoxyphenyl)-ethyl-O- $\beta$ -D-glucopyranoside, Phenyl-methyl-O- $\beta$ -D-glucopyranoside. Pennogenin, Pennogenin-3-O- $\alpha$ L rhamnopyranosyl-(1 $\rightarrow$ 3)-[ $\alpha$ -L-rhamnopyranosyl-(1 $\rightarrow$ 2)]- $\beta$ -D-glucopyranoside, Pennogenin-3-O- $\alpha$ -L rhamnopyranosyl-(1 $\rightarrow$ 4)-[ $\alpha$ -L-rhamnopyranosyl-(1 $\rightarrow$ 2)]- $\beta$ -D-glucopyranoside, 3-O- $\alpha$ -L-rhamnopyranosyl-(1 $\rightarrow$ 2)-[ $\alpha$ -L-rhamnopyranosyl-(1 $\rightarrow$ 3)]- $\beta$ -D-glucopyranosyl pennogenin (spiroconazol A), 26-O- $\beta$ -D-glucopyranosyl-(25R)-5-en-furost-3 $\beta$ ,17 $\alpha$ ,22 $\alpha$ ,26-tetraol-3-O- $\alpha$ -L-rhamnopyranosyl-(1 $\rightarrow$ 4)- $\alpha$ -L-rhamnopyranosyl-(1 $\rightarrow$ 4)-[ $\alpha$ -L-rhamnopyranosyl-(1 $\rightarrow$ 2)]- $\beta$ -D-glucopyranoside, 23 $\beta$ ,27-dihydroxy-pennogenin 3-O- $\alpha$ -L-rhamnopyranosyl-(1 $\rightarrow$ 4)- $\alpha$ -L-rhamnopyranosyl-(1 $\rightarrow$ 4)-[ $\alpha$ -L-rhamnopyranosyl-(1 $\rightarrow$ 2)]- $\beta$ -D-glucopyranoside, 4-hydroxy-[2-trans-3',7'-dimethylocta-2',6'-dienyl]-6-methoxy acetophenone.	Das (2008); Tang et al. (2014); Shriram et al. (2008); Adetoun & Ikotum (1989)

## 4.6 PHARMACOLOGICAL ACTIVITY

### 4.6.1 ANTI-CANCER ACTIVITY

Steroidal compound cancer therapy is becoming an enticing option for medical chemists, and several active molecules have demonstrated this activity (Selim, 2015). Diosgenin has also been investigated to demonstrate a chemopreventive/therapeutic effect against cancers of multiple organs, and

it has been determined that this chemical is extremely important as a possible anticancer drug (Chen et al., 2015).

#### **4.6.2 IN VITRO ANTI-CANCER EFFECT OF DIOSGENIN**

Diosgenin, the main steroidal sapogenin present in *Dioscorea*, has been shown to powerfully suppress constitutively activated pro-inflammatory and pro-survival signaling pathways and induce apoptosis in a different of cancer cells (Shishodia & Aggarwal, 2006). Shishodia and Aggarwal's previous research (2006) stated that in RAW 2647 macrophage cells, diosgenin abrogated TNF-alpha-induced NFkB activation and suppressed osteoclastogenesis. In Her-2 positive breast cancer cells, diosgenin downregulates the expression of AKT, mTOR, JNK and their related pro-survival signaling pathways, causing apoptosis (Chiang et al., 2007). Further, Li et al. diosgenin could inactive the STAT3 signaling pathway in cells of hepatocellular carcinoma (HCC). Diosgenin repressed STAT3 transcriptional activity as well as the expression of its downstream gene products implicated in proliferation, invasion, and metastasis. Further, HCC cells are made more sensitive to doxorubicin and paclitaxel by diosgenin, which promotes apoptosis in a synergistic way, indicating that diosgenin is a possible bioactive constituent for curing HCC and other cancers (Li et al., 2010). Diosgenin inhibited dose and time-dependent apoptosis in skin squamous cell carcinoma cells A431 and Hep2 (Das et al., 2012). It is noted that HT-29 colon cancer cells are immune to TRAIL-induced apoptosis. Moreover, inhibiting the p38/MAPK signaling pathway and DR overexpression, it strongly inhibited cell proliferation and triggered apoptosis (Lepage et al., 2011). In addition, Romero Hernandez et al. showed that diosgenin-derived thio (seleno) ureas and glycomimetics with 1,2,3-tiazolyl tether on C3 showed more potent anticancer potential in breast cancer cells of MDA-MB-231 and MCF7, hepatocellular carcinoma cells of HepG2 and induced apoptosis compared to their parent compound diosgenin. In another analysis, the combination of diosgenin and methotrexate was considered more effective than the parent diosgenin inhibitor in inhibiting both the growth of transport-resistant breast cancer cells and dihydrofolate reductase (the enzyme involved in DNA synthesis) (Cai et al., 2016). In chronic myeloid leukemia cells, diosgenin-induced autophagy disrupted the mTOR signaling pathway and triggered apoptotic cell death (Jiang et al., 2016). Diosgenin mediated cytotoxicity and significantly inhibited the dose and time-dependent growth and proliferation

of MCF-7 breast cells. Diosgenin has also been found to be effective in the prevention of breast cancer caused by N-nitroso-N-methylurea in rats (Jagadeesan et al., 2013). As a result, diosgenin exhibits antiproliferative effect on prostate cancer (PC-3 and DU 145 cells), colon cancer (HCT-116 and HT-29 cells), erythroleukemia (HEL cells), squamous carcinoma (A431, Hep2, RPMI 265 cells), hepatocellular carcinoma (HepG2 and HCC cells) (Selim, 2015; Kim, 2012; Yli, 2015). Gastric cancer (BGC-823 cells), breast cancer (MCF-7), lung cancer (A549 cells) (Mohammad, 2013), and human chronic myeloid leukemia (K562 cells) (Jiang, 2016). In various stages of tumorigenesis, diosgenin is assumed to cause apoptotic cell death and thus prevent its malignant transformation (Tong, 2012; Chen, 2015; Raju, 2012). The antimetastatic effect is also demonstrated by diosgenin reducing cell migration and incursion by decreasing the expression of matrix metalloproteinase (Chen, 2011). All of the studies listed above have made major disclosures about the possibility of diosgenin being used as a new cancer treatment. Efforts are therefore being made to exploit the ability of diosgenin as an individual drug and with several other bioactive compounds to monitor the growth and spread of different types of human tumors and to investigate their possible mode of action.

#### **4.6.3 ANTI-INFECTIOUS ACTIVITY**

Plant compounds have been assessed for their antimicrobial activity against fungi, bacteria, protozoa, and viruses. All tested species, such as *Candida albicans*, *C. glabrata*, and *C. tropicalis*, are associated with human pathogens (Sautour et al., 2004). Sapogenin was, on the other hand, sensitive to numerous Gram-positive (*Bacillus subtilis*, *B. cereus*, *Staphylococcus*, and *S. epidermis*) and various gram-negative (*E. coli* and *S. typhi*) pathogens (Khan et al., 2015). *D. bulbifera* L. (bulbils) has antimicrobial activity against *Klebsiella pneumonia*, *Escherichia coli*, *Proteus vulgaris*, *Staphylococcus aureus*, *Aspergillus niger*, *A. Flavus*, *A. fumigatus*, and *Rhizopus nigricans* was reported by Seetharam et al. in 2003. Furthermore, diosgenin has been proven to be effective due to its antioxidant properties in certain viral diseases and can be effective in HIV patients with dementia (Turchan et al., 2003) and also exhibits anti-viral activity in *in-vitro* studies against Hepatitis C Virus (HCV). Diosgenin works by reducing plasma cholesterol, and HCV needs cholesterol to multiply efficiently, which shows an anti-viral impact (Wang, 2011). In addition to throat pain, *D. bulbifera* has also

been used in Chinese medicine to treat gonorrhea and syphilis. The aqueous extract of *E. coli* was found to have most strong activity against *E. coli*, whereas the ethanol extract was found to be superior against *S. aureus* and *C. albicans* (Jiang et al., 2016). Recently, norditerpene compound 8-epidiobulin E acetate from *D. bulbifera* bulbs has broad range potential for the treatment of antibiotic resistance plasmid (R-plasmids) from clinical isolates, while low antimicrobial activity (MIC > 400 µg/mL) has been shown for all tested pathogens except *E. coli* (pUC18) with MIC=200 µg/mL. However, *Enterococcus faecalis*, *E. coli*, *Shigella sonnei*, *Pseudomonas aeruginosa*, and *Bacillus subtilis* inclinal strains of R-plasmid were cured effectively. The reduction in the MIC of antibiotics against MDR bacteria due to 8-epidiobulin E acetate R-plasmid treatment has given evidence for the novel mechanism behind the successful antibacterial treatment of *D. bulbifera* (Adetoun & Ikotun, 1989). *D. bulbifera* tubers are used against typhoid fever caused by *Salmonella typhi* and paratyphoid fever caused by *S. paratyphi* A and *S. paratyphi* B in the western highlands of Camerron. When tested against *S. typhi*, *S. paratyphi* A, *S. paratyphi* B, *Pseudomonas aeruginosa*, *E. coli*, *K. pneumonia*, and *S. aureus* using both agar diffusion and broth dilution techniques, two clerodane diterpenoids, bafoudiosbulbins A and b were revealed to have antibacterial activity. Bafoudiosbulbin A and B both selectively exhibited bactericidal activity against *S. typhi*, *S. paratyphi* A, and *S. paratyphi* B (Woo et al., 2014).

#### **4.6.4 ANTI-INFLAMMATORY AND IMMUNOLOGICAL ACTIVITY**

An anti-inflammatory activity in mice was conducted in which it was shown that diosgenin has an inhibitory effect on the development of superoxide in activated bone marrow neutrophils, and it was found that this steroid inhibited the generation of extracellular and intracellular superoxide anion effectively and concentration dependently. In addition, this effect was linked with the suppression of signaling pathways of cAMP, PKA, cPLA 2, Akt, and MAPKs (Lin, 2014). In addition, anti-inflammatory activity was observed in vascular smooth muscle cells (VSMC), and diosgenin was shown to decrease the adhesive ability of VSMC and TNF alpha cells by inhibiting mitogen-activated kinase (MAPK)/protein kinase B (ICAM-1) and vascular cell adhesive molecules (VCAM-1) in VSMC. Further, diosgenin may be beneficial in osteoarthritis, i.e., synovial inflammation and articular cartilage deterioration, due to its anti-inflammatory and immunomodulatory

activities. In this context, it was investigated that this compound inhibits IL-1  $\beta$ -induced expression in human osteoarthritis chondrocytes by inflammatory mediators, including metalloproteinase 3 and 13, iNOS, and COX-2 (Wang, 2015). Further, Diosgenin's role in food allergy regulation was also explored in Balb/c mice, and there was evidence of a suppressive effect on intestinal inflammation, including diarrhea, mast cell degranulation, and the presence of mucin-containing goblet cells in the duodenum. Further, diosgenin has been found to have anti-allergic action *in vivo* to be correlated with the suppression of the development of the IgE and the degranulation of mast cells. Additionally, long diosgenin therapy suppresses phthalic anhydride production-induced skin inflammation using transgenic IL-4/Luc/CNS-1 mice with human IL-4 promoter and enhancer IL-4 (CNS-1) regulated luciferase cDNA was also evaluated. The finding supported the association between IL-4 and the suppression of this steroid in skin inflammation caused by repeated dermal phthalic anhydride exposure. Owing to its anti-inflammatory and immunomodulating properties, diosgenin may also be of grossment in this illness because osteoarthritis is characterized by articular cartilage degeneration, and synovial inflammations are both on the rise. In this sense, diosgenin has also been shown to increase the expression of receptors for VEGF, angiopoietin, and endothelial tyrosine kinase and may, therefore, be a molecule of interest for rheumatoid arthritis.

#### **4.6.5 ANTI-DIABETIC ACTIVITY**

Different studies indicate that in experimental models, Diabetic effects have been observed in yam tubers containing diosgenin and other chemicals (Omoruyi, 2008). In fact, Diabetic treatment with diosgenin could be beneficial by encouraging adipocyte differentiation and suppressing inflammation in adipose tissues. As a result, diosgenin may be advantageous to the patient's health in the obesity-related glucose metabolic disorder. Diosgenin has been reported in other model system in this situation to contribute to a reduction in plasma and hepatic triglycerides, which could be effective in the treatment of hepatic dyslipidemia associated with diabetes. In streptozotocin-induced diabetic rats, diosgenin decreased blood plasma glucose levels. In addition, these studies have shown that diosgenin increases the function of vital enzymes involved in diabetes-changed glucose metabolism (MacAnuff, 2005). Further, studies on lipid accumulation in pre-adipocytes 3T3-L1 in type 2 diabetic rats have shown that diosgenin (0.1 to 10  $\mu\text{mol-L-1}$

concentration) can promote PPAR $\gamma$  (peroxisome proliferative-activated gamma receptor) expression and adipocyte differentiation leading to diosgenin hypolipidemic impact (Sangeetha, 2013). This compound also has a beneficial impact on IKK $\beta$ /IRS-1-dependent insulin resistance, is linked to endothelial dysfunction, and can be, therefore, useful in the prevention or therapy of cardiovascular disorders associated with resistance and diabetes (Gao et al., 2002). Diabetic rats were subsequently given chronic diosgenin administration, which was found to have a hypoglycemic impact as well as the ability to restore vascular responsiveness via endothelium-dependent and independent mechanism, at least partially countering lipid peroxidation, apoptosis, and inflammation (Adetoun & Ikotun, 1989). It was also found in another investigation that glucokinase activity of glucose-6-phosphatase and fructose-1,6-bisphosphatase increased in the liver. In addition, among other positive improvements in many diabetes-related parameters, diosgenin supplementation reduced blood glucose levels in diabetic rats relative to the group of rats who were fed a normal diet. This outcome is consistent with previous investigations suggesting that diosgenin has hypoglycemic characteristics (Komori, 1997).

#### **4.6.6 ANTI-HIV ACTIVITY**

Seven metabolites extracted from ethyl acetate and water fractions of *Dioscorea bulbifera* bulbils were evaluated for anti-HIV 1 integrase activity. The most potent anti-HIV 1 integrase activity (IC<sub>50</sub> 3.15 mM), followed by 2,4,6,7-tetrahydroxy-9,10-dihydrophenanthrenen (IC<sub>50</sub> 1/414.20 mM), quercetin-3-O-b-D-glucopyranoside (IC<sub>50</sub> 1/419.39 mM) and quercetin-3-O-b-D-galactopyranoside (IC<sub>50</sub> 1/421.80 mM) was shown by flavonoid myricetin. Asp64, Thr66, Glu92, Asp116, Gln152, Asn155, and Lys159 interacted with these compounds, which are involved in integrase enzyme 3' processing and strand transfer reactions (Ahmed et al., 2009; Okon & Ofenu, 2013).

#### **4.6.7 ANTIOXIDANT ACTIVITY**

Hydroalcoholic extract of *D. bulbifera* tuber (doses of 100, 200, and 400 mg/kg) reversed indomethacin-induced gastric ulcers associated with free radical alterations can boost antioxidant activity by causing a significant increase in peroxidase and catalase while reducing glutathione peroxidase,



decreasing glutathione and tissue lipid peroxidation. The scavenging ability of consecutive extracts viz. petroleum ether, ethyl acetate, methanol, and 70% ethanol of *D. bulbifera* bulbs was examined against pulse radiolysis produced by ABTS<sup>+</sup> and OH radicals using biochemical methods in addition to DPPH, superoxide, and hydroxyl radicals. Enzymatic assays of antioxidant activity (glutathione peroxidase, catalase, superoxide dismutase, glucose-6-phosphate dehydrogenase, and glucose-s-transferase) and non-enzymatic assays (reduced glutathione, Vitamin C, and E) have also been shown in ethanol extract from *D. bulbifera*.

#### **4.6.8 NEUROPROTECTIVE ACTIVITY**

Certain *Dioscorea* species have been traditionally used to alleviate memory problems and dementia, including Alzheimer's and other neurodegenerative diseases (Yang et al., 2009). The chloroform extract of *D. oppositifolia* rhizomes significantly decreased the dose dependent glutamate induced toxicity with a maximum neuroprotective effect of 10 µg/mL (Tang et al., 2009). Further, the chemicals extracted from *D. nipponica* rhizomes also had antineuroinflammatory and neuroprotective properties, with 3,7-dihydroxy-2,4,6-trimethoxy-phenanthrene being the most potent. With 162.36% stimulated and a strongly reduced nitric oxide (NO) level with an IC<sub>50</sub> value of 19.56 µM in LPS-activated BV2 microglial cells, the latter was the most effective nerve growth factor (NGF) inducer. It also greatly increased the outgrowth of neuritis in mouse neuro2a (N2a) cells and demonstrated considerable neuroprotective activity (Woo et al., 2014).

#### **4.6.9 ANTI-PANCREATITIS AND ANTI-ARTHRITIC ACTIVITIES**

Several compounds at a concentration of 0.5 mM were isolated from the rhizomes of *D. zingiberensis*, i.e., (3R,5R)-3,5-dihydroxy-1-(3,4-dihydroxyphenyl)-7-(4-hydroxyphenyl) heptane displayed anti-pancreatitis activities with an inhibitory effect of 19% on sodium taurocholate induced pancreatic acinary necrosis (Du et al., 2017). Another research recorded that the steroidal saponins extracted from the *D. zingiberensis* rhizomes demonstrated anti-arthritis activities on the 2,647 macrophage cells stimulated by the LPS by inducing both p65 and IκBα protein expressions (Zhang et al., 2014).

#### **4.6.10 ANTI-NOCICEPTIVE ACTIVITY**

The study of the anti-nociceptive effect of *D. bulbifera* L. var sativa (MEDB) bulb of methanol extract was carried out by Nguelefeck et al. (2010). After two doses, the effect of (MEDB) on CFA-induced hypernociception at 250 and 500 mg/kg lasted for 5 days. MEDB significantly inhibited pain caused by acute lipopolysaccharides (LPS) at 500 mg/kg, but it had little effect on spontaneous nociception induced by thermal hypernociception and capsaicin. Nitro-L-arginine methyl ester (1NAME) or glibenclamide antagonized that in the prostaglandin E2 (PGE2) model, MEDB has antinociceptive effects. This showed that the antinociceptive effect of the plant was due to partial activation of the NO-cGMP-ATP-responsive potassium channel pathway.

#### **4.6.11 ANTICOAGULANT AND ANTITHROMBOTIC EFFECTS**

In *in-vitro* and *in-vivo* models, diosgenin has been shown to exert dose-dependent antithrombotic activity in rats by inhibiting platelet aggregation and thrombosis and by prolonging APTT, PT, and TT. This compound also prolonged bleeding coagulation cycles and increased the rate of defense in mice, again in a dose-dependent way (Gong et al., 2011; Zhang et al., 2013). More recently, this steroid and its structural counterpart have been recently found to prevent blood clotting by blocking platelet aggregation (Zheng et al., 2016). Because of this interesting consequence, to increase the drug solubility of the medications and their distribution throughout the body, a diosgenin derivative (theophylline diosgenin) and uracil-ended poly(ethylene glycol) were combined to form a pro medication.

### **4.7 PATENT**

The invention concerns a *Dioscorea* extract and its use in improving the proliferating of some bone marrow and spleen cells, improving the immune system, and treating infections and cancer with immunotherapy. An extract from *Dioscorea* tuber was used to develop the new product, which can increase the activity of the NF-kB-inducible composite promoter ELAM1, promoter GMCSF, and protects animals against certain cancers. This extract can also help to strengthen your immune system for the treatment and

recovery from physical/chemical harm of pathogen infection and cellular transformations. An extract from *Dioscorea* tuber, which is soluble in water and insoluble in 70–80% ethanol, between 0°C and 25°C, is a feature of the invention. The extract can be prepared from *D. batatas* Decne, *D. alata* L., *D. pseudojaponica* or *D. alata* L. var. *purpurea* (Roxb.) M. Pouch. An immunogenic composition containing an antigen and an adjuvant agent is also included in the invention, wherein an extract from *Dioscorea* tuber is used as an adjuvant agent.

The other innovation offers a method for the treatment of osteoporosis in subjects in need of such treatment, including oral administration to subjects of an appropriate quantity of *Dioscorea* extract capable of promoting the proliferation and differentiation of bone marrow cells in subjects in which the species of *Dioscorea* is characterized by spontaneously amplified polymorphic DNA. The invention further includes methods for inducing drowsiness, reducing inflammation, and relieving pain employing a new extract from *Dioscorea hispida*. With certain sedatives, such as barbiturates, being linked to nasty drug reactions and being abused, as well as the problems connected with existing anti-inflammatory agents, *D. hispida* extract might be a possible option. This idea intends to provide a more effective but less expensive alternative to currently available sedatives, anti-inflammatory agents, and pain medications.

## KEYWORDS

- **anti-HIV activity**
- **antioxidant activity**
- ***Dioscorea* spp.**
- **distribution**
- **diversity**
- **immunological activity**
- **neuroprotective activity**
- **pharmaceuticals**
- **taxonomy**

## REFERENCES

- Abhyankar, R. K., & Upadhyay, R., (2011). Ethno medicinal studies of tubers of Hoshangabad, M.P. *Bulletin of Environment, Pharmacology and Life Sciences*, 1(1), 57–59.
- Adetoun, A., & Ikotun, T., (1989). Antifungal activity of dihydrodioscorin extracted from a wild variety of *Dioscorea bulbifera* L. *J. Basic Microbiol.*, 29, 265–267.
- Ahmed, Z., Chishti, M. Z., Johri, R. K., Bhagat, A., Gupta, K. K., et al., (2009). Antihyperglycemic and antidiyslipidemic activity of aqueous extract of *Dioscorea bulbifera* tubers. *Diabetologia Croatica*, 38(3): 69–72.
- Batugal, P. A., Kanniah, J., Lee, S. Y., & Oliver, J. T., (2004). 1 international plant genetic resources institute. In: Batugal, P. A., Kanniah, J., Lee, S. Y., & Oliver, J. T., (eds.), *Medicinal Plants Research in Asia: The Framework and Project Workplans* (Vol. I, p. 9).
- Caddick, L. R., Rudall, P. J., Wilkin, P., Hedderson, T. A., & Chase, M. W., (2002). Phylogenetics of *Dioscoreales* based on combined analyses of morphological and molecular data. *Bot. J. Linn. Soc.*, 138, 123–144.
- Cai, B., Liao, A., Lee, K. K., Ban, J. S., Yang, H. S., Im, Y. J., & Chun, C., (2016). Design, synthesis of methotrexate-diosgenin conjugates and biological evaluation of their effect on methotrexate transport-resistant cells. *Steroids*, 116, 45–51.
- Chiang, C. T., Way, T. D., Tsai, S. J., & Lin, J. K., (2007). Diosgenin, a naturally occurring steroid, suppresses fatty acid synthase expression in HER2-overexpressing breast cancer cells through modulating Akt, mTOR, and JNK phosphorylation. *FEBS Lett.*, 581, 5735–5742.
- Das, A. K., Dutta, B. K., & Sharma, G. D., (2008). Medicinal plants are used by different tribes of Cachar district, Assam. *Indian Journal of Traditional Knowledge*, 7(3), 446–454.
- Das, A., (2008). *Agro-Techniques of Selected Medicinal Plants* (Vol. 1, pp. 85–88). TERI Press, India.
- Das, S., Dey, K. K., Dey, G., Pal, I., Majumder, A., Maiti Choudhury, S., Kundu, S. C., & Mandal, M., (2012). Antineoplastic and apoptotic potential of traditional medicines thymoquinone and diosgenin in squamous cell carcinoma. *PLoS One*, 7, e46641.
- Fan, X. J., Jiao, J. J., & Zhao, Y. Q., (2008). Effects of dioscin on adenosine phosphates in rat myocardium with ischemia-reperfusion. *J. Tianjin Med. Univ.*, 14(4), 409–411.
- Firenzuoli, F., & Gori, L., (2007). Herbal medicine today: Clinical and research issues. *Evidence-Based Complementary and Alternative Medicine*, 4(s1), 37–40.
- Gao, H. Y., Kuroyanagi, M., Wu, L. J., Kawahara, N., Yasuno, T., & Nakamura, Y., (2002). Antitumor-promoting constituents from *Dioscorea bulbifera* L. in JB6 mouse epidermal cells. *Biol. Pharm. Bull.*, 25(9), 1241–1243.
- Gupta, D., & Singh, J., (1989). p-hydroxyacetophenone derivatives from *Dioscorea bulbifera*. *Phytochemistry*, 28, 947–949.
- Hans, D. N., (1996). *African Ethnobotany: Poisons and Drugs: Chemistry, Pharmacology, Toxicology* (pp. 423, 424). Chapman & Hall GmbH, D-69126, Heidelberg.
- Jadhav, V. D., Mahadkar, S. D., & Valvi, S. R., (2011). Documentation and ethnobotanical survey of wild edible plants from Kolhapur District. *Rec. Res. Sci. Technol.*, 3, 58–63.
- Jagadeesan, J., Langeswaran, K., Gowthamkumar, S., & Balasubramanian, M. P., (2013). Diosgenin exhibits beneficial efficiency on human mammary carcinoma cell line MCF-7 and against N-nitroso-N-methylurea (NMU) induced experimental mammary carcinoma. *Biomed. Prev. Nutr.*, 3, 381–388.

- Jasem, A., Khan, M., Taha, A., & Thiemann, T., (2014). Preparation of steroidal hormones with an emphasis on transformations of phytosterols and cholesterol—A review. *Mediterranean Journal of Chemistry*, 3(2), 796–830.
- Jiang, S., Fan, J., Wang, Q., Ju, D., Feng, M., Li, J., Guan, Z. B., An, D., Wang, X., & Ye, L., (2016). Diosgenin induces ROS-dependent autophagy and cytotoxicity via the mTOR signaling pathway in chronic myeloid leukemia cells. *Phytomedicine*, 23, 243–252.
- Karthikeyan, S., Jain, S. K., Nayar, M. P., & Sanjappa, M., (1989). *Florae Indicae Enumeration: Monocotyledonae* (p. 435). Botanical Survey of India, Calcutta.
- Khare, C. P., (2016). *Ayurvedic Pharmacopoeial Plant Drugs-Expanded Therapeutics* (pp. 227, 228). CRC Press, Boca Raton, London, New York.
- Komori, T., (1997). Glycosides from *Dioscorea bulbifera*. *Toxicol.*, 35, 1531–1536.
- Kuete, V., Bertrandponno, R., Mbayeng, A. T., Taponjou, L. A., Meyer, J. J., et al., (2012). Antibacterial activities of the extracts, fractions, and compounds from *Dioscorea bulbifera*. *BMC Complement Altern Med.*, 12, 228.
- Kumar, S., Das, G., Shin, H. S., & Patra, J. K. (2017). *Dioscorea* spp. (a wild edible tuber): A study on its ethnopharmacological potential and traditional use by the local people of simlipal biosphere reserve, India. *Front. Pharmacol.*, 8, 52.
- Lepage, C., Leger, D. Y., Bertrand, J., Martin, F., Beneytout, J. L., & Liagre, B., (2011). Diosgenin induces death receptor-5 through activation of the p38 pathway and promotes trail-induced apoptosis in colon cancer cells. *Cancer Lett.*, 301, 193–202.
- Li, F., Fernandez, P. P., Rajendran, P., Hui, K. M., & Sethi, G., (2010). Diosgenin, a steroidal saponin, inhibits the STAT3 signaling pathway, leading to the suppression of proliferation and chemosensitization of human hepatocellular carcinoma cells. *Cancer Lett.*, 292, 197–207.
- Liu, H., Chou, G. X., Guo, Y. L., Ji, L. L., Wang, J. M., et al., (2010). Norclerodane diterpenoids from rhizomes of *Dioscorea bulbifera*. *Phytochemistry*, 71(10), 1174–1180.
- Liu, Y. W., Shang, H. F., Wang, C. K., & Hou, W. C., (2007). “Immunomodulatory activity of dioscorin, the storage protein of yam (*Dioscorea alata* cv. Tainong No. 1) tuber. *Food and Chemical Toxicology*, 45(11), 2312–2318.
- Mbiancha, M., Kamanyi, A., Teponno, R. B., Taponjou, A. L., Watcho, P., & Nguelefack, T. B., (2011). Analgesic and anti-inflammatory properties of extracts from the bulbils of *Dioscorea bulbifera* L. var sativa (*Dioscoreaceae*) in mice and rats. *Evid-Based. Complement. Altern. Med.*, 2011, 912–935. doi: 10.1155/2011/912935.
- Ni, L., Xu, P., & Wu, X. S., (2007). Antioxidative effect of dioscin on cardiomyocyte following hypoxia/reoxygenation injury. *Shanghai J. Tradit. Chin. Med.*, 41(11), 76, 77.
- Ning, K. Y., Li, Y. K., & Gao, H. L., (2007). Effect of MPD on acute myocardial ischemia in dogs. *Tradit. Chin. Drug Res. Clin. Pharmacol.*, 18(6), 417–421.
- Ning, K. Y., Li, Y. K., & Gao, H. L., (2008). Therapeutic effects of methyl protodioscin for myocardial infarction in rats. *Tradit. Chin. Drug Res. Clin. Pharmacol.*, 19(1), 1–3.
- Okon, J. E., & Ofeni, A. A., (2013). Antidiabetic effect of *Dioscorea bulbifera* on alloxan-induced diabetic rats. *CIB Tech. J. Pharmaceut Sci.*, 2(1), 14–19.
- Sharma, M., Hotpet, V., Sindhura, B., Kamalanathan, A., Swamy, B. M., & Inamdar, S. R., (2017). Purification, characterization, and biological significance of mannose binding lectin from *Dioscorea bulbifera* bulbils. *Int. J. Biol. Macromol.*, 102, 1146–1155.
- Shishodia, S., & Aggarwal, B. B., (2006). Diosgenin inhibits osteoclastogenesis, invasion, and proliferation through the downregulation of Akt, I kappa B kinase activation, and NF-kappa B-regulated gene expression. *Oncogene*, 25, 1463–1473.

- Shriram, V., Jahagirdar, S., Latha, C., Kumar, V., Puranik, V., et al., (2008). A potential plasmid-curing agent, 8-epidiosbulbin E acetate, from *Dioscorea bulbifera* L. against multidrug-resistant bacteria. *Int. J. Antimicrob. Agents*, 32(5), 405–410.
- Sonibare, M. A., & Abegunde, R. B., (2012). *In vitro* antimicrobial and antioxidant analysis of *Dioscorea dumetorum* (Kunth) Pax and *Dioscorea hirtiflora* (Linn.) and their bioactive metabolites from Nigeria. *Journal of Applied Biosciences*, 51, 3583–3590.
- Tang, Y., Xue, Y. B., Zhou, L., Zhang, J. W., Yao, G. M., et al., (2014). New norclerodane diterpenoids from the tubers of *Dioscorea bulbifera*. *Chem. Pharm. Bull. (Tokyo)*, 62(7), 719–724.
- Teponno, R. B., Tapondjou, A. L., Donatien, G., Djoukeng, J. D., Mansour, E. A., et al., (2008). Bafoudiosbulbins F and G, further clerodane diterpenoids from *Dioscorea bulbifera* L var sativa and revised structure of Bafoudiosbulbin B. *Phytochemistry*, 69(12): 2374–2379.
- Wang, T., Choi, R. C., Li, J., Bi, C. W., Ran, W., Chen, X., Dong, T. T., Bi, K., & Tsim, K. W., (2012). Trillin, a steroidal saponin isolated from the rhizomes of *Dioscorea nipponica*, exerts protective effects against hyperlipidemia and oxidative stress. *J. Ethnopharmacol.*, 139, 214–220.
- Woo, K. W., Kwon, O. W., Kim, S. Y., Choi, S. Z., Son, M. W., Kim, K. H., & Lee, K. R., (2014). Phenolic derivatives from the rhizomes of *Dioscorea nipponica* and their anti-neuroinflammatory and neuroprotective activities. *J. Ethnopharmacol.*, 155, 1164–1170.
- Yang, M. H., Yoon, K. D., Chin, Y. W., Park, J. H., Kim, S. H., Kim, Y. C., & Kim, J., (2009). Neuroprotective effects of *Dioscorea opposita* on scopolamine-induced memory impairment in *in-vivo* behavioral tests and *in vitro* assays. *J. Ethnopharmacol.*, 121, 130–134.
- Zhang, X. X., Ito, Y., Liang, J. R., Liu, J. L., He, J., & Sun, W. J., (2014). Therapeutic effects of total steroid saponin extracts from the rhizome of *Dioscorea zingiberensis* CH Wright in Freund's complete adjuvant induced arthritis in rats. *Int. Immunopharmacol.*, 23, 407–416.

## CHAPTER 5

---

# *Eucalyptus* spp.: A Wonder Tree

MOUMITA MALAKAR

Assistant Professor, Department of Horticulture,  
Central University of Tamil Nadu, Neelakudy, Thiruvarur,  
Tamil Nadu, India

---

### ABSTRACT

*Eucalyptus* (*Eucalyptus* spp.) is a large genus of the Myrtaceae family, includes 900 species and subspecies. The enhanced popularity (for significant uses) and wide adaptability to different conditions of eucalyptus tree motivated many government and private organizations to adopt its cultivations at a commercial scale. In low fertile land or in wasteland, it can be grown successfully. It meets the requirements of people and industries and has helped to reduce pressure on natural forests. In recent decades, the demand for *Eucalyptus* plant-derived products for therapeutic uses has amplified. So, utilization of essential oils extracted from its multiple plant parts for clinical, industrial, and various biological purposes *viz.* antimicrobial, antioxidant, anti-inflammatory, antiseptic, astringent, antitumor, antihistaminic, anticancer cytochrome p450 inhibitor and hepatoprotective effects have been commercialized in food and cosmetic industries. *Eucalyptus* essential oil contains several constituents' like 1,8-cineole ('eucalyptol,' the principal component),  $\alpha$ -pinene,  $\beta$ -myrcene (1.5%),  $\beta$ -pinene, limonene,  $\alpha$  phellandrene,  $\gamma$ -terpinene, linalool, pinocarveol, terpinen-4-ol, and  $\alpha$ -terpineol extracted basically from leaves. Array of pharmaceutical components demonstrated a range of pharmacological effects including hypoglycemic action. The volatile and non-volatile constituents of *Eucalyptus* include monoterpenes (hydrocarbon and oxygenated monoterpenes), sesquiterpenes (hydrocarbon and oxygenated sesquiterpens) and tri-terpenoids, flavonoids, flavanols, gallotannins, quercetin, euglobals,

procyanidins, macro-carpals. Discrimination of inter-specific hybrids from contaminants like *E. urophylla*, *E. grandis*, and *E. saligna* using RAPD and Simple Sequence Repeat (SSR) markers to obtain an exclusive fingerprint of its hybrids with high potential for vegetative propagation used in breeding programs have also been executed. Overall, strong and effective Plant Variety Protection and Farmers Right (PVPFR) is important for strengthening the safety issues of grass-root level farmers.

## 5.1 GENERAL INTRODUCTION

Eucalyptus, is a member of the family ‘Myrtaceae’ (tribe – Eucalyptae), commonly known as ‘Eucalypt.’ Approximate 700–900 species of Eucalyptus are available which secure its position next to the largest genera namely *Acacia*. During 1850s, first Eucalyptus was introduced in 90 different countries among which Australia and Tasmania are most popular for having wide germplasm (Brooker, 2000) but some species had also found out from the outskirts of Australian territory (Eldridge et al., 1994). As for example, *Eucalyptus deglupta* is prevalent in Sulawesi and Ceram (Indonesian islands), Mindanao (Southern Philippines), Northern New Guinea and New Britain while *E. urophylla*, *E. orophila*, and *E. wetarensis* exist in Timor and Sunda group of islands (Pryor et al., 1995). Among all existing species, *E. globulus* (known as Australian Eucalyptus or ‘Blue gum’ [in English] or ‘Karpuramaram’ [in Tamil]) is widely distributed all over the world especially in subtropical and Mediterranean regions. By habit, it’s a tall, evergreen, flowering trees and shrub form woodlands. Their stem bark may be smooth, fibrous, hard or stringy, leaves sickle shaped with oil glands exude oil during extraction, tepals (when sepals and petals got fused with each other) form an ‘Operculum’ or ‘Cap’ above the stamens, fruit is woody capsule, known as ‘Gum-nut.’ They prefer to grow at high rainfall to semi-arid regions at the altitude ranges from sea level to subalpine. The potential of this tree to re-sprout after the fire issue prove its fire adaptation, one of the prime features of forest tree species. Since time immemorial, the use of Eucalyptus for ethnomedicinal purposes by aboriginals is well-known. Barring its utilizations as forest timber, fuel, paper pulp and food, its environmental uses, like erosion control caused by water and wind and also as a vital source of essential oils (used in perfumery and floral art and crafts industry) are noteworthy. Many countries are adopting eucalyptus plantations at commercial scale for its appropriateness in cosmetics, food, and beverage industry as well as for aromatherapy and phyto-therapy. In



contrast, the highly inflammable nature and growth inhibition impact on other plants existing in its vicinity sometimes restrict its cultivation. The 'Allelopathic' effect (chemical interaction b/w plants) (Naithani, 2017) caused due to allelochemicals of Eucalyptus is evident by various advanced research. The herbicidal properties of the identified allelochemicals had been reported by Zang & Fu (2009). They reported the weed control potential of those allelochemicals.

Eucalypts for its multifaceted uses (pulp and paper production, charcoal, energy, furniture, housing, etc.) got prime attention since ancient times. Rapid growth, sumptuous biomass production ability (good quality of wood, short cellulose fiber, etc.) and adaptability to wide range of environmental conditions are chief reasons for its successful cultivation and fame. During early 1900s, the eucalyptus plantations throughout the long stretch of railway tracks in Brazil and South Africa supplied significantly sumptuous amount of charcoal for locomotives. According to FAO (2000), total 16–19 million hectares of eucalyptus plantation was found in Asia, South America, Southern Europe and Africa. *E. grandis*, *E. globulus*, *E. camaldulensis* – these three are mostly used for commercial plantation purpose while *E. grandis* and *E. urophylla* used in tropical and subtropical regions and *E. globulus* in temperate regions (Potts, 2004).

Cloning techniques assist significantly for spreading of commercial plantations of Eucalyptus, introduced in Popular Republic Congo in 1975 (Delwaulle et al., 1983). The rooted cuttings of eucalyptus hybrids possess long, clear, straight trunk and could yield good quality of woods are employed for its extensive plantations. Uniform inheritance of traits from parents to offspring is one of the merits of asexual propagation which attract the attention of paper and pulp industries. High quality of timber and uniform biomass production – these two are prime factors for pulp production, hence, vegetative propagation gets utmost importance for Eucalyptus. Micropropagation for Eucalyptus had been introduced during mid of 1970s (Durand-Cresswell et al., 1985) and till date it is the most the most feasible way of propagation for selected genotypes of Eucalyptus at commercial scale. Due to its burgeoning demand, exclusively in South America and Africa province, it seems mandatory to approach for more advanced breeding programs and also to introduce exotic species from its native place Australia.

During last 1 decade, Agrobacterium was used as vector for the genetic transformation needed to develop transgenic eucalyptus trees (Gonz'alez et al., 2002). Diversity analysis with aid of genetic makers is also another effective mode for appropriate selection of eucalyptus cultivars for breeders to

get disease and stress tolerant and high-quality wood yield varieties. Except this technique, expressed sequence tag (EST) sequencing programs are most advanced biotechnological tools for further improvement of eucalyptus tree.

According to Kadambi (1944) eucalyptus tree was first planted in India by Tippu Sultan during 1790 in his Nandi hills garden at Bangalore but Bhatia (1984) cited that the ruler of Mysore, Tippu Sultan had summoned eucalyptus seeds from Australia followed by planting of about 16 species in India. In India *E. tereticornis*, *E. grandis*, *E. citriodora*, *E. globulus* and *E. camaldulensis* species are quite popular. Extensive research had been made on biologically active ingredients of Eucalyptus (Indian origin) essential oil and also on its antimicrobial potential. According to Bhatia (1984), there is no available information on chemical constituents of essential oil extracted from leaves of *E. globulus* grown in Dehradun, India. First fossil record of Eucalyptus was found in Laguna del Hunco deposit in Chubut province, Argentina during Eocene ear (51.9 Mya) (Hermsen et al., 2012). According to palynological survey report, the oldest eucalyptus fossil was found in South America which was of course not the endemic place for this genus but proves its Gondwanan distribution. Few authors also mentioned about the evidence of eucalyptus leaf fossils found during Miocene era in New Zealand where eucalypts are not endemic (Hermsen et al., 2012). Even after being the native place of Eucalyptus (contributes 75% of total vegetation), the fossil record of Cenozoic era is quite finite in modern Australia. Around 21-million-year oil tree-stump is the most authentic macrofossil of Eucalyptus among other available fossil records preserved in basalt rock at Lachlan Valley in New South Wales (Alley et al., 1999). Not a single specimen of Eucalyptus was found during the investigations made on fossil floras of Paleocene to Oligocene of South-Eastern Australia. Benrow et al. (1995) explained the aforementioned condition based on the hypothesis that the abundance of mesic non eucalypt vegetation (during mid-tertiary era) was found at the continental margins of Australia while the arid continental interior vegetations contained enough eucalypts. Eucalypts replaced the most of all mesic and rainforest vegetations situated at the continental margins due to successive drying phenomenon since Miocene (Berry, 1916). Afforestation programs are the key reasons of super-dominance of Eucalyptus in Australia. Callen & Cowley (1995) found the correlation between the increase of eucalyptus pollens and the increased sediments of charcoal although its rate varied all over Australia. The afore stated information proves a link between increased rates of artificial fire phenomenon by the intervention of aboriginals and the augmented number of this highly fire-tolerant genus in Australia.

Eucalyptus tree is distributed in tropical regions. According to Pandey (1992) in tropical Africa, 3 million hectares of land, in total, were under eucalyptus cultivation during 1990 but the total land area under its cultivation was reduced to 1.7 million hectares during 1980. In tropical America and Asia, the areas under eucalyptus plantation were 8.6 and 32.3 million hectares in 1990 respectively while 4.9 and 11.2 million hectares in 1980, respectively. Pandey (1992) reported the mean annual rate of 127, 373, and 2,112 for forest plantation using Eucalyptus in tropics. In these 3 regions, the total estimated areas under the plantation of key eucalyptus species (*E. globulus*) are 10.06 million hectares.

Modern trend of using eco-friendly products as compared to synthetic ones strengthening the utilization of plant-based products in food, drinks, toiletries, and cosmetics sectors. Eucalyptus essential oils are of great importance in diversified field (like food, pharmaceutical, aromatherapy, perfumes, antibacterial-antifungal, and insecticidal-pesticidal agents, etc.) (Vecchio & Clara, 2016). Foliage(s) of Eucalyptus are the chief source of essential oils, extracted using Steam/hydro-distillation method. The key component of eucalyptus essential oil is 1,8-cineole (cineole or eucalyptol) which makes it medicinally worthy (cineole or eucalyptol) (Begossi, 1996). Other range of chemical constituents like terpenes and its oxygenated derivatives (mono and sesqui-terpenoids), hydrocarbons, aromatic derivatives, esters, and alcohols found to be present in eucalyptus EO. Essential oil of Eucalyptus is used basically as folk medicine and also as anesthetic, vermifuge, sedative, suppurative, rubefacient, stimulant, disinfectant, deodorant, astringent, anodyne, antiphlogistic, antiseptic, diaphoretic, expectorant, febrifuge, antiperiodic, hemostat, inhalant, insect repellent, fumigant, preventative, tonic, and rubefacient (Lo Cantore et al., 2009). Barring the 9 commercially and medicinally vital eucalyptus species, *E. cinerea*, *E. cneorifolia* and *E. macarthurii* are also important. The former 2 species used extensively for its medicinal properties while the latter one in perfumery industry. The insect and pest repelling potential and antioxidant properties of leaf extracted essential oil of Eucalyptus is well-known. The Tasmanian Blue-gum (*E. globulus*) is the chief essential oil extracting species having straight, strong, blotched trunk, blue-green foliage(s) and creamy white blooms (Damjanović-Vratnica et al., 2011; Dixit et al., 2012). In Tasmania, it is mainly cultivated for its timber, pulp, and essential oils. The ethno-medicinal and therapeutic significance of *E. citriodora*, *E. camadulensis* and *E. urophylla* are noteworthy. The first species is used as analgesic, anti-inflammatory, and antipyretic to heal respiratory infections (like cold, flu, and sinus congestion, etc.) while the latter two

species used as antibacterial, antifungal, analgesic, and anti-inflammatory agents and also for their antioxidative and antiradical activities (Vecchio & Clara, 2016). The quantity and quality of *Eucalyptus* essential oils vary greatly owing to the time of harvesting and other environmental conditions.

## 5.2 AREA AND PRODUCTION

### 5.2.1 PLANTATION AREAS IN THE TROPICS

The afforestation strategies during 1981–1990 had been adopted with an aim to plant 2.6 million per ha of forest tree species annually to increase the green cover area in tropics of 43.8 million ha. In India, Indonesia, Brazil, Vietnam, and Thailand, 85% of the total green area was established. Around 60% of the total estimated areas were planted with other non-commercial tree species (those areas known as ‘non-industrial’ areas) and rest of the area (around 10 million ha) was planted with the genus *Eucalyptus* (Ball, 1995).

### 5.2.2 ASIA AND THE PACIFIC REGION

Major enhancement of the total forest areas was made during 1981–1990 in Tropical Asia and Pacific regions. The planting was made at the rate of 2.11 million ha year<sup>-1</sup> (81% of gross area). This percent of afforested areas has only covered ½ of the total deforested areas. Further plantations with more good quality wood harvesting species (like *E. globulus*) are needed although several provisos still existing (Ball, 1995). South Africa, Portugal, Spain, Brazil, Australia, Chile, and Swaziland – these are the significant producers of eucalyptus oil but China is the highest producer of it (contributes 75% of total world’s trade). Although the quality of oil produced by China is inferior due to its blending nature (cineole mixed with camphor) rather than the true eucalyptus oil (Gauthier, 1991).

The amount of major chemical constituents usually varies depending on the species. As for example, *E. kochii* and *E. polybractea* contain significant amount of cineole content (80–95%) although globally *E. globulus* has secured its position. According to British Pharmacopoeia, at least 70% of the cineole content in essential oils can qualify its pharmaceutical grade. According to Campinhos (1993), to meet the global requirement of medicinal and perfumery grade eucalyptus essential oil, 3,000 and 1,500 tons of total eucalyptus production per annum was needed during 1991. Piperitone, phellandrene, citral, methyl cinnamate and geranyl acetate – these are the non-cineole components of eucalyptus essential oil. Varying proportions of them require rectification

to upgrade the qualitative and quantitative value of essential oils. Based on the composition and end-use, *Eucalyptus* oils are classified into 3 groups viz. medicinal, perfumery, and industrial. The utmost important component is 'Cineole' (a transparent mobile liquid but may turn into yellow color as its age proceeds) of woody-sweet scent (Ball, 1995) (Table 5.1).

**TABLE 5.1** Reported Plantation Areas, Tropical Asia-Pacific Region ('000 ha)

Countries	Up to Year End 1980			Up to Year End 1990			Average Annual Rate
	Industrial	Non-Ind.	Total	Industrial	Non-Ind.	Total	
Bangladesh	128	32	160	189	146	*335	1,480
Bhutan	2		2	5		5	
India	1,536	2,950	4,486	5,670	13,230	18,900	
Nepal	19		19	55	25	80	
Pakistan	–	160	160	88	152	240	
Sri Lanka	112	18	130	180	18	198	
South Asia	1,797	3,160	4,957	6,187	13,571	19,758	
Laos	4		4	4	2	6	140
Myanmar	30	25.7	55.7	222	112.8	334.8	
Thailand	63	272.4	335.4	377	378.5	775.5	
Vietnam	60	1,340	1,400	600	1,500	2,100	
C.S.E Asia	157	1638.1	1795.1	1,203	1993.3	3196.3	
Indonesia	1,446	2,564	4,010	1,430	7,320	8,750	482
Malaysia	26		26	115.5		115.5	
Philippines	65	235	300	60	230	290	
S.E. Asia	1,537	2,799	4,336	1605.5	75.50	9155.5	
Fiji	40		40	90.2	13.8	164	16
N. Caledonia	7		7	10		10	
Papua N.G.	17	5	22	35	7.6	42.6	
Samoa	2		2	6		10	
Solomon Island	17		17	24.6		21.6	
Vanuatu	0	0	0	1	1	2	
Pacific Island	83	5	88	166.8	22.4	365.2	
<b>Total</b>	<b>3,574</b>	<b>7602.1</b>	<b>111176.1</b>	<b>9162.3</b>	<b>23136.7</b>	<b>32,299</b>	<b>2,112</b>

\*Excludes about 3,00,000 ha of homestead plantations.

Source: Pandey (1992).

### 5.3 MARKETING AND TRADE

*Eucalyptus*, native to Australia is now cultivated throughout the globe to meet the rising demand of its essential oil extracted using steam distillation method by diversified manufacturing industries. *Eucalyptus* oil furnishes antioxidant protection, boost immunity, and progresses respiratory circulation. The burgeoning demand for eucalyptus essential oil especially in aromatherapy is really noticeable but along with it in the perfumery, cosmetics, food and beverage industries too its mandate is significant. The inclination towards using eco-friendly products encouraging research communities to develop array of new beauty formulations with almost zero side-effects. Additionally, its antiseptic quality causes its uses in medicinal supplements, pharmaceutical products related to hypertension and lung ailments. This multifaceted use of eucalyptus essential oil has augmented its trade all over the world which will be nearly US \$900 million revenues by end of 2022 end.

Raw material used for the production of eucalyptus essential oil is 'Leaf.' To maintain the pace with the current demand, the major problem intrinsically associated is the depletion of source (i.e., raw material *alias* eucalyptus leaf) emerging now-a-days owing to massive quantity of leaf requirement for yielding of an ounce of eucalyptus oil. The initial investment for production of eucalyptus essential oil is very high due to employment of many advanced equipment. The situation become more whammy for new entrants as along with the huge capital investment during initial phase, the extreme obstacles posed by established, leading entrepreneurs. Overall, key challenges counting high capital investment and certification procedure by government ultimately slowing down the growth rate of eucalyptus oil industry throughout the world (Retrieved from: <https://www.factmr.com/media-release/79/eucalyptus-oil-market>).

#### **5.3.1 CURRENT AND FUTURE STATUS OF WORLD EUCALYPTUS OIL MARKET (SOURCE: BY FACT. MR REPORT, 2017 [LINK: [HTTPS://WWW.FACTMR.COM/MEDIA-RELEASE/79/EUCALYPTUS-OIL-MARKET](https://www.factmr.com/media-release/79/eucalyptus-oil-market)])**

1. Instead, the existing mode of distribution, the virtual distribution channel of eucalyptus oil can cause the highest CAGR by 2022.

2. According to the current statistics of global market for eucalyptus essential oil, the revenues earned by online selling of eucalyptus oil are not equivalent with the other segments of distribution channels.
3. In near future, Eucalyptus will experience the utmost demand from food and beverage industries followed by aromatherapy and therapeutic segments.
4. The sluggish rate of selling is envisaged for eucalyptus oil exclusively in perfumery industry by end of 2022.
5. The improved qualitative traits and eco-friendly nature of eucalyptus essential oil will enhance its sale with a moderate CAGR during 2022 end for consumers preference.
6. It is anticipated that the sale of organic eucalyptus oil will be more as compared to natural one during the forecasting period.
7. Europe could be the most potential market for eucalyptus oil trade securing the steady CAGR by 2022. It is anticipated that Europe continent will alone contribute around 1<sup>1/2</sup> of total market share during 2017–2022.
8. Barring few continents of Asia Pacific (like Japan [APEJ], Middle East and Africa [MEA], and North America), the overall eucalyptus oil market is to witness a sluggish expansion through 2022.
9. *Eucalyptus globulus* will witness the utmost demand in terms of revenues.
10. Another 2 species namely *E. kochii* and *E. polybractea* are also vital for trading. The former one is anticipated to show quick growth while the latter one the sluggish growth in the global eucalyptus oil market by end of 2022 (Figure 5.1 and Table 5.2).

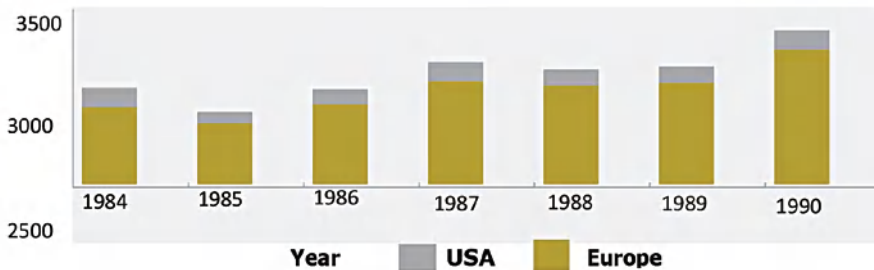


FIGURE 5.1 Comparison of Europe vs. USA imports 1984–1990 in tons.

Source: Foreign Agricultural Circular, USDA.

**TABLE 5.2** Market Taxonomy

Product Type	Nature	Application	T Channel
<i>Eucalyptus globulus</i>	Natural	Therapeutics	Modern trade
<i>Eucalyptus kochii</i>	Organic	Aromatherapy	Franchise outlets
<i>Eucalyptus polybractea</i>		Food and beverages	Specialty stores
		Cosmetics	Online
		Toiletries	
		Fragrances	
		Cleaning and home	
		Others	

Source: Adapted from Fact.MR (2022)

Defining the current world-wide market for *Eucalyptus* oils is difficult as outlined by United Nations Food and Agriculture Organization. Republic of China is well-known for its huge production and trade of cineole-rich medicinal eucalyptus oil (accounts for 70% of gross output and marketing) and also perfumery oil (source – *E. citriodora*). The gross global demand of eucalyptus oil is yet to be quantified. The bottlenecks of production and domestic consumption statistics published by Republic of China are of limited importance for making analytical reports on eucalyptus oil trade. Apart from this, Portugal, Spain, and Australia are also the notable processors and importers of eucalyptus essential oil while they also export the imported quantity. Previous studies and current data sources have been distilled to extract the essential features. In summary the world consumption of eucalyptus oils (all species) is estimated to be about 7,000 tons per annum and growing (Pain, 2007).

The study related to previous market needs the updated information on current and future markets and draws on useful insights from previous studies (Pain, 2007). The majority of the world's eucalyptus oil is applied where its distinctive aroma and flavor provides it with niche markets. Currently most is sold for use in pharmacy as liniments, inhalants, and expectorants, flavor, and aroma applications in household products such as cleaning products. Research and development have shown potential new markets in pharmacy, insect management, industrial solvents, fuel additives and as raw materials for a range of industrial processes. Along with the production of sumptuous amount of eucalyptus oil, China also contributes for timber/wood industry. The global need of eucalyptus oil for pharmaceutical and domestic uses is 7,000 tons year<sup>-1</sup> while currently it is expecting to witness a stable price



between US \$4,500–US \$5,000 tons<sup>-1</sup>. During the 1970s, several producers in Australia fell in the face of cheap imports from overseas, principally China. Recently there have been protests in India regarding cheap imports from China undermining attempts to expand the domestic industry. The eucalyptus oil industry in the Nilgiris has decided to approach the Union Government to impose an anti-dumping duty of 150% on Chinese oil imports in a bid to save the domestic industry. Domestic demand in India has been estimated at 400 tons per annum (Pain, 2007).

## 5.4 COMPOSITION AND USES

Among many other plant parts, ‘Leaf’ of eucalypts stores maximum amount of volatile oils. Key essential constituent of the volatile oil extracted from fresh laminae is 1,8-cineole while its quantity may vary from 54–95%. The other co-occurring constituents are like limonene,  $\alpha$ -terpineol, monoterpenes, sesquiterpenes, globulol, and  $\alpha$ ,  $\beta$  and  $\gamma$ -eudesmol, and few aromatic constituents. Gastrointestinal, anti-inflammatory, analgesic, antidiabetic, antioxidant, anticancer, antimicrobial, antiparasitic, insecticidal, repellent, properties, and oral, dental, dermatological, and nasal effects have been proved by several pharmacological studies.

### 5.4.1 CHEMICAL CONSTITUENTS OF THE LEAVES OF EUCALYPTUS GLOBULUS

The essential oil composed of basically oxygenated monoterpenes, monoterpenes, and oxygenated sesquiterpenes. Out of these, 1,8-eucalyptus (72.71%)  $\alpha$ -terpinene (2.54%), terpinene-4-ol (0.34%), and linalool (0.24%) are chief oxygenated monoterpenes, while  $\alpha$ -eudesmol (0.39%), (-)-globulol (2.77%), and epilobulol (0.44%) are chief oxygenated sesquiterpenes. Other range of compounds are  $\alpha$ -terpineol acetate (3.1%), geranyl acetate (0.71%), L-pinocarveol (0.36%),  $\beta$ -sabinene (0.25%), and terpinolene (0.19%) but only meagre percent (0.26%) of constituents are unidentified (Sebei et al., 2015).

### 5.4.2 CHEMICAL ANALYSIS AND CONSTITUENTS OF E. GLOBULUS FRUITS

Around 15 compounds have obtained from *E. globulus* fruits. The identified phytochemicals are beta-sitosterol, betulinic acid, stigmasterol, euscaphic acid, macrocarpol B and A, 3-O-methylellagic acid 4-O-(2''-O-acetyl)-alpha-L-rhamnopyranoside, 2a-hydroxybetulinic acid, ellagic, and gallic acid,

3-O-methylellagic acid and oleanic acid-3,4,3-O-trimethylelladic acid (Chalchat et al., 1995).

### **5.4.3 CHEMICAL CONSTITUENTS OF THE WOOD OF EUCALYPTUS GLOBULUS**

Sterols, triglycerides, fatty acids, steroid ketones, sterol esters and hydrocarbons are key components usually obtained from the woody portion of *E. globulus*. Other co-occurring compounds are fatty alcohol, mono, and diglycerides, waxes, and tocopherols (Chalchat et al., 1995).

Several bioactive chemical constituents (like cineole (70%–85%), aromadendrene limonene terpinene, pinene, cymene, and phellandrene) are known to heal some neurological diseases like headache, debility, and neuralgia. It has secured its reputation as immunity booster against chickenpox, cold, measles, and flu. Leucorrhoea, cystitis problem of genitourinary system, sinusitis, catarrh, bronchitis, asthma, and throat infections could be also healed by eucalyptus oils. Except these, dermatological issues like insect bites, wounds, herpes, lice, cuts, burns, etc., could be healed using its extracted and processed oils. Ali et al. (2015) reported the potency of eucalyptus EO to treat joint pains (rheumatoid arthritis) and muscle aches. Its other aforementioned properties also assist to recover several metabolic and infectious diseases. Hence, conclusively eucalyptus essential oil could be utilized to heal multidimensional human diseases (DamJaNoVić-VratNiCa et al., 2011; Tisserand & Balacs, 1995).

### **5.4.4 USE OF EUCALYPTUS OIL AS AN INGREDIENT**

‘Cineole,’ is an essential component to treat array of diseases (like inhalants, lozenges, ointments, cough, and cold, etc.) especially used to get rid of influenza and cold symptoms. Eucalyptol and  $\alpha$ -terpineol components give the oil a soothing and cooling nature, owing to that inhalation of eucalyptus oil vapor is a potential decongestant. Furthermore, for body massage and oral care, the potency of eucalyptus oil is unparalleled (Ali et al., 2015).

### **5.4.5 REPELLENT AND BIOPESTICIDE**

As bio-pesticide and insect repellent, cineole-based eucalyptus oil has secured its reputation. Vecchio et al. (2016) revealed that the registration of eucalyptus oil as insect and miticide was made during 1948 (Vecchio et al., 2016).

#### **5.4.6 FLAVORING AND FRAGRANCE**

The popularity of cineole-based eucalyptus oils in flavoring and perfumery industry is identified already. It is effective at the rate as low as 0.002%. In beverages, confectionaries, meat products and baked goods it is widely used as flavoring agent. Wide range of food spoilage microorganisms and pathogens could be effectively destroyed using the cineole-based eucalyptus oil. Cheap and low-quality flavoring agents like lemon ironbark, strawberry gum and non-cineole peppermint could be also used as optional items. In detergents, soaps, perfumes, and lotions its use as a fragrant component provides a soothing aroma while it also possesses pungent and intoxicating scent usually vary according to its concentration. The cleansing features allow it to use for oral rinses (Olayinka et al., 2012).

#### **5.4.7 INDUSTRIAL**

Mixing of 5% cineole-based eucalyptus oil, may fix difficulties associated with the separation between ethanol and petrol fuel mixtures. Eucalyptus oil can be also used as a fuel for having significant octane rating although sufficient confusions are there concerning its economic viability. In mining sector, the use of phellandrene- and piperitone-based eucalyptus oils is most conventional to separate sulfide minerals using flotation (Vecchio et al., 2016).

#### **5.4.8 CLEANING**

Anti-microbial and antiseptic properties allow range of eucalyptus oils to use for household cleaning purposes. It's a mandatory item (as solvent) used in commercial laundry (to clean woollens) especially to remove greasy and sticky residues/spots (Vecchio et al., 2016).

### **5.5 ORIGIN AND DISTRIBUTION**

The super-dominance of diversified species of *Eucalyptus* tree (Family: Myrtaceae; synonymously known as 'Gum tree,' 'Red iron tree' or 'Safeda of Nilgiri') throughout the globe (specifically in sub-tropical and warm temperate parts) is evident by the formation of its characteristic vegetation.

It is indigenous to Australia, Tasmania, New Guinea and the neighboring islands. It was first introduced in Nilgiri Hills, Tamil Nadu by Britishers in 1843 for fuel and timber purpose (Sharma et al., 1986).

Brooker et al. (2002) explained the geological base of dissemination of eucalypts from Australia to other parts of the globe resorting the plate tectonics theory, reinforced by fossil evidences. According to them, earlier the single super-continent Gondwana comprised of Madagascar, Africa, India, Arabia, South America and New Guinea while Australia was a part of that land mass but due to the splitting during Tertiary era, the drifting of Australian landmass northwards from Antarctica had taken place. They also stated that prior to the massive drifting, the Australian continent for huge rainfall later caused the uniform development rainforest. But due to weather-based circumstances, the landmass was entirely dehydrated and contracted towards eastern sea and consequently lost its fertility. Such conditions, disallowed rainforest vegetation to survive. At this juncture, evolution spawned few plant families, one of them is Myrtaceae (family of eucalypts) who can tolerate drought and less fertile conditions (Brooker, 2002).

Due to the wide range of adaptability at diversified conditions of soil and climate of Eucalyptus, Southern Europe and South and North Africa become suitable for eucalyptus plantation. South Africa, China, Indonesia, Brazil, and Congo are famous for growing inter and intra-specific hybrids while and in Philippines, Malaysia, Thailand, and Vietnam and South Americas (Paraguay, Uruguay, Chile, and Argentina) only little eucalyptus plantations are found. In Philippines, *E. deglupta* is quite dominant. Its further distribution in temperate countries is restricted for its less cold tolerance nature. Among the large number of its species (~700), only the negligible percentage is used for industrial purposes. Labate et al. (2008) mentioned its use for fuel, shelterbelts, windbreaks, and for hardwood fiber. In Australia, total 227,336,951 acres (92,000,000 hec.) of land are occupied by eucalyptus plantation. South-eastern Australia (Blue Mountain regions) is the hub of diversified eucalypts. At this place blue haze is often found, might be due to emission of volatile terpenoids by eucalypts. Australian continent also contained few non-Australian origin species too. Nevertheless, several occur naturally in the land mass of North Australia to New Guinea and certain species occur in some of the islands of the eastern part of the Indonesian archipelago, such as Timor, the Lesser Sunda Islands, Flores, and Wetar. One important species, *E. deglupta*, follows the line of active volcanoes which extends from New Guinea through Sulawesi (Celebes) and from Moluccas to Mindanao islands of the Philippines (Pryor, 1995).

Of the species found outside the territorial limits of Australia, two, *E. deglupta* and *E. urophylla*, have not been recorded from Australia. Aforementioned eucalyptus species are specially appropriate for planting at lower latitudes of the world. They are good species and tolerate lower latitudes than any found in Australia, where the northernmost point is 10°41'S. According to Wallace (1913) East side of "Wallace's Line" was the hypothetical limit of natural occurrence of eucalyptus vegetation. This region was called 'Indo-Malayan' and 'Austro-Malayan' region. This line crossed between Bali and Lombok (Wallace, 1869) while on Eastern side of the line Makassar Strait with Sulawesi, on Western side Borneo, on North-East side Celebes Sea and on Southern side Philippines islands were situated. According to him, on the West side of Mindanao the existence of *E. deglupta* was also evident but recent studies proved it incorrect according to the report of Times Cocise Atloas of the World (1973). Based on the report of Martin & Cossalter (1975–1976), except *E. alba* all other species of Eucalyptus were naturally occurred along the Est of amended line. According to them, the natural latitudinal range of eucalyptus occurrence is 7°N to 43°39'S which prove their Austro-Malayan origin although majority of cultivated species occur in South of the Tropic of Capricorn but North of tropic of Capricorn also contain significant diversity of Eucalyptus (Pryor, 1995).

## 5.6 BOTANY AND TAXONOMY

Leaves of Eucalyptus are generally broad, sessile, leathery textured studded with oil gland, alternate phyllotaxy, 6–12 inches long, mature leaves are of sickle-shaped (4–5 years after) and blueish-green in hue. They hang diagonally or vertically. Sometimes, their arrangement differs based on climate. Flowers borne either singly or in cluster, sessile in nature (without pedicel) while flower buds are encased by a cup-like structure but during anthesis this covering gets splitted for easy expansion of flower. Its fruit is enveloped by a woody, cup-shaped container possessing numerous minute seeds (Eyles et al., 2009).

There are three main behaviors that species can divide into:

- i. Long, single trunked woodland trees are featured for their small crown;
- ii. Emergence of small branches often found in case of single-stemmed woodland trees; and
- iii. Multi-stemmed eucalyptus trees (known as 'Mallees') are >10 m (33 ft.) in height.

Tree sizes follow the convention of:

- i. Small – to 10 m (33 ft) in height;
- ii. Medium-sized – 10–30 m (33–98 ft);
- iii. Tall – 30–60 m (98–197 ft.);
- iv. Very tall – over 60 m (200 ft) (Al-Snafi, 2017).

### **5.6.1 BOTANICAL CHARACTERISTICS OF DIFFERENT PARTS OF EUCALYPTUS**

#### **5.6.1.1 BARK**

As long as the subero-phellodermal layer on the juvenile branches and their twigs functions uninterruptedly, the primary bark is usually smooth and continuous. When this layer ceases to function, a new layer is pointed deep down and is retained for another year or several years. Later, other layers may appear still deeper at various time intervals. These successive layers are distinguishable either over the whole surface, or on parts of the trunk and branches. Moreover, the rhytidome, that is, the complex mass outside successively generating layers, may vary in color, texture, and persistence or shedding following renewal of the subero-phellodermal layer (Eyles et al., 2009; Saveyn et al., 2010). Usually, smooth bark is observed in young branches but the lower portion of trunk of mature tree possesses its characteristic ‘Rhytidome,’ composed of partially disintegrated and enlarged secondary phloem tissue situated in between phellem cells, is quite persistent in nature and deeply furrowed. Various types of barks are described as follows:

- 1. Deciduous Bark:** Peeling off of the bark of Eucalyptus is species specific. The new growth of bark causes the shedding of the old one in long strips, exclusively found in *E. globulus* but in case of *E. camaldulensis* and *E. saligna* shedding of peel is found in broad plate form rather than the previous form. *E. citriodora* or *E. astringens* show their characteristic bark shedding in small scales or flakes form. Two features (i.e., color, and texture) are impossible to determine due to adjoining form with other patches of varied age. Generally, new patches are fine, shiny, and bright textured with different hues while old patches are dull and grey colored with moderately rough surface.
- 2. Persistent Bark:** Non-renewal of subero-phellodermal layer or the periodic non-shedding of dorsal parts of rhytidome, form the

‘persistent’ bark. With the progression of age, conversion of its bark hue from light to dark occurs basically due to oxidization and become more pulverulent and consequently, loses its characteristics.

3. **Ironbark Type:** The bark is featured for its tough, little fibrous or non-fibrous nature which may form minute polyhedrons of hard, corky texture after successful crumbling along the longitudinal furrows. Normally, this type of bark contains dark hues and also ‘Kino’ nothing but minute masses of gum rich in tannin.
4. **Box Type (Shortly Fibrous):** Fibrous texture, obliquely reticulated or furrowed (finely) bark surface, and faded grey color are the key features of this type.
5. **Long-Fibred Brown Bark:** The basic features of this type of bark are its characteristic hue (dark brown), long fibers and longitudinal furrow. The removal of the extramural bark layer usually exposes the texture of long fibers. This type of bark is found in *E. robusta* and *E. botryoides* and while ‘stringy barks’ are often found in *E. obliqua* and *E. globoidea*.
6. **‘Peppermint and Bloodwood’ Types:** The pattern of furrowing is its key feature. Shallow, irregular furrowing takes place in two directions, results in creation of oblong shaped scale effect (e.g., *E. elata*, ‘peppermint’ type and *E. gummifera* ‘bloodwood’ type).

#### 5.6.1.2 LEAVES

The leaves of most species of eucalypt vary, sometimes markedly, from the seedling to the mature tree. The leaves are important aids to identification. The system of classifying the various types of leaf used by Blake (1953) has been followed here:

1. **Seedling Leaves:** These are the early leaves developed on seedlings in their first year. Pairs of leaves develop from the growing tip on opposite sides of the stem and successive pairs are arranged at right angles to each other, an arrangement known as ‘decussate.’
2. **Juvenile Leaves:** These are the leaves found in a nursery seedling when four to six pairs of leaves have developed from the young growing tip. They are also common in the forest when shoots develop from lignotubers or from the ‘reversion shoots’ which develop on most eucalypt trunks following serious damage by fire

or other factors. They are sometimes spectacularly different from adult leaves, e.g., *E. globulus*. It is widely believed that juvenile leaves, such as those seen on seedlings or reversion shoots, reproduce vanished ancestral characters of the species.

3. **Intermediate Leaves:** These are frequently larger than juvenile or adult leaves, and many pairs of them may be produced by the growing tip after the juvenile stage and before the more or less stable adult foliage is produced.
4. **Adult Leaves:** These leaves are emerged from the crown of well-grown eucalyptus plants. Anatomically, these leaves are coriaceous, thick, and stiff in nature due to heavy cut in deposition. Enriched sclerenchymatous content also contributes towards the thick and stiff nature of adult leaves. They are usually alternate, only in a few species are they opposite or sub-opposite. The shape of leaf is commonly lanceolate but sometimes may vary from narrowly and broadly lanceolate to linear, elliptical, oblong, oval or orbicular. They are frequently falcate. Their dimensions vary considerably. In the same species, and sometimes on the same tree, there is an appreciable variation in the shape and dimensions of the leaves. Thus, the dimension of leaf should be calculated by adding length, breadth, and petiole too.

### 5.6.1.3 REVERSION (EPICORMIC) SHOOTS

When a eucalypt is damaged by fire or other agency, new shoots and juvenile foliages develop from the many dormant epicormic buds present on the trunk and branches. These shoots are known as 'Reversion shoots.' The key importance of 'reversion shoots' is to make the eucalyptus plant mechanically stable as these shoots aid in reestablishment of crown part. The reversion shoots emerge from mechanically stable portions of damaged plants to rejuvenate the growth of damaged eucalyptus plant. They soon produce mature foliage. Reversion shoots may be seen at appropriate places in most large crowns.

### 5.6.1.4 OPPOSITE AND ALTERNATE LEAVES

The vast majority of eucalypt growing tips grow in length between nodes which develop opposite or sub-opposite pairs of leaves, decussately arranged. That is, each successive pair of leaves is at right angles to the



previous pair on the stem. In a few species the opposite, decussate foliar arrangement is retained beyond the juvenile stage, when the leaves may be cordate, amplexicaul or connate in most species the intermediate and mature leaves become alternate. There is then some extension of the shoot between the leaves of each pair developed from the growing point. The length of the internode between the leaves of each pair is shorter than the internode between successive pairs of leaves. The alternate leaf arrangement is usually accompanied by some twisting of the internode between each pair and sometimes between the leaves of each pair. This enables the leaves to be ranked on either side of the stem, so that they adopt a posture that intercepts maximum sunlight. Occasionally, successive nodes of a eucalypt growing shoot may throw off a whorl of three leaves. This may happen on nursery seedlings but more frequently on coppice shoots.

#### 5.6.1.5 LEAF FACES

All eucalypt leaves have an inside and an outside face, representing the way the leaves oppose each other when each leaf pair opens from the growing tip. In some species the two faces are markedly different in color as the leaves attain their final size; in other species there is little obvious difference between the faces. The two leaf faces are frequently referred to as ‘upper’ and ‘lower,’ because they are most noticeable on shoots where the leaves are ranked on either side of horizontally oriented shoots, thereby effectively intercepting sunlight. In these cases, the upper surfaces are darker than the lower surfaces. The upper, darker surfaces were the inside leaf faces when opening from the growing tip.

#### 5.6.1.6 VENATION

Leaf venation is also another taxonomical feature for eucalypts. The leaves of most species have a readily recognizable midrib from which the succession of lateral veins diverge and cross the leaf to join an intra-marginal vein which follows the contour of the edge of the leaf. The lateral veins maintain a fairly regular ‘angle of venation’ relative to the midrib, particularly in the middle portion of the leaf. The following types of venations can be recognized.

1. **Penniveined:** In this type of the lateral veins are fairly numerous and parallel at an angle of 60° or more with the midrib. The intra-marginal vein is usually fine and close to the leaf edge.

2. **Oblique:** In this type of the angle of venation is less than 60° with the midrib. Penniveined type is more in number as compared to the lateral veins which anastomosed frequently while intra-marginal vein is somewhat sinuous and comparatively distant from the leaf edge.
3. **Longitudinal:** In this type of the lateral veins make an angle of 30° or less to the midrib and are sometimes almost parallel to it.
4. **The Inflorescence:** This type is dichasial cyme. Characteristically, the stunted central flower and lateral branches with extended peduncles of single whorl of blooms are found. In many species, multiple bracts fuse with each other and appear as single pair. Sometimes, the fused bracts are also found to envelope the young inflorescence immediately after bolting or prior to anthesis. In the subgenus *Corymbia* this process takes a few months, in *Symphyomyrtus* (Subgroup) one year and in *Monocalyptus* about two years. Because of the dichasial structure, the flower clusters have precise numbers and show precise orientation. In the few species which have solitary flowers in the leaf axils, such as *E. globulus*, the cymose nature of the inflorescence is not displayed, but in those with other numbers it may be clearly seen. Thus, in the simplest, there is a three-flowered axillary cyme (as in *E. viminalis*) or a seven-flowered flower cluster (as in *E. saligna*), each of which is in accord with the structure of a regular dichasium. As the number of flower buds in each flower cluster becomes greater, precise regularity of the dichasial branching is lost and some of the branches become monochasial. The number of buds in the flower clusters then becomes less precise; they begin to vary within the same species and even within the same individual, especially when numbers exceed 15. In the so-called compound inflorescence, each cymose cluster behaves as a single unit, these being arranged in accordance with the decussate nature of the normal leafy shoot.

The outstanding feature of each Eucalyptus flower is the presence of anoperculum which occurs with three variations. In a few species, especially those in the subgenus *Eudesmia*, there is only one operculum present which is surrounded by four small teeth at the top of the hypanthium. These teeth were recognized by Brown as separate sepals, whereas the operculum lying within them is a single structure resulting from the fusion of the four petals. Sometimes there is an indication of the sutures which are the meeting lines of

separate petals. In a great many species, particularly those in the subgenera Blakella, Corymbia, and Symphyomyrtus, there are two opercula, an outer one covering an inner. The outer operculum sometimes breaks into separate pieces or it may remain intact, but in either case it is shed before abscission of the inner operculum at anthesis. In the part of the subgenus Corymbia comprising the true bloodwoods the outer operculum dehisces imperfectly and usually sheds with the inner at anthesis. In the subgenus Monocalyptus, which embraces some 100 species, there is only one operculum present and no sign of calyx teeth. There is some uncertainty as to whether this is made only of fused sepals, or petals, or whether in its derivation it is a more complicated structure resulting from the intimate fusion of petals and sepals. It is customary to give the name ‘bud’ to what is in reality the flower of the eucalypt up to the time of abscission of the operculum at anthesis. The ‘bud’ comprises operculum, hypanthium, and pedicel (Pryor, 1995).

#### 5.6.1.7 SHAPES OF OPERCULA

The shapes of the opercula are described in the following terms:

Shape	Example
Conical	<i>E. rudis</i>
Obtuse conical	<i>E. cladocalyx</i>
Acute conical	<i>E. tereticornis</i>
Homed or long	<i>E. occidentalis</i>
Hemispherical apiculate	<i>E. amygdalina</i> or <i>E. diversicolor</i>
Rostrate	<i>E. carnaldulensis</i>
Ovoid	<i>E. salubris</i>
Biretta operculum	<i>E. erythrocorys</i>
Boss-shaped	<i>E. globulus</i>
Flattened	<i>E. concinna</i>

It will be found in practice that in the same species, and often on the same tree, the shape of the operculum is variable and can only be described with the help of at least two or three of the above comparisons.

#### 5.6.1.8 STAMENS

The classification of eucalypts established by botanists has been based up to now upon the characteristics of the stamens. In the series Comutae, e.g., *E. occidentalis* is, the operculum is long and conical and all the filaments are

accommodated erect and are surmounted by the anthers. In the red gums Exsertae, e.g., *E. tereticornis*, the outer filaments at least are erect and surmounted by the anthers. Exceptions in the red gums are the forms of *E. camaldulensis* with strongly beaked buds. In these the filaments may be completely inflected. In jarrah, *E. marginata*, the filaments are also quite erect and this is the only species of *Monocalyptus* where this condition is seen (Naithani, 2017).

In many species of *Eucalyptus*, e.g., *E. sieberi*; and some *Symphomyrtus*, e.g., *E. leucoxylon*, the filaments are at first erect then strongly inflected with the anthers placed toward the bottom of the bud cavity. In other species, particularly of the two largest subgenera, the filaments form no recognizable pattern and are variously twisted in bud. The use of this character in identification is clearly illustrated in the separation of two unrelated ironbark species which look alike and occur together in the field, viz., *E. beyeri* and *E. crebra*. A simple bud dissection shows that *E. beyeri* has inflected filaments and *E. crebra* has twisted filaments (Blakeley, 1934).

#### 5.6.1.9 FRUITS

The enlarged hypanthium with ovary form the fruit of *Eucalyptus*. Four segments form the upper part of its fruit. The lid shaped ‘operculum’ sheds with maturity to remove the scar ultimately form an external ring or ‘Calycine ring’ followed by an internal ring or ‘Staminal ring.’ The bottom and inward segments of the disc hold the upper portion of the ovary, although the true ontogenesis is yet to be known. After attaining maturity, the disc splits forming distinct valves. Calycine ring, in few species, disappears after the development of fruits while in *E. leucoxylon* and *E. melliodora* the prominent ring protrudes clearly beyond the disc. For these species, even after complete maturity of fruits, the ring may adhere partially at one end of fruits. So, hypanthium with pedicel of disc and the position and shape of valves are the characteristic features of eucalyptus fruits (Brooker, 2002).

#### 5.6.1.10 SHAPE OF THE HYPANTHIUM AND THE PEDICEL

Hypanthium is basically globular, ovoid, urceolate, campanulate, hemispherical, cylindrical or conical in shape. It usually gets merged with its pedicel which might be attenuated. Hypanthium with long attenuated pedicel form pyriform shaped fruits while combination of hypanthium with short, attenuated pedicel produces turbinate fruit. Furthermore, short, club shaped

fruits are also formed by the combination of cylindrical/urceolate hypanthium with attenuated pedicel (Chippendale, 1968).

#### 5.6.1.11 *SHAPE OF THE DISC*

The existence of disc at the upper part of ovary in fresh flowers or fruits are usual. With the maturity and desiccation of fruits, the distance between two parts (upper and lower) are usually increased and become more prominent during opening of valves. The ovary develops into a capsule and results in formation of protuberant, flat, thin or depressed disc. Protuberant disc either concave or convex. The latter one develops ‘Dome-shape.’

#### 5.6.1.12 *POSITION AND SHAPE OF VALVES*

In *E. camaldulensis* the valves are short and triangular in shape either show the upper portion of ovary or contain sharp pore developed from the ruptured base of persistent style. In *E. oleosa*, the valves are joined together continuously at a point for the existence of persistent whole style. In certain species, with the progression of fruit’s maturity, valves become fragile and drop off quickly.

#### 5.6.1.13 *EXSERT VALVES*

In *E. camaldulensis* this type of valve is found. When the position of the base of valve is at or above the level of calycine ring and points protrude beyond the whole fruit, then it is called ‘Exsert’ valve.

#### 5.6.1.14 *ENCLOSED VALVES*

This type is completely reverse than the earlier type. Here, valves will be at the lower position of calycine ring.

#### 5.6.1.15 *LEVEL VALVES*

In ‘Level’ valves, the base will be situated with or slightly below the calycine ring.

#### 5.6.1.16 *SEED*

The flowers of eucalypts are pollinated in the main by insects, particularly bees, blowflies, and ants, and rarely by wind. Nectar is secreted in the cup

of the flower. The stored nectar in the cup of flower is very attractive to insects.

Many numbers of ovules are found in eucalypt fruits. Some, but never all of these ovules, are fertilized during pollination. It is important to remember that each ovule must be fertilized by a separate pollen grain, so while each seed in a fruit is from the same female parent, then there is high chance of the involvement of male parents in the seed within a capsule. So, if other species which can hybridize with the female parent are also flowering in the vicinity, it is possible that there may be one or more hybrid seeds in the fruit.

The fertilized ovules expand in about six months, or even less, after pollination. The seed is usually viable as the capsules are changing in color from green to brown. Mature capsules are brown and usually remain closed for several months or even two or more years if they remain attached to their parent branches. If fruits or the branches are detached from the tree the valves which hold the seed in the capsules open in the course of hours or days and the seed is shed, together with the unfertilized ovules, which are usually smaller and lighter in weight than the fertile seed, and are known as 'chaff' (Chippendale, 1983, 1988).

#### 5.6.1.17 SEED CHARACTERISTICS

The size of Eucalyptus seeds range from <1 mm (*E. populnea*) to >2 cm (*E. calophylla*); in color, from black in *E. tereticornis* to yellow in *E. camaldulensis*; in shape, from spherical (*E. wandoo*) to cuboid (*E. tetradonta*) and subulate (*E. curtisii*); and in sculpture, from shallowly reticulate in *E. leucoxydon* to deeply pitted in *E. griffithsii*. The seed of many species of the woody-fruited bloodwoods (subgenus *Corymbia*) is prominently winged; that of the paper-fruited bloodwoods (subgenus *Blakella*) saucer-shaped and unwinged. The seed of some species, e.g., *E. pyriformis*, may resemble that of some species in *Monocalyptus* but the high percentage of subulate chaff in *E. pyriformis* clearly distinguishes it (Chippendale, 1968; Pryor, 1995).

According to the scientific classification, *Eucalyptus* belongs to the Kingdom 'Plantae,' Sunkingdom 'Trachebionta,' Super division 'Spermatophyta,' Division 'Magnoliophyta,' Class 'Dicotyledons,' Subclass 'Rosidae,' Order 'Myrtales,' Family 'Myrtaceae.' The common, cultivated species of *Eucalyptus* is *E. globulus* Labill (Table 5.3).

**TABLE 5.3** List of Hybrids (from FAO Eucalyptus)

<b>Taxon</b>	<b>Probable Parents</b>
<i>E. affinis</i> Deane and Maiden	<i>E. albens</i> x <i>E. sideroxylon</i>
<i>E. algeriensis</i> Trabut	<i>E. camaldulensis</i> x <i>E. rudis</i>
<i>E. antipolitensis</i> Trabut	<i>E. globulus</i> X <i>E. viminalis</i>
<i>E. biangularis</i> Simmonds in Maiden	<i>E. globulus</i> x <i>E. urnigera</i>
<i>E. cordieri</i> Trabut	Probable hybrid of <i>E. nortonii</i>
<i>E. gornphocornuta</i> Trabut	<i>E. gomphocephala</i> X <i>E. cornuta</i>
<i>E. huberanct</i> Naudin (as applied by Blakely)	Quite common in Australia. <i>E. viminalis</i> X several related species giving seven-flowered umbels in contrast to the three flowers of <i>E. viminalis</i> . Chippendale (1976) states that <i>E. huberarza</i> Naudin. is now accepted as a taxon.
<i>E. kirtoniana</i> F. Muell.	<i>E. robusta</i> x <i>E. tereticornis</i>
<i>E. longifolia</i> var. <i>multiflora</i> Maiden	<i>E. longifolia</i> x <i>E. robusta</i>
<i>E. maidenii</i> var. <i>williamsonii</i> Blakely	<i>E. botryoides</i> x <i>E. pseudoglobulus</i>
<i>E. mcciatchiei</i> Kinney	<i>E. globulus</i> x <i>E. ovata</i>
<i>E. nortonniana</i> Kinney	<i>E. pseudo globulus</i> x <i>E. maidenii</i>
<i>E. oviformis</i> Maiden and Blakely	<i>E. pseudoglobulus</i> x <i>E. tereticornis</i>
<i>E. patentinervis</i> R.T. Bak.: Syn. <i>E. kirtoniana</i>	<i>E. robusta</i> x <i>E. tereticornis</i>
<i>E. populifolia</i> Hook. var. <i>obconica</i> Blakely	<i>E. microtheca</i> x <i>E. populnea</i>
<i>E. trabutii</i> Vilmorin	<i>E. botryoides</i> x <i>E. camaldulensis</i>

Source: Adapted from: <http://www.fao.org/3/ac459e/ac459e.pdf>.

## 5.7 VARIETIES AND CULTIVARS

There are over 500 species of Eucalyptus. It has many Indian vernacular names, depending on the geographical region or the language, for example: Nilgiri (Kannad), Neelgir (Hindi), *E. globulus* (Latin name), Sugandh Patra (Sanskrit name), Gum Eucalypts (English), Gum tree, Harit Parn or Tail Parn (Gujrati), and Gum eucalypt (English). Other commonly available species are *Eucalyptus bicolor* (English name: red box), *Eucalyptus camaldulensis* (syn: *Eucalyptus rostrata*) (English name – blue gum), *Eucalyptus incrassata* (English name – yellow mallee), *Eucalyptus microtheca* (Syn: *Eucalyptus coolabahs*) (English name – western coolibah), *Eucalyptus torquata* (English name – Christmas tree) (Naithani, 2017).

### 5.7.1 MAJOR SPECIES OF EUCALYPTUS

---

<i>Eucalyptus amygdalina</i>	<i>Eucalyptus microtheca</i>
<i>Eucalyptus australiana</i>	<i>Eucalyptus nitens</i>
<i>Eucalyptus botryoides</i>	<i>Eucalyptus ovate</i>
<i>Eucalyptus calophylla</i>	<i>Eucalyptus pauciflora</i>
<i>Eucalyptus camaldulensis</i>	<i>Eucalyptus perriniana</i>
<i>Eucalyptus citriodora</i>	<i>Eucalyptus pilularis</i>
<i>Eucalyptus cladocalyx</i>	<i>Eucalyptus polyanthemus</i>
<i>Eucalyptus consideniiana</i>	<i>Eucalyptus polybractea</i>
<i>Eucalyptus cypellocarpa</i>	<i>Eucalyptus populnea</i>
<i>Eucalyptus dives</i>	<i>Eucalyptus radiate</i>
<i>Eucalyptus gigantean</i>	<i>Eucalyptus regnans</i>
<i>Eucalyptus globulus</i>	<i>Eucalyptus risdonni</i>
<i>Eucalyptus gomphocephala</i>	<i>Eucalyptus robusta</i>
<i>Eucalyptus grandis</i>	<i>Eucalyptus rossi</i>
<i>Eucalyptus gunnii</i>	<i>Eucalyptus rostrata</i>
<i>Eucalyptus incrassate</i>	<i>Eucalyptus saligna</i>
<i>Eucalyptus kino</i>	<i>Eucalyptus sideroxylon</i>
<i>Eucalyptus largeflorens</i>	<i>Eucalyptus sieberiana</i>
<i>Eucalyptus lesouefii</i>	<i>Eucalyptus smithii</i>
<i>Eucalyptus macrocarpa</i>	<i>Eucalyptus tereticornis</i>
<i>Eucalyptus macrorhyncha</i>	<i>Eucalyptus tetradonta</i>
<i>Eucalyptus maculate</i>	<i>Eucalyptus umbra</i>
<i>Eucalyptus marginata</i>	<i>Eucalyptus urophylla</i>
<i>Eucalyptus melanophloia</i>	<i>Eucalyptus viminalis</i>
<i>Eucalyptus melliodora</i>	<i>Eucalyptus wandoo</i>

---

### 5.7.2 COMMERCIALY CULTIVATED VARIETIES EUCALYPTUS IN INDIA

*Eucalyptus globulus*, *Eucalyptus citriodora*, *Eucalyptus hybrid*, *Eucalyptus camaldulensis*, FRI-4 and 5 (Reddy, 2015).

- **Clonels:** 316, 3, 271, 7, 288, 2045, 413, and 411.

On the other hand, there is several *Eucalyptus* species don't produce cineole based and non-based essential oil since it is the key compound of *Eucalyptus* essential oil. The examples are as follows:



- **Eucalyptus species used commercially for extraction of cineole-based Eucalyptus-oil:** *E. tereticornis*, *E. viridis*, *E. cneorifolia*, *E. globulus*, *E. horistes*, *E. kochii*, *E. dives*, *E. smithii*, *E. radiata*, *E. oleosa*, *E. leucoxylon*, *E. goniocalyx*, *E. dumosa*, *E. sideroxylon*, *E. polybractea*.
- **Eucalyptus species used commercially for extraction of non-cineole-based Eucalyptus-oil:** *E. radiata*, *E. dives* (phellandrene variant), *E. dives*, *E. elata* (piperitone variant), *E. olida* (methyl cinnamate), *E. staigeriana* (citral, limonene) and *E. macarthurii* (geranyl acetate).

Furthermore, *E. citriodora* (commonly known as ‘Lemon Eucalyptus’) is classified as *Corymbia citriodora* – used for the production of citronellal-based eucalyptus oil.

### 5.7.3 DESCRIPTION OF DIFFERENT SPECIES AND CULTIVARS

1. ***Eucalyptus Bicolor*:** This species of Eucalyptus attains the height of 20 m. It possesses persistent, fibrous-flaky (box) bark which is grey to black grey in color. Leaves are dull grey-green in color, texture glaucous, linear (at juvenile stage) to narrow-lanceolate (adult stage) in shape. Its leaves at any stage of maturity remain disjunct. A fully mature leaf is usually 9–18 cm long and 0.8–1.8 cm wide. Inflorescence is compound umbel-asters, hold 7–11-blooms, peduncle terete, 3–11 mm long. Floral buds are ovoid in shape and 4–5 mm long and 2–3 mm in diameter with some scars. The calyptra is hemispherical/conical but smaller and thinner than hypanthium. Stamens are fertile and style persistent. Fruits hemispherical/ovoid-truncate shaped, usually 3–6 mm in length and 3–5 mm in diameter. They have depressed disc and valves enclosed or positioned at the rim-level (Hill, 1991).
2. ***Eucalyptus camaldulensis*:** Its height commonly ranges from 20 m to 50 m while trunk attains the diameter of 1–2 m. Under natural growing conditions, it contains short, thick bole with large, spreading crown while it possesses a clean, erect bole of 20 m width with less spreading and branched crown. Its bark is smooth textured but 1–2 m length from the base of the trunk has rough bark. White,

grey, yellow-green, grey-green or pinkish grey – are the ranges of its bark color. The characteristic peeling off takes place in strips or in irregular flakes. Leaves are sickle shaped, tapered, and short pointed at the base, grey-blue in color, drooping with alternate phyllotaxy. The full-grown leaves are 8–22 cm long and 1–2 cm wide. Axillary inflorescence bears 7–11 flowers, flower buds are white and globular, rostrate or ovoid-conical in shape. The lid like structure, i.e., operculum is hemispherical, rostrate or conical, obtuse with a size of 4–6 × 3–6 mm. Fruits are very small capsules, 5–8 mm in size. These tetra locular fruits contain minute seeds (Al-Snafi, 2017).

3. ***Eucalyptus griffithsii***: White/grey/red-brown colored smooth, continuous bark is one of its distinguishing features. Its disjunct leaves are lanceolate – ovate in shape with entire margin, petiolate, and dull grey-green in color. Shape of adult leaves are more or less same as the juvenile leaves but much thicker, basally tapered and deep grey-green in color with glossy texture, its petioles are narrowly flattened or channeled, lateral vein system with obscure and acute veins. Inflorescence is simple, axillary, and 3-flowered while peduncles flattened/angular (3 mm wide). Flower buds are clavate shaped but not glaucous or pruinose. Calyx calyptrate shed when flowers are immature while calyptra is hemispherical shaped, corrugated, and wider than ribbed hypanthium. Flowers are white in color, campanulate fruits with depressed disc. Its valves re exert (Al-Snafi, 2017).
4. ***Eucalyptus incrassata***: Grey or grey-brown colored smooth, continuous bark which sheds longitudinally is found in this species with green branchlets at juvenile stage. Juvenile leaves are dull-grey-green – dull-green in hue, elliptic–ovate shaped with entire margin and petiolate while fully matured, deep grey-green colored petiolate leaves are disjunct, lanceolate in shape with tapered base and semi-glossy to glossy textured, and thick. Their sizes range from 10–11 cm in length and 1.5–5 mm in width. Petioles length range from 10–20 mm may be flattened or channeled. Lateral veins are obscure, acute, and moderately spaced. Simple, axillary inflorescences are 3–7 flowered, with peduncle (narrowly flattened/angular) of 13–20 mm long. Cylindrical/fusiform shaped flower buds with a size of 12–20 × 6–8 mm. Pedicellate cream colored flowers are 3–5 mm long, calyx calyptrate. Calyptra is conical and 2–3 times bigger than

smooth/ribbed hypanthium. Fruits are cylindrical or ulcerate with pedicel, depressed disc, valve enclosed, tri or tetra locular with a size of 8–13 x 7–11 mm. Chaff is dimorphic, linear, and cuboid shaped with the color identical of its seeds (Al-Snafi, 2017).

5. ***Eucalyptus microtheca* (Syn: *Eucalyptus coolabah*):** Its grey or grey-black colored persistent, continuous, fibrous-flaky bark peels off in patch (box). The characteristic features of its leaves are almost akin like that of the *E. griffithsii* and *E. incrassata*. Inflorescence is compound, terminal or axillary usually 3–7 flowered. Peduncles terete. Its flower also shares similar features like earlier 2 species except its hue which is white in color here. Hypanthium is smooth. Fruits are hemispherical shaped; disc is flat while valves positioned at rim-level or exserted. Chaff dimorphic, linear, and cuboid (Al-Snafi, 2017).
6. ***Eucalyptus torquata*:** It is a small-medium-sized tree with a height range from 4–10 m with branched, spreading crown and trunk with persistent bark. Its greyish-green leaves are lanceolate in shape with a size of 90–120 mm × 15–20 mm. The flower buds are distinct with rough and corrugated base and having operculum tapered to a long point. Its bloom usually large (max. 35 mm in diameter) is multihued like coral-pink to white or cream or may be red colored (Al-Snafi, 2017).

## 5.8 SOIL

Soils range from loamy to clay are suitable for eucalyptus plantation. Soils must be fertile enough with good moisture holding capacity required for optimum growth and yield. Sandy, saline, and highly alkaline soils found inappropriate for it. In contrast, alkaline and saline soils are appropriate for its hybrid cultivation. Optimum soil pH ranges from 6–7.5 (Reddy, 2015).

## 5.9 CLIMATIC REQUIREMENT FOR EUCALYPTUS FARMING

Varied climatic condition can allow Eucalyptus to grow. Wide range of temperature of 2–47°C can favor its growth. Tropical climatic condition can cause best growth but it can thrive also under temperate climatic condition. It can grow up to 2000 to 2200 m altitude, annual downpour of 4–10 cm is

needed. Owing to drought resistant potential its cultivation could be adopted in waste lands or drought areas.

## **5.10 PROPAGATION**

Various propagation methods have been developed to meet the growing demand for eucalypt products. These ranges from seeds, cuttings, *in vitro* propagation, to somatic embryogenesis.

### **5.10.1 PROPAGATION BY SEEDS**

Naturally grown and hybrid species of *Eucalyptus* provide broad genetic bases for commercial eucalyptus plantation and also cause an authentic genetic diversity resource. Substantial genetic variation assists to select superior eucalypt genotypes in tree improvement programs. Once preferred genotypes are identified, large quantities of seeds are collected and planted out to establish 'seed orchards,' from which inferior trees are identified early and removed. Generally, propagation using seeds are discouraged owing to ill growth, slow development and inferior quality timber while introgression of undesirable heredity materials could be also avoided by not adopting this method of propagation. Also, many eucalypts exhibit irregular flowering and high abortion rates, which results in unreliable and often limited seed supply. In order to maintain competitiveness and to preserve superior genotypes, more efficient and reliable methods are needed. Seed and vegetative propagation are often integrated in commercial plantation management, combining, and exploiting the advantages of each. Seed propagation entails relatively low technological investment and is favored when genotype-site matching has not been well established, when planting sites are highly variable, or when faced with recalcitrant rooting of cuttings. However, propagation by seed is a relatively slower process, requiring trees to reach maturity before producing seeds, compared to vegetative propagation from practically any explant. The production of vegetative propagules from superior selected *Eucalyptus* genotypes addresses the limitations of seed-propagated plantations. The successful rooting of stem cuttings in the mid-1950s, and its potential in supplying clonal material to the ornamental and forest industries led to the global implementation of this technology. Clonal plantations display greater uniformity in crop height, diameter, and wood properties. Being superior to sexual regeneration through the preservation of superior genotypes, growers

recognized the importance of vegetative or clonal propagation in meeting the objectives of crop improvement programs. Unlike seeds, however, many explants for vegetative propagation do not contain meristems. As a result, these have to be differentiated from existing plant tissues, a process that relies on the supply of growth regulators (Nakhooda & Jain, 2016).

### **5.11 LAND PREPARATION FOR EUCALYPTUS FARMING**

Weed free land should be selected for eucalyptus plantation while land free from any underground plant parts is one of the basic criteria of land selection for Eucalyptus. Soil should be ploughed unless it comes down to fine tilth and it should be initiated at least 3 months prior the Ridging, harrowing, and levelling – these additional operations must be completed by April for monsoon plantation (Reddy, 2015).

For pit preparation a pit (size approx. 30 cm × 30 cm × 30 cm) has to dug in advance of planting. The soil of the top half of the pit has to be separated followed by filling up of that soil back into the pit at the bottom and rest soil on top.

### **5.12 PLANTING AND SPACING**

Conventional planting time in case of Eucalyptus is monsoon but sometimes it could be also region-specific (as for example: June-July and Feb-March are the planting time in North India while only June-July in South India). The time of planting for colonies is all around the year.

For getting the commercial yield, proper management practices should be adopted. Hence, spacing between plants certainly play a vital role. According to Reddy (2015), 1.25 × 1.5 m spacing using ‘Ridge plantation’ method without incorporation of any intercrop could accommodate 2120 number of plants per acre. He also recommended 1.5 x 1.5 m (ridge plantation) and 2 x 2 m (without any intercropping) distances for planting of 1,675 and 1,184 number of plants acre<sup>-1</sup>. The standardized spacing for Eucalyptus is 2 × 2 m.

### **5.13 INTER-CROPPING**

Integrated cultivation and intercropping system could be also adopted during the early stage of eucalyptus plantation. Except paddy, any other

easy-growing minor crops (like ginger, turmeric for their shade loving nature and also some medicinal crops) could be grown initially could generate additional income. But optimum nutrient management is a crucial factor here.

#### **5.14 NUTRIENT MANAGEMENT**

Eucalyptus plants respond very well to manures and chemical fertilizers. Chemical fertilizers and FYM could apply together. In the 1<sup>st</sup> year, after 90 days of plantation, N:P:K @ 30 g plant<sup>-1</sup> and FYM@ 2 kg plant<sup>-1</sup> year<sup>-1</sup> could be applied. In 2<sup>nd</sup>, 3<sup>rd</sup>, and 4<sup>th</sup> years 50, 80, and 150 g plant<sup>-1</sup> of N:P:K and 3, 4, and 6 kgs plant<sup>-1</sup> year<sup>-1</sup> of FYM could be applied to get optimum growth (Reddy, 2015). The rate of nutrients application should be commensurate with plants age.

#### **5.15 IRRIGATION MANAGEMENT**

Immediately after transplantation of seedlings watering is mandatory. Usually drip irrigation system is most preferred for maintaining optimum soil moisture tension. Frequency of irrigation depends on soil type and weather conditions. Although, eucalyptus trees are drought tolerant but growers must attain the minimum water requirement (at least 25 irrigations are needed during dry spell) for utmost growth and yield too. But supplemental irrigation could be withstood during monsoon although Eucalyptus is partially tolerant to water stagnation condition but under exceptional condition surplus water should be drained out (Reddy, 2015).

#### **5.16 WEED CONTROL**

Manual weeding and harrowing, two times during summer and 3 times during winter should be done.

#### **5.17 TRAINING AND THINNING, PRUNING**

Crop management practices are integrally related with training, pruning, and thinning operations. 'Training' provides desired shape of trees while 'Thinning' helps to get large size and straight poles (the most economic plant

part) and ‘Pruning’ promotes plant growth. All these 3 processes involve eliminating weak, lanky, diseased, unwanted branches and shoots. These are vital to maintain high-density plantations. Up to 1<sup>st</sup> year of planting any of these operations are not needed while pruning should be carried out at the far end of 2<sup>nd</sup> year or early part of 3<sup>rd</sup> year. However, for cloned species, thinning, and pruning operations could be eliminated throughout its growing period.

Apart from its commercial uses, in landscaping industry as ‘Specimen Tree’ it could be also used to create focal point. Green hue of foliage(s), blotched bark, unique habit with clean trunk and branching pattern can add another dimension to the winter garden.

### **5.17.1 RULES OF PRUNING**

Although, any heavy pruning is not essential for *Eucalyptus* but to maintain its architectural habit the followings could put forth:

1. Sharp bypass-style secateurs, loppers, and a sharp saw are the appropriate implements for pruning eucalyptus. Selection of implement is another concern since too sharp device may cause tearing or ripping of branches and bark.
2. Pruning strategies should meet the requirement to develop strong, central trunk.
3. Formation of angles employing weak branches should be avoided.
4. A clean cut above the bud is important without any uneven protrusions.
5. ‘Gouging’ into the central trunk is not ideal.
6. South facing branches should be chosen for pruning (i.e., for making a clear slanting cut without making any wound in adjacent bark) for their quick healing.
7. ‘Arbrex Seal’ and ‘Heal’ or ‘Medo’ are popular wound sealant used to color the pruned ends.

Lateral branches emerged from central trunk shouldn’t be eliminated during first 2–3 years as they’re the fundamental components to form a strong habit. Their early removal may weaken the trunk and consequently, produce lanky structure due to not having photosynthesizing and feeding primary branches. Unplanned and inexperienced pruning cause damage to the trees (such as ‘Wind-throw’). During the early phase of growth, the concerned species should be allowed to be bushy being emerged lower side

shoots (familiar as ‘feather’ shoots for juvenile trees) from multi-stemmed branches but for single stemmed structure, the side branches along with 2 to 3 pairs of leaves after nipping shoot end could be retained. In case of liberal branch growth, repeated pruning will be beneficial but complete removal of branches is discouraged. Natural shedding of old, over-mature branches usually takes place. During early stages of growth, it’s very easy to lop off branches to give economic habit owing to vigorous growth pattern without causing any ill effects. It results in development of strong epicormic growth of trunk and large branches along with healthy root system. Furthermore, it should be remembered that the plant height shouldn’t interfere with any overhead wires (such as telegraph wires or power cables, etc.). Hence, conclusively measured and thoughtful pruning can yield a unique architectural habit (Retrieved from: [file:///G:/AAP/Eucalyptus/Training%20and%20pruning%20\\_%20Hardy%20Eucalyptus.pdf](file:///G:/AAP/Eucalyptus/Training%20and%20pruning%20_%20Hardy%20Eucalyptus.pdf)).

### **5.17.2 TIME OF PRUNING**

April and September is the time for eucalyptus pruning. Late summer or much delayed pruning may result in ill growth since wounds which are making during pruning can’t get sufficient time for healing before the onset of winter season. Frost condition immediately after the pruning is not desirable since it causes peeling away of bark from the trunk and results in complete dying of the whole tree. Pruning season not needed to be followed critically in tropical countries.

### **5.17.3 COPPICING OF EUCALYPTUS TREE**

Tall trees or shrubs are headed down near the ground level, this process is known as ‘Coppicing.’ It encourages the emergence of new shoots from root collar and bottom portion of trunk frenetically. This technique is most appropriate for rejuvenation of old, leggy trees especially which are already seasoned with hard pruning. It helps to boost up tree vigor (more clearly multi-stemmed structure). Early of March-May is the appropriate time for adopting this special operation for Eucalyptus. Here, in Eucalyptus, its trunk is headed down to its stump along with the total removal of all lateral branches using a sharp bypass lopper. The height of stump usually varies but conventionally 100–120 mm (4–5 inches) to 450 mm (180 inches) is followed. It facilitates the dormancy breaking of lignotuber and subcutaneous



shoots. Without which generation of weal shoots will take place (Retrieved from: file:///G:/AAP/Eucalyptus/Training%20and%20pruning%20\_%20Hardy%20Eucalyptus.pdf).

#### **5.17.4 POLLARDING OF EUCALYPTUS**

‘Pollarding’ operation could be defined as the decrease of overall plant height than its natural height. Owing to having dormant meristematic tissues in cambial layer enhances the ‘Pyrophytic’ (fire tolerant) feature of *Eucalyptus*. It is their survival adaptation which assists them to regenerate after the forest fire. Pollarding operation causes the break-down of the effects of few suppressive growth hormones present in shoot tips of branches. After getting release from those hormones, epicormic shoots start to develop from tissues just below the pruned end. Quick shift from juvenile and intermediate phase to adult phase of foliage(s) emerged from pollard shoots takes place. Soon new shoots form canopied multiple branches but sometimes dominant growth of one shoot may suppress other shoot growths. Pollarding is a temporary remedy to slow down its frenetic growth but genetically they possess the fast growth pattern. According to the growth pattern of individual species, the frequency of pollarding is determined. Usually, in case of quick growing species (as for example *E. glaucescens*, *E. deanei*, *E. dalrympleana*, *E. regnans*, *E. rubida*, *E. nitens*, *E. gunnii*, *E. oblique*, *E. rubida* and *E. urnigera*), every year pollarding may be needed to perform. After removal of lower lateral branches, these species quickly form the crown leaving the trunk which gives a straight, clean, tall trunk. The main branches sprout towards the crown. Only 2 years old trees should be subjected into pollarding operation otherwise trees will not get sufficient energy to resume its growth (Retrieved from: file:///G:/AAP/Eucalyptus/Training%20and%20pruning%20\_%20Hardy%20Eucalyptus.pdf).

#### **5.17.5 OVERCOMING OF SOCKETING AND WIND-THROWING**

Uprooting of eucalyptus tree due to strong wind is a common phenomenon. Hence, as protective measure the young Eucalyptus may be gently tied by a soft flexible fabric strap, so that it can sway little. Collaterally, removal of extra canopies is also required to reduce the top-crown weight. Appropriate balancing during the pruning is needed so that the tree does not take on a lop-sided appearance. In case the tree has been uprooted from its root itself,

then it is advised to remove it completely without adopting any further strategies (Retrieved from: file:///G:/AAP/Eucalyptus/Training%20and%20pruning%20\_%20Hardy%20Eucalyptus.pdf).

#### 5.17.5.1 PLANT GROWTH

The girth of the plant should be measured at 1.4 m height above the ground level. According to Reddy (2015), the optimum girth size indicates the health of eucalyptus plants. To explain this, he had stated some target girth size according to the age of plants (like girth sizes of 4–8, 6–12, 12–18, 18–22, 22–26, 26–30, 30–34, 34–38, 38–42, and 42–46 inches should be the target for 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup>, 4<sup>th</sup>, 5<sup>th</sup>, 6<sup>th</sup>, 7<sup>th</sup>, 8<sup>th</sup>, 9<sup>th</sup>, and 10<sup>th</sup> years old plants, respectively). Clones usually start to enhance the vigor from 6<sup>th</sup> years onwards.

### 5.18 PESTS AND DISEASES

Eucalyptus is the key source of fuelwood, timber, transmission poles, building materials and fencing posts. Hence, for having the commercial utilities, it is vital to maintain its productivity, quality of produces and essentially to protect them from diseases and pests. Here, the followings are the major diseases and pests found in Eucalyptus grown in central highlands eco-region.

#### 5.18.1 INSECT-PESTS

1. **Blue Gum Chalcid (BGC) (*Leptocybe invasa*):** In Kenya 2002 first this minute gall-forming wasp was found. Seedlings and saplings canopy are the chief sites of their attack. After attacking they develop the symptoms of producing typical bump-shaped galls on the respective sites especially on leaf midrib, petioles, and newly gawn stems. ‘Confidor’ and ‘Methomex’ are 2 effective systematic pesticides used to control this. Optionally, *Selitricoides neseri* could be used as biological control agent.
2. **Eucalyptus Snout Beetle (*Gonipterus scutellatus*):** The adults feed the margin while the larvae take the whole epidermis of leaves. *Anaphes nitens* as biological control agent (collected from South

Africa) was introduced first during 1945 in Kenya. Kieni, Kinangop, and Kiserian are few places greatly affected by this pest.

3. **Termites:** The field grown Eucalyptus grown in Kenya are got effected by termites. It mainly attacks the bole. First, it makes hole on the bole followed by ring barking and the successive death of the seedlings. In fact, they're also able destroy the established tree cause major losses. Gladiator, Confidor, and Imaxi could be used successfully against them.
4. **Winter Bronzing Bug (*Thaumastocoris peregrines*):** The main site of attack of this sap-sucking bug is foliage(s). During initial infestation, only foliage(s) turn reddish-brown but in case of intense infestation, foliage(s) turn into yellow-brown color (winter bronzing). Unless introducing a biological control agent, there is no other way to control this pest.

### 5.18.2 DISEASES

1. **Powdery Mildews (*Erysiphe cichoracearum*):** A whitish coating often found to occur on leaves grown under nursery conditions. The existence of this symptom for prolonged period results in puckered leaves. *Erysiphe cichoracearum*, the causal organism of Eucalyptus Powdery mildew is responsible for this. Regular spraying with fungicides can only control this.
2. **Leaf Spots (*Mycosphaerella* sp.):** Blackish spots on ventral side while purplish brown spots on dorsal side of old, aged leaves of Eucalyptus usually appear due to its attack. It can also attack the seedlings. Application of suitable fungicides and use of disease-free planting materials can merely control this disease.
3. **Cankers (*Botyrosphaeria* sp.):** It's the most frequently occurred disease in Eucalyptus (canker prone species are *E. grandis* and *E. camaldulensis*). Its onset is related with stress/offsite planting. Stem is its key site of attack. In severe cases, gum starts to ooze out from cankered stem followed by development of dwarf tree. Formation of brown ring in sapwood is another anatomical symptom of this disease.

## 5.19 HARVESTING AND YIELD

To harvest its economic part, first the entire tree is felled followed by uprooting of its stump. Best crop management practices, healthy soil status and high-density planting could yield significantly. Spacing of 2 m × 2 m could yield 80–100 tons/ha of timber while 1 m × 1 m spacing gives 25 tons/ha yield after 8 years of plantation.

### 5.19.1 ESSENTIAL OILS YIELDS

Essential oils are mainly extracted from eucalyptus leaves. The amount of extracted oil is very much species specific varies from 0.10 to 9.0% on dry weight basis. Tree age, leaf age, altitude, season, harvest time and fertilizer application are essential factor greatly influence the oil yield. Among these factors, altitude factor is most vital than others but oil content is quite season specific. For example, leaves of *E. citriodora* amassed during summer in Pakistan contained 0.9% oil than 1.3% during winter. Interestingly, the oil content in immature, juvenile leaves are higher as compared to the mature, old leaves but net quantity of harvested leaves are more in older trees. In central Thailand, January to July is the optimum time for leaf harvesting, used specially for essential oil production. Application of N<sub>2</sub>, Ph, and K fertilizers could enhance essential oil content (Zhang et al., 2010).

## 5.20 PROCESSING TECHNIQUES

Eucalyptus oil, empirically known as C<sub>10</sub>H<sub>18</sub>O. It is the most vital essential oil with complex chemical nature. Fresh and desiccated leaves, including branch tips, could be utilized for its essential oil extraction. It is famous for its antibacterial, antiviral, and antifungal properties, and biological effects on cold, influenza, other respiratory infection, rhinitis, and sinusitis. Each chemical components of its essential oil plays significant role. Its molecular structure consists of C atoms attached with each other by H atoms contribute towards its organic nature. Oxygen, sulfur, and nitrogen atoms often found in their molecular structure (Basma et al., 2013). They're classified into two groups:

1. **Volatile Fraction:** Essential oil contains 90–95% of the oil in weight.
2. **Non-Volatile Residue:** This consists of 1–10% of the oil with fatty acids, sterols, carotenoids, waxes, and flavonoids.

The properties of eucalyptus oil are shown below (Singla et al., 2013):

<b>Description:</b>	Colourless to pale yellow liquid with an aromatic and camphoraceous. Odor and pungent, cooling, spicy taste.
<b>Molecular Formula:</b>	$C_{10}H_{18}O$
<b>Molecular Weight:</b>	154
<b>Specific Gravity at 25°C:</b>	0.920–0.925
<b>Refractive Index at 20°C:</b>	1.4550–1.4600
<b>Optical Rotation at 20°C:</b>	–0.5°–+0.5°
<b>Freezing Point:</b>	0°C –+1°C
<b>Boiling Point at 760 mmHg:</b>	176–177°C.
<b>Flash Point:</b>	49°C
<b>Melting Point at 760 mmHg:</b>	1.5°C
<b>Solubility:</b>	Slightly soluble in water, soluble in ethanol, ether, chloroform, and hexane

### 5.20.1 EXTRACTION PROCEDURE

Wide range of procedures are used for eucalyptus essential oil extraction but conventionally ‘Steam Distillation’ method is followed. Recently, owing to technological advancement much more effective, efficient, and economical extraction methods are now in market counting solvent extraction, supercritical fluid extraction, and microwave extraction. Appropriateness usually varies according to individual species and varieties. But overall, the adoption of advance extraction methods is quite limited due to the initial investment and operational expenditures associated with these (Kabuba & Huberts, 2009).

### 5.20.2 PRINCIPLES OF DISTILLATION

Liquid boils at the temperature at which its vapor pressure equals the atmospheric or surrounding pressure. Whole number of molecules in two immiscible liquids *viz.* vapor phase and pure liquid, will be always higher in first phase than the second one even at identical temperature condition. Thus, the exerted pressure will be greater in vapor mixture than the pure vapor alone (Ernest, 1948). Consequently, the vapor pressure of the whole system increases that cause to evaporate essential oil at temperature below its boiling point. Hence, the vapor pressure of essential oils with high boiling point must be equivalent to the atmospheric pressure (Handa et al., 2008).

### **5.20.3 WATER DISTILLATION**

To extract the essential oils from the botanicals using water distillation method, first the materials have to immerse in liquid (water) followed by boiling. Sadlon & Ramson (2010) stated the key characteristic feature of this process, i.e., the direct contact of materials with boiling water. Movement of boiled water within plant tissues due to high temperature condition and pressure fluctuations during distillation process, create better condition for osmosis which increase the diffusion force at certain point when whole amount of volatile oils start to come out from plant tissues for collection. One of the economic measures of this distillation process is the reuse of distillate water after successful separation of oil for re-boiling purpose. To mitigate the losses of oxygenated components, this technique is followed. Along with the efficiency of this method, inexpensive, hazardless construction and portable nature of steel containers and also its appropriateness for open field utilization, are few supplemental merits. Extracted oils could be protected against overheating due to the presence of water surrounding it.

### **5.20.4 EXTRACTION METHODS**

Stress, infection or parasitic attack chiefly influence the production of essential oils (nothing but the secondary metabolites) by plants. Eucalyptus essential oils are volatile, organic compounds present in range of plant parts like fruits, flowers, bark, seeds, wood, and roots but leaves are the key source (Zhang et al., 2010). Several authors (Barazandeh, 2005; Bignell et al., 1997) narrated the following method of extractions:

- 1. Hydro-Distillation:** Here, a container containing botanicals and water is heated below which allows to release aromatic vapor followed by its condensation into liquid mixed with hydrosol. Amount of total oil yield is positively related with the distillation time. But prolonged distillation process may deteriorate the quality of extracted essential oil (Barazandeh, 2005).
- 2. Steam Distillation:** Here, steam is forced to move through the plant materials placed in a flask, so that the vaporization of volatile oils could take place. This process is almost identical with the prior one but results in higher yield (Sefidkon et al., 2008).

3. **Vacuum Distillation:** This process requires lower temperature. This condition reduces the chances of alteration of chemical compositions during distillation process using eucalyptus botanicals (Bignell et al., 1997).
4. **Supercritical Fluid Extraction (SFE):** This process involves the use of carbon-di-oxide (CO<sub>2</sub>) as non-polar solvent at fixed temperature and pressure conditions. It helps to extract the oil very rapidly. Its efficiency is more as compared to the hydro-distillation procedure (Rozzi et al., 2002).
5. **Subcritical-Water Extraction (SWE):** Hot water (100–374°C) as extractant and high pressure – these are two major components for this method of extraction. Major merits of this process are short span of extraction, superior quality of extract, cost-effective extractant and eco-friendly nature (Jimenez-Carmona & Luque de Castro, 1999; Herrero et al., 2006).

## 5.21 CHARACTERIZATION OF PHYTOCONSTITUENTS

Among other plant parts of Eucalyptus, ‘leaf’ is the vital one regarding plentiful essential oil storing. Essential oils are stored in minute glands of eucalyptus leaves. Generally, eucalyptus species contain 0–1.7% of oil of the fresh weight of the leaves. Key constituents of leaf derived eucalyptus essential oil are 1,8-cineole, the content of which may 54–95%. 1,8-cineole content may vary due to seasonal causes. Maturity of leaves also affect its chemical content. Barring this, oil also contains monoterpenes such as cymene,  $\alpha$ -pinene,  $\beta$ -pinene and limonene, geraniol, and camphene, aromadendrene, cuminaldehyde, globulol, and pinocarveol (Dhifi et al., 2016). The common co-occurred chemicals limonene,  $\alpha$ -terpineol (both could be derived from menth-1-en-8-yl cation, the identical biogenetic precursor of cineole probably), monoterpenes (such as  $\alpha$ -pinene), sesquiterpenes (such as aromadendrene), globulol, and  $\alpha$ ,  $\beta$  and  $\gamma$ -eudesmol, and aromatic constituents (such as methyl cinnamate) (Sebei et al., 2015). Beside the oil, the genus *Eucalyptus* also contained complex mixtures of plant secondary metabolites, including terpenoids, cyanogenic glycosides, hydrolysable, and condensed long chain ketones, tannins, formylated phloroglucinol compounds and flavonoids (Ben Jemâa et al., 2012). In extracted oil of *E. bicolor*, 26 compounds were found; using chemical isolation method, in which p-cymene (17.4%), neoisoverbenol (9.1%) and 1,8-cineole (37.5%) were the

key compounds (Sebei et al., 2015). Based on the reports of phyto-chemical analysis, it has found that wide ranges of chemical components (like flavonoids, tannins, terpenoids, saponins, glycosides, steroids, anthraquinones, etc.) are present in different plant parts of *E. camaldulensis*. The principal chemical constituents of its EO are oxygenated monoterpenes (34.9%), oxygenated sesquiterpenes (31.8%), monoterpene hydrocarbons (29.0%) and sesquiterpene hydrocarbons (4.3%). Analysis (by gas chromatography, GC-ion trap Mass Spectrometry [MS] and FID) of extracted essential oil by steam distillation method utilizing aerial parts of *E. camaldulensis* grown in Sardinia–Italy resulted in the identification of 37 compounds among which spathulenol (2.1–15.5%), crdypnone (3.2–10.2%), p-cymene (27.8–42.7%), beta-phellandrene (3.9–23.8%) and 1,8-cineole (4.1–39.5%) are main. Total yield ranged from 0.2–5% of its dry weight. Oils also contained moderate quantity (1.4–4.7%) of phellandral, cuminal, and other 2 not common aldehydes (Sebei et al., 2015; Elaissi et al., 2011).

Analysis report of essential oil extracted from *E. camaldulensis* leaves proved the existence of 24 chemical constituents from saline sample while 27 chemical constituents from non-saline samples. Chemical constituents of EO from saline and non-saline samples (%) respectively were:  $\alpha$ -Pinene  $14.68 \pm 0.42$  and  $12.43 \pm 0.37$ , Camphene  $0.87 \pm 0.07$  and  $2.96 \pm 0.12$ ,  $\beta$ -Pinene  $6.66 \pm 0.17$  and  $2.33 \pm 0.19$ , Eucalyptol  $34.42 \pm 1.21$  and  $40.05 \pm 1.20$ ,  $\gamma$ -Terpinene  $9.42 \pm 0.36$  and  $7.48 \pm 0.29$ ,  $\delta$ -Terpinene  $1.11 \pm 0.06$  and  $1.17 \pm 0.05$ ,  $\alpha$ -Linalene epoxide  $0.27 \pm 0.02$  and  $0.28 \pm 0.02$ , Isoamyl isovalerate  $1.07 \pm 0.09$  and  $1.10 \pm 0.07$ , Fenchyl alcohol  $0.79 \pm 0.03$  and  $0.89 \pm 0.05$ ,  $\alpha$ -Camphdenic Aldehyde  $0.66 \pm 0.03$  and  $0.67 \pm 0.02$ , *t*-Pinocarveol  $8.36 \pm 0.40$  and  $3.32 \pm 0.11$ , Myrtenal  $0.94 \pm 0.03$  and  $0.97 \pm 0.06$ , *Z*-Carveol  $1.15 \pm 0.04$  and  $1.25 \pm 0.07$ , *d*-Carvone  $0.51 \pm 0.03$  and  $0.36 \pm 0.02$ , *o*-Cymene 5-ol  $0.46 \pm 0.03$  and  $0.54 \pm 0.02$ , Benzyl valerate – and  $0.14 \pm 0.01$ ,  $\alpha$ -Gurjunene – and  $0.26 \pm 0.02$ , b-gurjunene – and  $0.22 \pm 0.03$ , Aromadendrene  $2.63 \pm 0.16$  and  $2.78 \pm 0.20$ , Alloaromadendrene  $0.89 \pm 0.05$  and  $0.97 \pm 0.07$ , Phenethyl Isovalerate  $0.90 \pm 0.03$  and  $1.01 \pm 0.06$ , Ledene  $0.45 \pm 0.05$  and  $0.52 \pm 0.03$ , Epiglobulol  $1.83 \pm 0.09$  and  $1.96 \pm 0.03$ , Ledol  $7.42 \pm 0.05$  and  $7.67 \pm 0.08$ , Viridiflorol  $1.13 \pm 0.04$  and  $2.76 \pm 0.06$ , Eremophilene  $0.78 \pm 0.03$  and  $0.85 \pm 0.02$  and g-Cadinene  $0.29 \pm 0.01$  and  $0.33 \pm 0.02$  (Al-Snafi, 2017; Ashraf et al., 2010). EO, saline, and non-saline samples of *E. camaldulensis*'s leaves are: oil content (% fresh matter basis)  $0.98 \pm 0.10$  and  $0.96 \pm 0.12$ ; refractive index (40°C)  $1.4620 \pm 0.01$  and  $1.4580 \pm 0.02$ ; solubility (ml/5 ml of 70% ethanol)  $0.93 \pm 0.10$  and  $1.05 \pm 0.16$ ; density (25°C)  $0.938 \pm 0.04$  and  $0.936 \pm 0.04$ ; specific gravity (25°C)  $0.920 \pm 0.04$  and  $0.919 \pm 0.04$ ; physical



appearance: colorless-dark yellow (Ashraf et al., 2010). New triterpenoid acids (eucalyptanoic acid) were isolated from the fresh uncrushed leaves of *Eucalyptus camaldulensis* var. 'Obtusa' along. Its structure has been established as 3 $\beta$ -hydroxyolean-9 (Al-Snafi, 2015), 12-dien-28-oic acid (Begum et al., 2002). A new triterpenoid camaldulin (3 $\beta$ -formyloxyurs-11-en-28,13 $\beta$ -olide) along with ursolic acid lactone acetate, ursolic acid lactone, betulinic acid and  $\beta$ -sitosterol 3-O- $\beta$ -d-glucopyranoside were isolated from *Eucalyptus camaldulensis* var. *obtus*e leaves (Begum et al., 2000). Triterpenoid amirinic acid (2 $\alpha$ ,3  $\beta$ ,7 $\beta$ -trihydroxy-11 $\alpha$ -methoxyurs-12-en-28-oic acid and 2 $\alpha$ , 3 $\beta$ , 7 $\beta$ -trihydroxyurs-11-en-28,13 $\beta$ -olide), ursolic acid lactone, betulinic acid, oleanolic acid and ursolic acid, were isolated from fresh, uncrushed leaves of *Eucalyptus camaldulensis* var. 'Obtuse.' Total phenolics in the *Eucalyptus camaldulensis* leaves was 364.1  $\pm$  8.2 (mg gallic acid equivalent/g) and total flavonoids was 80.5  $\pm$  0.9 (mg quercetin equivalent/g) *Eucalyptus camaldulensis* leaves contained many phenolic groups and compounds including ellagitannins, flavonoids, phloroglucinol derivatives and galloyl esters (Singab et al., 2011). *Eucalyptus incrassata* leaf sample yielded 2% w/w (dry leaves) of essential oils. 1,8-cineole (30%),  $\alpha$ -pinene (18%), aromadendrene (13%) were the main constituents of *Eucalyptus incrassata* leaves essential oils, however, the oils of *Eucalyptus incrassata* contained: 1,8-cineole; Allo-aromadendrene; Alpha-bulnesene; Alpha-campholenic-aldehyde; Alpha-copaene; Alpha-cubebene; Alpha-eudesmol; Alpha-fenchene; Alpha-gurjunene; Alpha-phellandrene; Alpha-pinene; Alpha-selinene; Alpha-terpineol; Aromadendrene; Beta-caryophyllene; Beta-cis-ocimene; Beta-cubebene; Beta-elemene; Beta-eudesmol; Beta-phellandrene; Beta-pinene; Beta-selinene; Beta-trans-ocimene; Bicycloelemene; Bicyclogermacrene; Cadina-1,4-diene; Calacorene; Calamenene; Caryophyllene-oxide; Cis-p-menth-1,8-dien-6-ol; Cryptone Leaf; Delta-cadinene; Delta-elemene; Fenchol; Gamma-eudesmol; Gamma-terpinene; Geraniol; Globulol; Isoamyl-isovalerate; Isobutyl-isovalerate; Limonene; Myrcene; P-cymen-8-ol; P-cymene; Palustrol; Pinocarvone; Sabinene; Spathulenol; Terpinolene; Torquatone; Trans-p-menth-1,8-dien-6-ol; Trans-p-menth-2-en-1-ol; Trans-p-mentha-1(7),8-dien-2-ol; Trans-pinocarveol, Trans-piperitol, Viridiflorene, and Viridiflorol (Bignell et al., 1994). New euglobals, euglobal-In-1, euglobal-In-2, euglobal-III, and euglobal-V having an acylphloroglucinol-sesquiterpene structure were isolated from the juvenile leaves of *Eucalyptus incrassata* (Takasaki et al., 1994).

The total amount of the oil in the leaves of the *Eucalyptus griffithsii* was 0.3% of the dry weight. The main constituents of the *Eucalyptus griffithsii*

leaves essential oils were 1,8-cineole (26%), *trans* pinocarveol (11%) and  $\alpha$ -pinene (8%) (Bignell et al., 1994). The Phytochemical analysis of *Eucalyptus microtheca* leaves extracts revealed the presence of essential oils, flavonoids, tannins, and alkaloids (Mahmoud, 2012). The major components of *Eucalyptus microtheca* essential oils were 1,8-cineole (34.0%), p-cymene (12.4%),  $\alpha$ -pinene (10.7%),  $\beta$ -pinene (10.5%) and viridiflorene (5.2%). However, in the oil of *Eucalyptus microtheca* flowers, 88 compounds were identified including (%):  $\alpha$ -thujene 0.504;  $\alpha$ -pinene 16.246;  $\alpha$ -fenchene 0.078; Camphene 0.271; Verbenene 0.051;  $\beta$ -pinene 11.082;  $\beta$ -myrcene 0.263;  $\alpha$ -phellandrene 7.006;  $\alpha$ -terpinene 0.367; o-cymene 13.522; Sabinene 2.131; Limonene 2.713; cis-ocimene 0.149;  $\gamma$ -terpinene 0.868; Isopropenyltoluene-cymene 0.093;  $\alpha$ -terpinolene 0.189; Linalool L 0.058; Appel oil 0.113; D-fenchyl alcohol 0.085; Hexadecane 0.147; *Trans*-pinocarveol 0.365; Pinocarvone 0.303; 4-methyl-1,3-heptadiene 0.088; 2,4-hexadiene, 2,5-dimethyl-0.070; 4-terpineol 1.052; Myrtenal 0.202;  $\alpha$ -terpineol 0.425; Myrtenol 0.160; Dodecane 0.392;  $\beta$ -citronellol 0.365; Piperitone 0.167; Citrol 0.063; Citronellyl formate 0.115; Diglycol dimethacrylate 0.787; Carvacrol 0.494; 2-butylpyridine 0.129; soledene 0.170; Copaene 0.150; Tetradecane 0.063;  $\beta$ -elemene 0.063;  $\alpha$ -gurjunene 0.542; Seychelene 0.040; *Trans*-Caryophyllene 0.227;  $\gamma$ -selinene 0.122; Calarene 0.112;  $\beta$ -gurjunene 0.073; Aromadendrene 7.444;  $\alpha$ -humulene 0.080; Alloarmadendrene 1.632;  $\alpha$ -amorphene 0.400;  $\beta$ -selinene 0.311;  $\alpha$ -guaiene 0.320; Ledene 2.135;  $\alpha$ -muurolene 0.318;  $\gamma$ -cadinene 0.667; Calamenene 0.248;  $\delta$ -cadinene 1.040; Cadina-1,4-diene 0.045;  $\alpha$ -calacorene 0.070; Epiglobulol 0.975;  $\beta$ -maaliene 0.253; Plustrol 0.221; Spathlenol 1.848; Globulol 5.419; Veridiflorol 1.044; Ledol 0.631; Hexadecane 0.212;  $\alpha$ -ylangene 0.196; Isospathulenol 0.217; Tau-cadinol 0.791;  $\alpha$ -cadinol 0.444; Cadalene 0.120; N-octadecane 0.246; Tetradecanamide 0.321; n-hexadecanoic acid 0.375; Ecosane 0.167; Hexadecanamide 0.918; Octadecanoic acid 0.425; Docosan 0.145; 9-octadecanamide 5.414; Di-[2-ethylhexyl] phthalate 0.584; 4-methylenespiro [2,4] heptane 0.055; (2-methylprop-1-enyl)-cyclohexa-1,3-diene 0.098; 1-(2'-hydroxy-3',4'-dimethylphenyl) ethenone 0.603; 7,9-di-tert-butyl-1-oxaspiro (4.5) deca-6,9-diene-2,8-dione (0.117), *trans*-1,6-dimethyl bicycle (4.3.0) non-2-en-7-one (0.346), 2-methyl-5-(1-methylethyl), 1,3-cyclohexadiene, 1H-cyclopropa[e] azulene, monoepoxide (0.139), decahydro-1,1,7-trimethyl-4-methylene and [1aR (1a.1alpha.4a.beta.7b.alpha)]-7.alpha, 7a beta (0.243). In the EO extracted from *E. microtheca* leaves, 101 compounds had been identified (%):  $\alpha$ -thujene 0.742;  $\alpha$ -pinene 6.752; camphene 0.079;  $\beta$ -pinene 5.006;  $\beta$ -myrcene 0.533;  $\alpha$ -phellandrene 16.487;

$\alpha$ -terpinene 0.832; p-cymene 5.251;  $\beta$ -phellandrene 2.194; Limonene 1.503; Cis-ocimene 1.655;  $\beta$ -ocimene Y 0.101;  $\gamma$ -terpinene 1.235; Cymene 0.024;  $\alpha$ -terpinolene 0.425; Rosefuran 0.024; Cycloheptanmethanol 0.061; Linalool L 0.093; Isoamyl isovalerate 0.529; Isoamyl valerate 0.056; Fenchol 0.076; Trans-pinene hydrate 0.062; Allocimene 0.049; 1-terpineol 0.045; 1-methylnorcarane 0.051; Ethylbenzoate 0.124; 4-terpineol 1.256; 1-(adamantly)cyclohexene 0.042;  $\beta$ -fenchol 0.203; cis-sabinol 0.224; Thiophene, 2-ethyl-5-methyl 0.120; Ascaridole 0.085; Dicyclobutylidene oxide 0.084; Divinyl dimethylsilane 0.114; Piperitone 0.196; 1-methoxyhept-1-yne 1.809; Citronellyl formate 0.029; Carvacrol 0.420;  $\alpha$ -cubebene 0.160; Isoledene 0.278; Copaene 0.308; 2-pentene-1-ol, 2-methyl 0.215;  $\alpha$ -gurjunene 1.897; Trans-caryophyllene 0.539; Aromadendrene 12.773; Epizonaren 0.067;  $\alpha$ -humulene 0.142; Alloarmadendrene 2.520;  $\gamma$ -gurjunene 0.327;  $\alpha$ -copaene 0.755;  $\beta$ -selinene 0.525;  $\beta$ -panasinsene 0.702; Ledene 5.665;  $\alpha$ -muurolene 0.398; Geremacrene B 0.099;  $\alpha$ -amorphene 1.666; cis-calamenene 0.207;  $\delta$ -cadinene 2.663; Cadina-1,4-diene 0.103;  $\alpha$ -calacorene 0.087;  $\alpha$ -cadinene 0.163; Ledane 0.092; Epiglobulol 1.167;  $\beta$ -maaliene 0.306; Palustrol 0.190; Spathlenol 1.915; Globulol 5.997; Veridiflorol 1.243; 1,3-dimethyl-5-ethyladamantane 0.285; Ledol 0.753;  $\gamma$ -curcumene 0.391; Isospathulenol 0.300; Tau-muurolol 1.580;  $\delta$ -cadinol 0.231; Guaia-3,9-diene 0.292;  $\alpha$ -cadinol 0.806; Vulgarol A 0.129; Hexadecanoic acid 0.093; 2-tridecanol 0.028; Hexadecanoic acid ethyl ester 0.025; Decyltetraglycol 0.025; Tricosane 0.012; Benzonitrile, m-phenethyl 0.032; Pentacosane 0.073; Pentaethoxylated pentadecyl alcohol 0.036; 1-cyclohexene-1-carboxaldehyde, 4-(1-methylethyl) 0.170; Cyclohexene, 3-methyl-6-(1-methylethyl) 0.108; Furan, 2,3-dihydro-4-(1-methylpropyl) (0.458), 2-cyclohexane-1-ol, 2-methyl-5-(1-methylethenyl)-trans (0.059), 10-dioxido-dodeca-3,11-diene-5-ol (0.268), 2,6,10-trimethyl-2,5,7,10-dioxido-dodeca-3,6,10,11,11-t5-etramethyl (0.138), 2,3-dimethyl-cyclohexa-1,3-diene 0.390; 2-methyl-5-(1-methylethyl) (0.026)-(1R, 2S, 4R, 7R)-7-isopropyl-5-methyl-5-bicycle [2.2.2] octen-2-ol (0.140), decahydro-1,1,3a-trimethyl-7-methylene, 1H-cyclopropa[a] naphthalene, [1a.s]1a.1.alpha, 3a.alpha, 7a. Beta, 7b.beta, 7b.alpha) (0.235), Bicyclol [3.1.0] hex-2-ene, Naphthalene-1,2,3,4,4a,7-hexahydro-1,6-dimethyl-4-(1-methylethyl) (0.139),  $\alpha$ -campholonic acid 0.049; (E)-3-isopropyl-6-oxo-2-heptenal 0.058; 1,5,5-trimethyl-6-methylene-cyclohexene 0.056; 2,6,10-trimethyl-2,5,7, Tricyclo [6.3.0.1] undec-7-ene, 1-methyl-4-isopropyl-cis-3-hydroxycyclohex-1-ene-6-one 0.230; and 1,6-dimethyl-2-cyano-3-ethyl-3-piperidine 0.612 (Maghsodlou et al., 2015; Al-Snafi, 2017).

## 5.22 BIO-PROSPECTION

### 5.22.1 PHARMACOLOGICAL EFFECTS

Out of 900 *Eucalyptus* species, >300 species produce volatile oils in their leaves. Medicinal, industrial, and perfumery/flavoring – these are three major categories of eucalyptus oil based on their uses. According to British Pharmacopoeia, ‘medicinal oils’ should contain <70% of cineole while ‘industrial oils’ must be comprised of piperitone and phellandrene and ‘perfumery/flavoring oils’ should contain higher concentrations of citronella-1 (a lemon scent) and geranyl acetate (a rose scent). The former type basically used as decongestant agent and for its antiseptic properties (used widely in-hale, sprays, embrocations, gargles, and lozenges). For other medicinal formulations like emulsions, and ointments, it is also used. To produce disinfectants, deodorants, liquid soaps, germicides, synthetic menthol and thymol, industrial oil plays significant role. For food flavoring purpose or as scenting agent or for synthesis of other flavoring agents the perfumery and flavoring oils are used. Medicinal Eucalyptus oil was produced from *Eucalyptus globulus* in China, Portugal, Spain, India, Brazil, Bolivia, Uruguay, and Paraguay; and from *Eucalyptus smithii* in South Africa, Swaziland, and Zimbabwe; from *Eucalyptus polybractea*, *Eucalyptus viridis* and *Eucalyptus dives* in Australia; from *Eucalyptus radiata* in South Africa and Australia; and from *Eucalyptus camaldulensis* in Nepal. Perfumery Eucalyptus oil was produced from *Eucalyptus citriodora* in China, Brazil, and India; and from *Eucalyptus staigeriana* in Brazil. Industrial Eucalyptus oil was produced from *Eucalyptus dives* in South Africa and Australia; and from *Eucalyptus campanulata* in Australia.

### 5.22.2 GASTROINTESTINAL EFFECTS

The potency of methanolic extracts of leaves of *E. camaldulensis* to heal ulcer ailment had been proved in rat model (Lawal et al., 2014). They confirmed that the dose rate of 500 mg kg<sup>-1</sup> of body weight continuously for 5 days at an interval of 24 hours could effectively reduce the size of ulcer. The size (diameter) of ulcer in induced-ulcer rats were reduced by 46.67 ± 3.33% as compared to control treatment using distilled water and ranitidine (Lawal et al., 2014). According to Adeniyi et al. (2009), the MIC (Minimum Inhibitory Concentration) of crude extract of *E. camaldulensis* against 6 strains of *Helicobacter pylori* (A2, T18984, 019A, A6, ATCC 4504, and ATCC 47619)

was 12.5–400  $\mu\text{g ml}^{-1}$  proved in *in-vitro* anti-*Helicobacter pylori* experiment. Triperpenoid and eucalyptanoic acids compound and their acetyl and acetylmethyl derivatives obtained from *E. camaldulensis* var. *obtusa* whole-fresh leaves possess some spasmolytic activity (Begum et al., 2002). These acetylmethyl derivatives@ 1  $\text{mg ml}^{-1}$  block the calcium influx and resulted in spasmolytic activity. Other chemical compounds like triterpenoid camaldulin (), ursolic acid lactone acetate and ursolic acid lactone (extracted from *E. camaldulensis* var. *obtusa*) also possess calcium antagonist activity and cause spasmolytic activity (Begum et al., 2000).

### 5.22.3 ANTI-INFLAMMATORY AND ANALGESIC EFFECT

1,8-Cineole (cineole) has anti-inflammation potential proved in animal model. It had successfully inhibited the experimental inflammation (paw oedema induced by carrageenan and cotton pellet-induced granuloma) in rats. Enhanced peritoneal capillary permeability, intra-plantar induced nociception and intraperitoneal acetic acid content could be effectively modulated by cineole oral administration at the dose rate of 100–400  $\text{mg/kg}$  in mice. In this experiment, the pre-treatment with naloxone@ 1  $\text{mg/kg}$  of body weight (a mu-opioid receptor antagonist) was ineffective to counter the anti-nociceptive effect of cineole in mice may be due to non-opioid mechanism. Santos & Rao (2000) revealed the significant anti-locomotive effect of cineole while it could too increase the central nervous system's depressant effect proved by the pentobarbital sleeping time in mice. For the treatment of bronchial asthma, 1,8-cineole could be also effective as evaluated by arachidonic acid (AA) metabolism. In this investigation, authors (Juergensa et al., 1998) measured *ex vivo* the production of LTB<sub>4</sub> and PGE<sub>2</sub> (AA-metabolites representative) by monocyte isolation process before the treatment, after 3 days of treatment and 4 days after the discontinuation of treatment using 1,8-cineole (3 x 200  $\text{mg/day}$ ). Consequently, they found that the production rate of representative AA-metabolites had been impaired significantly from monocytes *ex vivo* due to the blocking of AA-metabolism pathways in case of bronchial asthma patients treated with cineole at the afore mentioned dose rate for 3 days. The potential of cineole for inhibition of polyclonal boosted by cytokine production proved its anti-inflammatory efficacy. The therapeutic concentration of 1.5  $\mu\text{g/ml}$  of cineole could lower down the cytokine production in lymphocytes and monocytes of TNF- $\alpha$ , IL-1 $\beta$ , IL-4, IL-5 by 92, 84, 70, and 65% and TNF- $\alpha$ , IL-1 $\beta$ , IL-6, IL-8 by

99, 84, 76, and 65% respectively (Juergensa et al., 2004). The phagocytic effect of eucalyptus essential oil (EO) had been also evaluated by Serafino et al. (2008) in case of human monocyte derived macrophages (MDMs) *in vitro* and rat peripheral blood monocytes/granulocytes *in vivo*. This effect could be also obtained without any chemical immune-suppression administration (5-fluorouracil [FU] – a chemotherapeutic agent). The EO-induced MDM activation stimulated the phagocytic response intensely while enhanced innate cell-mediated immune response could also be attained *in vivo* after EO administration. The augmentation of phagocytic activity of the granulocytic or monocytic system had been evident by the use of 5-FU and eucalyptus EO in blended form. This combination treatment obstructed the production of 5-FU induced myelotoxicity. Juergensa et al. (1998) revealed the dose-dependent positive effect of cineole on suppression of tumour necrosis factor (alpha, interleukin-1 $\beta$ , leukotriene B4 and thromboxane B2) production. 1,8-cineole and beta-pinene – are 2 monoterpenes found from *E. camadulensis* EOs (plant part – leaves). The antinociceptive properties of these two compounds had been proved (using Tail-flick and Hot-plate methods) on rat model administered using morphine and naloxone (effective analgesics) by Atta & Alkofahi (1998); and Liapi et al. (2007). The authors confirmed the potency of cineole higher than beta-pinene. On the other hand, the synergistic impact of cineole and morphine had been evinced while the antagonistic potential of another potential analgesic, i.e., naloxone to counter the cineole effect was not evinced.

#### **5.22.4 ANTIOXIDANT EFFECT**

To reduce the oxidative stress and systolic blood pressure (SBP), the efficacy of dose-dependent 1,8-cineole was really noteworthy as described by Siramon & Ohtani (2007). About 0.1 mg kg<sup>-1</sup> and 1 mg kg<sup>-1</sup> of 1,8-cineole could significantly lower down SBP and enhance plasma nitrite concentrations as proved in rat model. Rats exposed to nicotine showed higher lipid peroxidation and plasma corticosterone levels but treatment using 0.01 and 0.1 mg/kg 1,8-cineole successfully antagonized the elevation (Siramon & Ohtani, 2007). DPPH (2,2-diphenyl-1-picrylhydrazyl) method and  $\beta$ -carotene-linoleic acid assay were useful to evaluate the *in vitro* antioxidant activities of eucalyptus EO and also the chemical composition of methanolic extracts prepared using leaves of *E. largiflorens* (*E. bicolor*) (Zhao et al., 2008). Through DPPH method, it was proved that in case of methanolic

extract, the  $IC_{50}$  value of polar sub-fraction was lower than the non-polar one while inhibition of linoleic acid oxidation by non-polar sub-fraction of methanolic extract (92–94.5%) proved its efficacy equivalent to synthetic antioxidant BHT. The methods authors used for evaluation was independent of eucalyptus oil content. Authors found the positive correlation between the antioxidant activity and the amount of total phenolics present in polar sub-fraction. These authors also studied the antioxidant activity of *E. bicolor*'s EO (essential oil) *in vitro* and reported about the superiority of extracts than EO regarding their antioxidant activity. High radical-scavenging activity and inhibition capacity (%) had been found in polar and non-polar sub-fraction of methanolic extracts. Zhao et al. (2008) also measured the antioxidant potential of *E. camadulensis*'s EO (81.9%) by evaluating its scavenging potential for stable DPPH radicals. They exhibited that the antioxidant activity of *E. camadulensis*'s EO was lower as compare with the ascorbic acid and butylated hydroxyanisole but its extracts possessed strong radical scavenging activity comparable to ascorbic acid and BHT for having chelating ferrous ions. Zhao et al. (2008) also investigated the antioxidant potential of *E. camadulensis* var. *Brevirostris* grown in Nile delta, Egypt. The methods of extraction are also vital to maintain the qualitative attributes of extracts. Supercritical fluid extraction and ethanol digestion – these two are most effective method of extractions to obtain significant antioxidant activities of the extracts. After going through the reverse-phase HPLC method of separation of both these extracts to identify the biologically active compounds, the presence of gallic and ellagic acid, common antioxidants, had been found in ethanolic extract (Zhao et al., 2008). The evaluation of antioxidant activity of EOs obtained from *Eucalyptus camaldulensis* leaves by DPPH-test revealed the values between 0.5 and 5.8 mmol l<sup>-1</sup>. The antioxidant activities of *E. camaldulensis*, *E. camaldulensis* var. *obtusa* and *E. gomphocephala* essential oils were also assessed using 2,2'-diphenylpicrylhydrazyl chemical (Takeuchi et al., 2003). The values ranged from 70 ± 3.13%, 50 ± 3.34% and 84 ± 4.64% for *E. camaldulensis*, *E. camaldulensis* var. *obtusa* and *E. gomphocephala*, respectively. The maximum antioxidant activity (84 ± 4.64%) denoted raised level of spathulenol (37.46%) (Takeuchi et al., 2003). The potential of *E. camadulensis* EO's extracted from its blooms on melanogenesis were assessed spectrophotometrically and by Western blotting technique on rat model. The antioxidant properties of the same was also found significant which caused the inhibition of melanogenesis. Bonaldo et al. (2007) stated that *E. camadulensis* flower EO-mediated depigmentation method was dependent on mitogen-activated protein kinases (MAPK) and

protein kinase A (PKA). So, the outcome of this investigation could affirm the use of eucalyptus EOs as beauty product. Zhang et al. (2010) measured the antioxidant activity of *E. microtheca*'s EO by DPPH method and found the radical scavenging activity as high as 81.8%.

### 5.22.5 CYTOTOXIC EFFECT

The anti-proliferative and cytotoxic effect of cineole was investigated by several researchers. The potency of eucalyptus EOs as an antiproliferative agent has been investigated on human colon cancer cell lines (HCT116 and RKO) using WST-8 and BrdU assays while LDH activity and TUNEL staining methods are considered as most efficient for its cytotoxicity evaluation. The apoptotic effect of cineole was analyzed *in vivo* by Murata et al. (2013) by injecting RKO cell lines inside the mice body. It is evident that the onset of apoptosis on HCT116 and RKO cell lines could be made by 1,8-cineole. Survivin, Akt, and p38 – these 3 molecules incite cleaved PARP and caspase-3 which in turn cause the induction of apoptosis. Clearly, cineole controls the functionality of these 3 molecules (cause inactivation of survivin and Akt and activation of p38). Polymerase chain reaction (PCR), DNA fragmentation and Flow cytometry are 3 effective methods to express *Bcl-2*, *Bcl-X*, *PARP-1*, *p53*, and *Bax* genes associated with apoptosis. Murata et al. (2013) noticed the inhibition potential of cineole against the tumor formation in xenotransplanted mice. According to Al-Fatimi et al. (2005), among all other commonly used traditional medicinal plants, the cytotoxic efficacy of *E. camadulensis* EO (extracted from leaf) against ECV-304 human cell lines were noteworthy. Except the above cell line, WEHI-3, HT-29 and HL-60 cell lines were also showed their responsive behavior. The cytotoxic effect was less in HT-29 and HL-60 cells ( $IC_{50} = 50.5$  and  $42.10 \mu\text{g/ml}$ , respectively) while WEHI-3 was highly sensitive ( $IC_{50} = 16.10 \mu\text{g/ml}$ ). But Mubarak et al. (2015) stated about the attenuated impact of its EO in RAW 264.7 cells. The dose-dependent aqueous acetone extract of eucalyptus could bring the cytotoxic effect on MCF-7, Hep-2, HepG-2, HeLa, HCT-116 and Caco-2 cell lines ( $IC_{50}$  ranged from 33.3 to  $57.7 \mu\text{gml}^{-1}$ ) (Singhab et al., 2011). The cytotoxic effects of essential oil of *Eucalyptus camaldulensis* was evaluated in different cancer and normal cell lines, the essential oil showed high potent cytotoxic effect on colon, prostate, and breast cancer cell lines as well as moderate potency against liver and lung cell lines with  $IC_{50}$  19.8, 31.5, 34.9, 51.7, and  $64.0 \mu\text{g/ml}$ , respectively. In the same pattern,



the oil showed high cytotoxic effect on normal epithelial retina cell line and moderate effect on normal skin fibroblast cell with  $IC_{50}$  41.3 and 60.6  $\mu\text{g/ml}$ , respectively (Rahimi-Nasrabadi et al., 2013). Jelena (2012) studied the efficacy of *in vitro* cytotoxicity of water, ethyl acetate, methanol, and *n*-butanol extracts prepared using leaves of *E. camadulensis* against human breast cancer cell lines viz. MCF 7 and MDA-MB-231 adopting MTT and SRB assays. Consequently, author found the  $IC_{50}$  value ranged from 3–250  $\mu\text{g ml}^{-1}$  proved the noteworthy cytotoxic potential of all eucalyptus extracts. Islam et al. (2015) also studied the anticancer potential of *E. camadulensis* extracts. EC-1 (*p*-menth-1-ene-4,7-diol) compound was isolated from earlier stated eucalyptus species and its potency was tested on EAC (Ehrlich Ascites Carcinoma) cells. Authors opined that this compound could improve the hematological parameters and also inhibit the growth (vol.) of cancer cells as evident in EAC-bearing mice model. They also revealed that the proliferation of EAC cells could be hindered by EC-1 administration at S-phase of cell cycle also. Cytological observation using fluorescence microscope and DNA fragmentation assay resulted in enhanced mRNA expressions of *p53* and *Bax* genes while undesirable expressions of *Bcl-2* and *Bcl-X* genes in EC-1 administered cells (Adeniyi et al., 2015). These authors also found the average cytotoxic impact of *E. camadulensis*'s crude methanolic extract on L20B (genetically engineered mouse cell line) and RD (rhabdomyosarcoma) human cells. The methanolic extract made from stem bark of *E. camadulensis* had showed *in vivo* antitumor effect tested in mice model (Islam et al., 2014). The treatment caused 96% and 81.4% inhibition and reduction in EAC cell growth and tumor burden, respectively as compared to control group. The dose rate as high as 1,120  $\text{mg kg}^{-1}$  ( $LD_{50}$ ) could cause low host toxic effects. Barring these, methanolic stem bark extract of *E. camaldulensis* could effectively cause some apoptotic features (membrane blebbing, chromatin condensation, nuclear fragmentation) in treated EAC cells. Gel electrophoresis also ascertained its apoptotic impact (Islam et al., 2014).

### 5.22.6 ANTIPARASITIC, INSECTICIDAL, AND REPELLENT EFFECTS

In studying anti-schistosomal effect of Eucalyptus essential oil, the scanning electron microscope observation showed that of essential oil produced sever damage in schistosoma worm's typography (El-Baz et al., 2015). The effect of the leaves, stem, and root barks extracts of *Eucalyptus camaldulensis*

was investigated in *Trypanosoma brucei* infected mice. The treatment using hexane, ethyl acetate, methanol, and water extracts @ 200–600 mg kg<sup>-1</sup> body weight day<sup>-1</sup> for consecutive 21 days could be effective enough against *T. Brucei*. In this experiment, authors used a 'Control' group (Berenil @ 3.5 mg kg<sup>-1</sup> body weight was used to treat) also. As a result, they found that the degree of cure was high in those groups of mice which were treated using *E. camadulensis* leaf extracts along with the standard drug (berenil treatment) but without berenil treatment the survival rate was quite less. They also found that the fresh infection induced using CSF (Cerebrospinal Fluid) in cured mice was ineffective which denote the strength of healing. Based on the bioassay-guided fractionation using *E. camadulensis* leaf, Kabiru et al. (2013) found that out of 10 fractions, 8 and 9 fractions merely expressed the minimal antitrypanosomal activity but it was incomparable to the standard drug ( $p \leq 0.05$ ). Nosratabadi et al. (2015) incubated the promastigotes of *Leshmania major* for 72 hrs. to evaluate the impact of methanolic and aqueous extracts of *E. camadulensis* on them followed by evaluation adopting MTT method. They employed 'Tartar emetic' in control group. They registered the IC<sub>50</sub> values of  $586.2 \pm 47.6$ ,  $1108.6 \pm 51.9$  and  $32.5 \pm 6.8$  µg ml<sup>-1</sup> for methanolic extracts, aqueous extracts and control group, respectively. Range of extracts like total extract, diethyl ether, chloroform, ethyl acetate, and water fractions of *E. camaldulensis* were used to evaluate their inhibitory potential on *T. vaginalis* growth (Hassani et al., 2013). As a consequence, crude extract @ 12.5 mg l<sup>-1</sup> exhibited 80%, diethyl ether extract @ 25 mg ml<sup>-1</sup> showed 100%, ethyl acetate extract @ 12.5 mg ml<sup>-1</sup> showed 100% and water extract @ 50 mg ml<sup>-1</sup> showed 80% growth inhibition after 24 hours of incubation but increased rate of growth inhibition with increased incubation period was observed in case of water extract (100% inhibition after 72 hours of incubation). The use of eucalyptus EO as a natural insecticide and pesticide is of huge significance especially environmental and toxicological point of view and also to mitigate the use of synthetic compounds (Batisha et al., 2008). The larvicidal activity of dose-dependent leaf extract and EOs of *E. camaldulensis* was investigated by Sedaghat et al. (2010) against *Anopheles stephensi*. Authors confirmed the 320 ppm of dose rate for 100% mortality of the above stated populations. In fact, EOs vapor of the same species also found to be toxic against *Aedes aegypti* adults could be proved by counting the total number of knocked-down mosquitoes at an interval of 30 mins. Excellent anti-larvicidal activity of EO extracted from leaves of *E. camadulensis* had been evinced especially in case of *Aedes aegypti* and *Aedes albopictus* larvae (Cheng et al., 2009). Authors confirmed that

alpha-terpinene was the key component for the afore mentioned activity. Lucia et al. (2009) stated that the efficacy of any fumigants usually depends on its volatility. They found a correlation between the cineole content and its toxic effect. Eucalyptus essential oil can act directly as a natural insect repellent. Eucalyptus essential oil can protect plants against rice weevils, pine processionary moths and mushroom flies. Essential oils extracted from the dried fruits of *Eucalyptus camaldulensis*, and essential oils of many other plants were tested for their repellency against the adult females of *Culex pipiens*. The essential oils showed repellency in varying degrees, Eucalyptus, basil, and anise being the most active (Erler et al., 2006). The insecticidal effects of hot and cold aqueous *Eucalyptus microtheca* leaves extracts were studied on mosquito *Culex pipiens*. Hot water extract was more effective on immature stages of insect. Eggs mortality rate of the hot and cold extracts was 51% and 47.3% respectively at a concentration of 20 mg/ml. Larval mortalities rate was significantly increased in hot and cold-water extracts as compared with control. The hot and cold extracts caused 31.5% and 28.6% pupal mortality at concentration of 20 mg/ml, respectively (Tysyar, 1997). The accumulative and non-accumulative effects of aqueous and organic extracts of the leaves of *Eucalyptus microtheca* was investigated on larvae of *Culex quinquefasciatus*. The petroleum ether extract was the most effective, however, all extracts increased the duration of larval stage and caused morphological changes of larva (Saleh et al., 2010).

### 5.22.7 ANTIMICROBIAL EFFECT

1,8-cineole is the key antimicrobial component. *Klebsiella spp.*, *Proteus spp.*, *Pseudomonas spp.*, *Escherichia coli*, and *Staphylococcus aureus* – these range of bacteria(s) are highly sensitive in respect of eucalyptus oil administration. The doses ranging from 5–25  $\mu$ l could brought significant antibacterial effect on *Escherichia coli* and *Klebsiella spp.* while 50  $\mu$ l was found appropriate for *Pseudomonas* and *Proteus spp.* (Trivedi & Hotchandani, 2004). They found that the measured area of zone of inhibition was positively correlated with dose rate irrespective of microorganisms. Interestingly, the extracts of *E. bicolor* is effective on wide ranges of bacteria, yeast, and molds. Methanolic extracts and also the volatile oils produced from *E. largiflorens* (Syn. *E. bicolor*) showed antimicrobial activity *in vitro* against *Aspergillus niger* ATCC 16404, *Candida albicans* ATCC 10231, *Pseudomonas aeruginosa* ATCC 27853, *Bacillus subtilis* ATCC

6633, *Staphylococcus aureus* ATCC 29737, *Escherichia coli* ATCC 10536, *Klebsiella pneumoniae* ATCC 10031, *Staphylococcus epidermidis* ATCC 12228, *Shigella dysenteriae* PTCC 1188, *Proteus vulgaris* PTCC 1182 and *Salmonella paratyphi*. The polarity index of the respective solvent (methanol here) is actually liable to its strong activity against almost all microorganisms while the non-polarity index doesn't possess any inhibitory effect except *Escherichia coli* as reported by Rahimi-Nasrabadi et al. (2013). Safaei-Ghomi & Ahd (2010) revealed that the anti-bacterial, microbial, and fungal potential of eucalyptus essential oil (major component cineole) was higher than its methanolic extracts as proved based on the results of minimum inhibitory concentration (MIC). For this experiment, authors used synthetic antibacterial (gentamicin [ $10 \mu\text{g disk}^{-1}$ ] and rifampin [ $5 \mu\text{g disk}^{-1}$ ]) and antifungal (nystatin [ $100 \mu\text{g disk}^{-1}$ ]) agents as reference controls. The antimicrobial activity of aqueous extracts and EOs of *E. incrassata* leaves were evident using disk diffusion method of assay against *Staphylococcus aureus* (a multidrug-resistant bacteria) (Salman et al., 2014). The range of 7–14 mm was the diameter of inhibition zone but utmost diameter was obtained in aqueous extract. Pandey & Singh (2014) studied the dose-dependent efficacy of acetone, methanol, and water extracts prepared from stem, bark, and leaf of *E. camadulensis* to evaluate the antimicrobial activity *in vitro* against *Bacillus megaterium*, *Bacillus subtilis*, *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Micrococcus luteus* and *E. coli* following agar well diffusion method of assay. They reported the utmost anti-bacterial and microbial potency against range of bacteria(s) (including gram [+] and [-]) using acetone and methanolic extracts derived from leaf and bark of *E. camadulensis*. Several research reports showed the sensitivity of *Escherichia coli*, *Staphylococcus aureus*, *Salmonella typhi*, *Proteus mirabilis* and *Klebsiella pneumoniae* towards the crude leaf extracts of *E. camadulensis*. About 50 mg is the most effective concentration for all type of extracts to suppress the diversified bacterial growth. El-Mahmood (2010) reported the least sensitivity of *E. coli* (7 mm), *K. pneumoniae* (9 mm), *P. mirabilis* (13 mm), *S. typhi* (12 mm) and *S. aureus* (12 mm) to aqueous extract while maximum efficacy of acetone extract against *E. coli* (12 mm), *K. pneumoniae* (13 mm), *S. typhi* (14 mm), *P. mirabilis* (15 mm) and *S. aureus* (14 mm). He evaluated the sensitivity based on the diameter of zone of inhibition. Salem et al. (2015) also investigated the antibacterial potential of EOs extracted from *E. camaldulensis*, *E. camaldulensis* var. 'Obtusa' and *E. gomphocephala* to evaluate their efficacy against gram (+) and (-) bacteria(s) adopting agar disc diffusion

and MIC methods. EO of *E. camadulensis* at the dose rate of 4 and 2 mg ml<sup>-1</sup> (these values are considered as Minimal Bactericidal Concentration [MBC]) could be potential enough to prevent biofilm formation by *Staphylococcus mutans* and *S. pyogenes* *in vitro* and *in vivo*, respectively (Rasooli et al., 2009). Both the MBCs of *E. camadulensis*'s EO could significantly reduce the exposure time. The effective exposure time of *S. mutans* in EO was 2.8 mins while it was 12.8 mins in case of Chlorhexidine treated group. Based on the consequences, researchers (Rasooli et al., 2009) deduced that all strength of eucalyptus EOs could effectively cause antibacterial and *in vivo* biofilm prevention effect. The investigation on the efficacy of blended version of *E. camaldulensis* EOs and common antimicrobial agents (ciprofloxacin, gentamicin, and polymyxin B) were carried out by Knezevic et al. (2016) against *Acinetobacter baumannii*, a common MDR bacteria, using broth microdilution method. Authors found the synergistic antibacterial impact evinced by time kill curve of this blended form. They also identified the essential constituents liable to this activity adopting bioautographic analysis. The effect of combination of polymyxin B and essential oil of *E. camdulensis* was maximum as confirmed by authors (Knezevic et al., 2016) resorting on a key parameter, i.e., reduced bacterial count only after brief incubation time (6 hrs.). According to Bachir & Benali (2014), the use of crude leaf extract of *E. camdulensis* could cause a significant reduction in the diameter of zone inhibition in case of *Escherichia coli* (gram negative) (10–31 mm) and *Staphylococcus aureus* (gram positive) (10–26 mm) but the resistance potential of the latter one higher than the former one. The IC (Inhibitory concentration) value ranged from 12.5–400 µg ml<sup>-1</sup> of the crude extract of same species *in vitro* was confirmed by Adeniyi et al. (2009) against *Helicobacter pylori* strains (ATCC 4504, ATCC 47619, A2, TI8984, 019A, and A6). Hexane, chloroform, methanol extracts of *E. camdulensis* and its 2 spectrophotometrically identified compounds (i.e., hydroxy-myristic acid methyl ester and pyrenyl ester [a sterol]) was also found effective (MIC of 4–64 µg ml<sup>-1</sup>) against *Mycobacterium tuberculosis* H37Rv (MtbH37Rv) (Lawal et al., 2012). El-Baz et al. (2015) confirmed the range of diameter of inhibition zones of 9.3–12.5 mm for yeast and fungi obtained using EOs extracted from *E. camadulensis* leaves while the identical range was also obtained regarding gram (+) and (-) bacteria(s). For other wide range of microorganisms (like *L. monocytogenes*, *S. aureus*, *E. coli*, *K. pneumoniae*, *S. cerevisiae*, *C. albicans*, *M. ramamnianus* and *A. ochraceus*) the potency of exclusively *E. camadulensis*'s EO had been proved by many scientists. The span of zone of inhibitions was 28 and 12

mm in case of *A. niger* and *R. solani*, respectively obtained using *E. camadulensis*'s EO (Ghaffar et al., 2015). Methanolic leaf extracts of the same species showed antifungal properties *in vitro* against *Microsporum canis*, *Microsporum gypseum*, *Tricophyton rubrum*, *Tricophyton schoenleinii*, *Tricophyton mentagrophytes* and *Epedermophyton floccosum* (Falahati et al., 2005). Furthermore, the antifungal capacity of eucalyptus essential oils at minimal concentrations against few phytopathogenic fungi had been reported by Barra et al. (2010). The sensitivity percentage of 50, 53.3, and 90 were found by El-Baz et al. (2015) in case of Rotavirus Wa strain, Cocksackievirus B4, and herpes virus type 1 respectively towards the leaf extracted EO of *E. camadulensis* proved its antiviral potency, but this extract remained ineffective for adenovirus type 7. Efficiency of methanolic extracts of the same species had also been evaluated in case of Poliovirus type I, Cocksackievirus B and Echovirus 6 (human enterovirus) (Adeniya et al., 2015) and authors reconfirmed its viricidal potential. Except benzene extract, the aqueous, ethanolic, chloroform, and acetone extract of *E. microtheca* was found effective against *S. aureus* and *S. typhimurium* but synergy of blended form (EO + conventional antibiotic) was only evident in case of *S. aureus* not against *S. typhimurium* (Suliman & Al-Dulimi, 2008). Al-Jeboury (2013) standardized the dose rate of 1 mg ml<sup>-1</sup> of methanolic (range of zone of inhibition 17–25 mm) and ethanolic extracts (range of zone of inhibition 20–29 mm) of *E. microtheca* against *Pseudomonas aeruginosa*. The minimum inhibitory concentration and minimum bacterial concentration were also evaluated against *Bacillus cereus*, *Staphylococcus aureus*, *Salmonella typhi*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and *Proteus mirabilis* by the same author. SEM (scanning electron microscope) analysis revealed that the exposure to methanolic and ethanolic extracts could cause structural changes (especially changes in cell wall active constituents) in certain bacteria(s) especially *E. coli* (MIC value was 8 mg ml<sup>-1</sup>), *Bacillus cereus* (MIC and MBC values were 8 and 16 mg ml<sup>-1</sup>) and *P. aeruginosa* (MIC & MBC values were 8 and 16 mg ml<sup>-1</sup>) (Seyyednejad et al., 2014). *Eucalyptus microtheca*'s antibacterial efficacy had been too proved against *L. monocytogenes*, *S. aureus*, *E. coli*, *K. pneumoniae*, *S. cerevisiae*, *C. albicans*, *M. ramannianus* and *A. ochraceus* by Ghaffar et al. (2015). The effectiveness of *E. microtheca*'s leaf extracts had been evaluated by Mahmoud (2012) against *Penicillium digitatum* and *Aspergillus niger* using agar well diffusion method while its alcoholic extracts showed inhibitory effect on mycelial growth of both fungi.

### 5.22.8 EFFECTS ON ORAL AND DENTAL HEALTH

The efficacy of aqueous and alcoholic extracts of eucalyptus leaves against *Mutans streptococci*, *Lactobacilli* (the most carcinogenic oral bacteria[s]) and *Candida albicans* had been evaluated by Qanbar & Al-Mizraqchi (2009). The sensitivity levels of these bacteria(s) were found maximum in case of alcoholic extracts (100 mg ml<sup>-1</sup>) at very low concentration than its aqueous extract (150 mg ml<sup>-1</sup>). In fact, the potency of both these extracts was higher as compared to conventional antibacterial agent namely chlorhexidine@ 2 mg ml<sup>-1</sup> especially against *Mutans streptococci* and *Candida albicans* as confirmed by earlier authors. The same authors standardized the MBC of 5–8, 6–10, and 3–7 mg ml<sup>-1</sup> for aqueous extracts and 4–8, 6–10, and 2–6 mg ml<sup>-1</sup> for alcoholic extracts against *Mutans streptococci*, *Lactobacilli*, and *Candida albicans*, respectively. The significant effect of eucalyptus extract on human periodontal health was evaluated by Nagata et al. (2008). For their investigation, they used eucalyptus extract containing chewing gums on three groups viz.: (i) group with deep periodontal pockets; (ii) group with minor periodontal pockets; and (iii) placebo group. Authors had applied 0.6% eucalyptus extract containing chewing gums (90 mg ml<sup>-1</sup>) to the 1<sup>st</sup> group for 3 months while 0.3% eucalyptus extract containing chewing gums (60 mg ml<sup>-1</sup>) to the 2<sup>nd</sup> group and chewing gums without any eucalyptus extract to the placebo group. The efficacy of these treatments was evaluated based on certain parameters like Plaque accumulation (PLA), gingival index (GI), bleeding on probing (BOP), periodontal probing depth (PD), and clinical attachment level (CAL) at an interval of 0, 4, 8, 12, and 14 weeks. Authors found significant improvements in treated group as compared to the placebo group.

### 5.22.9 DERMATOLOGICAL EFFECTS

The change in texture of hair strands was evinced after long-term application of eucalyptus extracts (Mamada et al., 2008). Authors carried out an investigation employing 4 groups viz. Japanese female, Japanese senior female, Japanese male, and Caucasian female. In their study they applied scalp lotion with eucalyptus oil either on half-head or whole head. Consequently, the lustrous and bouncy hair was noted after the long-term usages irrespective any race, age, and gender. They had also studied the elasticity of treated and placebo group's new hair growth by AFM (atomic force microscopy)

nano-identification method. They recognized improvement in the treated hair of new growth part of the cortex. Authors confirmed the change in physical properties of hair fiber of the treated groups was due to decreased alpha-helix structure and enhanced beta-sheet structure.

#### **5.22.10 NASAL EFFECT**

The effectiveness of 1,8-cineole on mucus hypersecretion in induced rhinosinusitis had been investigated by Sudhoff et al. (2015). An *ex vivo* nasal slice cultures were treated using lipopolysaccharides to mimic bacterial infection which resulted in the augmented number of mucin-filled goblet cells but numbers lowered down significantly after co-treatment by cineole. Real-time PCR analysis exhibited that cineole reduces the expression of mucin genes (MUC 2 and 19) related with the attenuation of NF- $\kappa$ B-activity.

#### **5.22.11 ANTIDIABETIC EFFECT**

The anti-hyperglycemic potential of ethanolic extract of *E. camaldulensis* leaves was investigated by Dawoud (2015). The author found, ethanolic extract@ 500 mg kg<sup>-1</sup> of body weight as optimum dose to get efficacious antidiabetic effect.

### **5.23 PROCESSING TECHNIQUES IN PHARMACEUTICALS**

Selection of phenotypic characters for further breeding approaches is a vital step but field dependence always poses constraints in the form of delay. Hence, to get rid of this problem marker assisted breeding approach could be a viable option. Available germplasms, selection method of phenotypic features and breeding strategies – these three influence a successful breeding program significantly. Earlier statistics of successful eucalyptus breeding program reflected a significant improvement in its average productivity, as for example in 1990 the productivity rate was 60 m<sup>3</sup> ha<sup>-1</sup> year<sup>-1</sup> which was significantly higher as compared to 12 m<sup>3</sup> ha<sup>-1</sup> year<sup>-1</sup> productivity rate in 1960 (Camargo, 2001). The above stated enhancement in eucalyptus productivity was due to some improved features like highly improved clones with quick growth rate, high wood quality, adaptability to poor soil condition and disease-pest resistance obtained through advanced silvicultural breeding strategies. Marker assisted selection (MAS) augments the selection efficiency through appropriate choice of heritable and environmental traits. Genetic



marker is a small piece of DNA proficient to make effective segregation between progenitors and progenies characterized by its highly polymorphic nature, higher degree of stability and detection potential between unlinked loci. The segregation analysis outputs have shown the efficacy of molecular markers for linkage map construction and estimation of gene frequency which found highly advantageous for genetic diversity analysis and to adopt further improved breeding approaches (Mori, 1993). To develop superior eucalyptus clones, breeding biology viz. parentage testing and evaluation of variable mating system plays a meaning role (Camargo, 2001).

#### 5.24 CHARACTERIZATION OF GENETIC DIVERSITY

The importance of molecular markers for diversity analysis of populations are well-known especially for its potential to construct populations, families, clones, cultivars, and also to segregate various populations from a gene pool. Polymorphic evaluation between *E. urophylla*, *E. grandis*, and *E. saligna* were made by Mori et al. (1996) based on isoenzyme loci to distinguish true-to-type inter-specific hybrids from others. They found the equal distribution of *Est-1*, *Est-2*, and *Idh-1* loci while another locus distribution pattern was unequal. Mori & Kageyama (2001) analyzed 5 and 69 clones and progenies of *E. grandis* and *E. urophylla* based on isoenzyme loci and consequently they obtained higher degree of genetic diversity at intra-population levels than inter-population levels. Genetic diversity analysis helps to explore the heterozygosis existing among the populations. Targeting to develop improved hybrids, prediction of degree of heterozygosis is sufficiently significant. Pigato & Lopes (2001) made genetic linkage maps after identifying 72 loci employing RAPD markers to discriminate 12 eucalyptus progenies. The genetic distances found (0.40) using Jaccard's coefficient analysis method between the groups didn't correspond the phenotypic grouping made based on various bark pattern. Furthermore, Caixeta et al. (2003) studied the genetic relatedness of 44 natural hybrids of eucalyptus using RAPD markers. Around 54% of genetic distances and 24–73% of genetic divergence level proved the discriminating efficiency of this DNA marker. The obtained consequences also demonstrated wide genetic base considered as basic requirement in all breeding programs. UPGMA (Unweighted Pair Group Method with Arithmetic Mean) analysis established 9 distinct groups with average genetic divergence > 60%. Muro-Abad et al. (2005) analyzed genetic diversity of 40 species of *E. grandis* and *E. urophylla* using 17 microsatellite markers. During their previous study, they made two 10 x 10 circulate partial diallel

crosses. Around 26.1% of heterozygosity was found while genetic diversity ranged from 10–100% and 64.6% of mean genetic distances was obtained after the amplification of 75 alleles by 17 microsatellites. Phylogenetic tree obtained by cluster analysis showed 2 groups with high level of diversity. In these 2 groups inclusion of some odd species of eucalyptus genus was also evident. They made comparative study based on the outputs of RAPD and microsatellite markers which revealed low and negative correlation values of RAPD analysis and presented the higher discriminating efficiency of microsatellite markers.

#### **5.24.1 FINGERPRINTING**

DNA fingerprinting using DNA markers is the most reliable method to characterize, identify, and segregate any populations. The origin, genetic distance and clustering of related genotypes are vital to know for adopting specific breeding programs (Pimenta et al., 2001) which could be ascertained using DNA fingerprinting technique. Neaylon et al. (2001) used RAPD markers to investigate the relationships among 3 hybrid species of eucalyptus viz. *E. macrocarpa*, *E. pyriformis*, and *E. youngiana*. The UPGMA dendrogram formed 2 clusters based on the genetic similarities, in other words, relative proximity and genetic distances among employed individuals had obtained. The analysis of dendrogram revealed that in 1 cluster all species and a hybrid of *E. macrocarpa* was included while another cluster contained *E. youngiana* and *E. pyriformis* genotypes and their respective hybrids. Later, Rocha et al. (2002) characterized 15 eucalyptus hybrid genotypes with high potency of asexual propagation using RAPD and SSR markers. As a consequence, they got unique set of markers, highly effective for identification purpose of all employed genotypes.

#### **5.24.2 QTL MAPPING**

Inter-specific hybridization is one of the ways to understand the interactive effects between alleles at the same locus (Genetic Dominance) and at different loci (Epistasis). For eucalyptus breeding mostly this method of hybridization is followed understand the non-additive genetic variance. MAS (Marker Assisted Selection) and recombination techniques of breeding could be adopted especially in vegetative propagated eucalyptus since they utilize genetic similarities (i.e., genetic linkages) to make breeding approaches successful (Grattapaglia & Sederoff, 1994) especially

using RAPD (Verhaegen et al., 1997), AFLP (Gaiotto & Grattapaglia, 1997) and SSR (Brondani et al., 1998) markers. Linkage maps are useful to recognize different genomic locations could cause the meaningful manifestation of economically viable attributes of eucalyptus. QTL (Quantitative Trait Locus) mapping is a way to draw a relationship between genotypic and set of quantitative phenotypic traits. It was used to study various characters including rooting (Marques et al., 2002), insect-pest resistance (Shepherd et al., 1995), plant growth (Squilassi & Grattapaglia, 1998), and *Puccinia psidii* rust resistance characters in *E. grandis* (Junghans et al., 2001). Few quantitative features such as wood volume and density of range of eucalyptus species have significant silvicultural importance which could be detected using QTL mapping. According to Marques et al. (2002), few loci are effective in controlling significant proportion (10–40%) of total phenotypic variation for set of quantitative traits in eucalyptus. Interestingly, the consequences of the study on QTL mapping in eucalypts for wood volume character had been made by Squilassi & Grattapaglia (1998) revealed that MAS methods are inefficient for selection of eucalyptus species both at individual and family level. 201 inter-specific hybrids of *E. urophylla* and *E. grandis* had been studied by Gion et al. (2001) to identify 8 genes and 3 Myb-transcription factors involved in lignin biosynthesis. The identified genes are [PAL (phenylalanine ammonia-lyase), COMT1 (caffeate/5-hydroxyconiferaldehyde O-methyltransferase 1), COMT2, 4CL (4-coumarate:coenzyme A ligase), C4H (cinnamate 4-hydroxylase), CCoAOMT (caffeoyl coenzyme A O-methyltransferase), CAD2 (cinnamyl alcohol dehydrogenase 2), and CCR (cinnamoyl-coenzyme A reductase)]. After identification, the identified genes were mapped single strand conformation polymorphism (SSCP) technique which revealed their 2 parental locations constructed with PCR (Polymerase Chain Reaction)-based markers. Thioacyolysis method is used generally to evaluate monomeric compositions (S/G ratio) of lignin while for QTL analysis of the same (S/G ratio) interval mapping procedure has found appropriate (Gion et al., 2001). The total variance obtained by QTL mapping ranged from 18.5–38% in case of *E. urophylla* and *E. grandis* which could hint the possibility of eucalyptus's lignin quality manipulation through MAS.

### 5.24.3 MARKER-ASSISTED SELECTION (MAS)

The key principle of using MAS is to attach molecular markers with a gene or group of genes for easy and efficient identification. Use of isoenzyme

and acid phosphatase isoenzyme markers for the selection of superior genotypes of eucalyptus are well-known. Menck (1996) used acid phosphatase isoenzyme markers to select superior genotypes which have rapid growth rate and also the efficiency to use phosphorous (ph). He had found a correlation between field grown genotypes and higher acid phosphatase enzyme activity. He reported that the tight linkage of markers with resistance alleles could cause effective and fast transmittance of the target alleles in plants. In this case, the process of pyramiding resistance alleles could be the effective one. Diameter of pole at breast height, wood growth and quality – these are key commercial features of eucalyptus but with low heritability. Hence, MAS could be an effective measure in this case. Squilassi & Grattapaglia (1998) studied the full-sib families of *E. grandis* and *E. urophylla* to assess the efficiency of MAS linked QTL method and conventional phenotypic selection for pole diameter feature of eucalyptus. The level of effectiveness of MAS based assessment usually depends on set of phenotypic and QTL data of all involved progenitors in the crossing procedure. The study made by above authors was insufficient since they evaluated only the maternal QTL allelic input not of all possible crosses. Bortoloto (2006) developed SCAR (Sequenced Characterized Amplified Region) marker to spot the blooming time of *E. grandis* using BSA (Bulked Segregant Analysis) method and consequently found its linkage to EMBRA 7 (Brondani et al., 1998) microsatellite marker. Interestingly, Brondani et al. (1998) reported the linkage of *EgLFY* gene (controls flowering) to EMBRA 6 which represented the chance to manipulate the flowering of *E. grandis*.

## 5.25 POTENTIAL BIOMOLECULES AND CLINICAL TRIALS

Osteoarthritis, the predominant chronic musculoskeletal disorder cause pain, stiffness, inflammation, and swelling especially in knee joints (Salaffi et al., 2005; Brooks, 2002; Hochberg et al., 2012). Except total knee replacement (TKR) (Carr et al., 2012; Lee et al., 2009), the use of Eucalyptus (*Eucalyptus globulus*) oil as folk medicine could be an effective nonsurgical alternative to get respite from this problem (Kumar & Laxmidhar, 2011). According to them, not only osteoarthritis, osteoporosis, upper respiratory infections, gastritis, and diabetes could be also healed using value-added products of eucalyptus.  $\alpha$ -pinene and 1,8-cineole (accounts for 70–90% [w/w] of the total content)– these 2 are key chemical constituents of eucalyptus essential oil (Singh et al., 2009). Santos & Rao (2000) proved the efficacy of oral administration of cineole on lowering the edema induced inflammation and

pain in rat model. Silva et al. (2003) reconfirmed the analgesic properties of eucalyptus oil. Juergens et al. (2004) found that the efficacy of cineole was for the restriction of cytokine secretion by T-lymphocytes. To get the myorelaxant effect and for promotion of emotional stability eucalyptus oil is of great use (Gobel et al., 1994). To assess the analgesic potency of eucalyptus oil through inhalation on patients who have undergone TKR (Total Knee Replacement) surgery, Jun et al. (2013) conducted an experiment. They recorded the responses of participants after TKR surgery and divided into 2 groups (1:1 ratio) viz. (i) intervention group (eucalyptus oil inhalation group); and (ii) control group (Inhalation group using almond oil). Authors made the evaluation using certain parameters viz. WBC (white blood cell) count, CRP (C-reactive protein) reaction, pain on a visual analog scale (VAS), heart rate and blood pressure half an hour (30 mins) prior and after the inhalation treatment of continuous passive motion (CPM) on 3 consecutive days. Jun et al. (2013) reported that the degree of TKR induced pain relief and hypertension level were significantly low in 'Intervention Group' (eucalyptus oil inhalation group) as compared to the 'Control' one which validate the potency of eucalyptus oil as pain reliever equally applicable for animal model and human being too (Table 5.4).

The antimicrobial potential of eucalyptus EOs is less investigated. Earlier, the multifaceted actions of 1,8-cineole (e.g., antitussive, antimicrobial, mucolytic, anti-inflammatory, bronchodilator, ciliary transport promotion and improved lungs infection) on human being as well as on animal model were investigated thoroughly and proved also. Antitussive in low concentration, quick nasal decongestion, ease of respiratory discomfort and reduction of dyspnea – these are proved impact of menthol treatment on several respiratory activities. Comprehensively, both could be used to heal diversified respiratory ailments (Baser & Buchbauer, 1987). Several authors recommended eucalyptus EO to heal chronic bronchitis, asthma, common cold, COPD, sinusitis, etc. Albeit the topical applications of EOs which contain high concentration of 1,8-cineole and menthol especially for infants or children should be restricted (Sebei et al., 2015; Dey & Mitra, 2013).

To heal range of respiratory tract infections (chronic bronchitis, bronchial catarrk, etc.) in adolescents (age  $>$  or  $=$  12 years) and adults both, eucalyptus EO could be highly recommended as stated by Aldoghaim et al. (2018). They used Pinimenthol® ointment consisted of eucalyptus and pine-needle EOs and menthol to study its tolerability effect for  $8.0 \pm 3.4$  days. This product was used for inhalation (17.3% of patients), inunction (29.6% of patients) or both inunction and inhalation (53.1% of patients). Based on the outcomes,

authors had recommended the use of Pinimenthol® ointment for adolescents and adults since the response regarding tolerability level ranged from excellent–good.

Barring its usefulness, the simple and cost-effective extraction procedures of eucalyptus essential oil are the key reasons of its huge commercial acceptance. Its wide range of chemical constituents (1,8-cineole, p-cymene, eucamalol, limonene, linalool,  $\alpha$ -pinene,  $\gamma$ -terpinene,  $\alpha$ -terpineol, alloocimene, and aromadendrene) are enough worthy for pest management purpose. The antimicrobial, fungicidal, insecticidal/insect repellent, herbicidal, acaricidal, and nematocidal properties of transparent and cool liquid of spicy and camphor odor eucalyptus oil have intensified its uses as eco-friendly insect and pesticide. The use of eucalyptus EO to control the indiscriminate use of synthetic chemicals, the toxicological implications and the serious issues of enhanced pest resistance against wide range of synthetic insect and pesticides become mandatory (Singla et al., 2013). The potential of eucalyptus EO as rat repellent was proved by Singh et al. (2013). In the experiment, they registered the daily food consumption from the food bowls kept inside the laboratory at an interval of 24 hr. from Tuesday–Friday. Depending on the average daily food consumption data, the repellence percent was determined using the formula mentioned below:

$$\text{Percent Repellency} = \frac{\text{FUT} - \text{FT}}{\text{FUT}} \times 100 \quad (1)$$

where; FUT is the mean daily food consumption from untreated side; and FT is the mean daily food consumption from treated side (Singla et al., 2013).

## 5.26 CONCLUSION

The multifaceted uses of eucalyptus EOs are the major reasons for its augmented demand. Its commercial uses as insect repellents, fragrant, and traditional medicines are well-known although the effective studies on diversified eucalyptus species are very finite in reality. The potency of range of biologically active constituents usually vary from species to species, so vast research is the need of the hour. Furthermore, the utility of its essential oils in diversified field has been recognized already but some cutting-edge research (as for example the new mode of actions and biosynthesis of eucalyptus oil may be required to make more improved natural pesticides, metabolically engineered pathways to increase the yield, etc.) should be carried out. In this regard, advanced molecular and biochemical approaches could act as effective

**TABLE 5.4** Patents on *Eucalyptus* Extracts

Sl. No.	Patent No.	Title	Description of Patent	Inventor
1.	WO2008011699A1 (Retrieved from: <a href="https://patents.google.com/patent/WO2008011699A1/en">https://patents.google.com/patent/WO2008011699A1/en</a> )	Fungicide with eucalyptus oil	Organic fungicide using eucalyptus essential oil (EO) where a natural emulsifier [NE] (rice or gum lecithin) has been used. The emulsion of EO in aqueous solution is made in such a way, so that the formulation becomes ready to use for plantations. It effectively minimizes the use of agrochemicals for the cultivation of farm crops. It is featured for the unique emulsification of colloiddally dispersed eucalyptus EO with natural emulsifier at the proportion of 10 (eucalyptus EO):10 (NE): 80 (water) by volume.	Walter Szortika Tessmann
2.	US20090324754A1 (Retrieved from: <a href="https://patents.google.com/patent/US20110129554A1/en">https://patents.google.com/patent/US20110129554A1/en</a> )	Method of eucalyptus extract preparation and its therapeutic value.	As drug or dietary supplement, eucalyptus extract could be used to heal neuro-mediator recapture disorder induced symptoms. It's a nutrient rich content which contains either a compound possess formula (I) or its diastereoisomers where R1 forms C=CH <sub>2</sub> replacing the carbon atom and join with formula (II) and R2 represents an isobutyl, $\alpha$ or $\beta$ -isobutyl substituent.	Christel Fiorini-Puybaret, Bernard Fabre, Cécile Chauvin, Philippe Joulia
3.	US20140100279A1 (Retrieved from: <a href="https://patents.google.com/patent/US20140100279">https://patents.google.com/patent/US20140100279</a> )	Treatment of hyperglycemia and hypertension using <i>E. camadulensis</i> extracts derived from its leaves.	The key chemical constituents of leaf extract of <i>E. camadulensis</i> are carboxylic acids (like valproic acid) where carboxyl groups are joined in chain of 7 or > carbon atoms (like stearic, palmitic, and archidic acids) or joined with 1 or 2 double bonds (like oleic and linoleic acids).	Denise Daley-Beckford, Trevor Herbert Yee, Ruby Lisa Alexander-Lindo, Paul Bancroft Reese

solution. Quantitative trait loci associated eucalyptus EO's biosynthesis in *E. grandis* × *E. urophylla* hybrids could prove the degree of advancement on its scientific research. Conclusively, long-term productive collaborative work with plant biologists, biochemists, molecular biologists, and plant breeders may make some innovative approaches towards eucalyptus.

## KEYWORDS

- **antifungal**
- **anti-inflammatory**
- **cultivation**
- **essential oil**
- ***Eucalyptus***
- **pharmaceuticals**
- **pharmacological**
- **RAPD**
- **SSR**

## REFERENCES

- Adeniyi, B. A., Ayepola, O. O., & Adu, F. D., (2015). The antiviral activity of leaves of *Eucalyptus camaldulensis* (Dehn) and *Eucalyptus torelliana* (R. Muell). *Pakistan Journal of Pharmaceutical Science*, 28(5), 1773–1776.
- Adeniyi, C. B., Lawal, T. O., & Mahady, G. B., (2009). *In vitro* susceptibility of *Helicobacter pylori* to extracts of *Eucalyptus camaldulensis* and *Eucalyptus torelliana*. *Pharmaceutical Biology*, 47(1), 99–102.
- Aldoghaim, F. S., Flematti, G. R., & Hammer, K. A., (2018). Antimicrobial activity of several cineole-rich Western Australian *Eucalyptus* essential oils. *Microorganisms*, 6(122), 1–11. doi: 10.3390/microorganisms6040122.
- Al-Fatimi, M., Friedrich, U., & Jenett-Siems, K., (2005). Cytotoxicity of plants used in traditional medicine in Yemen. *Fitoterapia*, 76(3, 4), 355–358.
- Ali, N., Al-Wabel, N. A., Shams, S., Ahmad, A., Khan, S. A., & Anwar, F. (2015). Essential oils used in aromatherapy: A systemic review. *Asia Pacific Journal of Tropical Biomedicine*, 5(8), 601–611.
- Al-Jeboury, G. H., (2013). *In vitro* antibacterial activity of *Eucalyptus microtheca* and *Cinnamomum zeylanicum* crude extracts against *Pseudomonas aeruginosa* isolates. *Medical Journal of Babylon*, 10(4), 784–793.



- Alley, N. F., Clarke, J. D. A., Macphail, M., & Truswell, E. M., (1999). Sedimentary infillings and development of major Tertiary palaeo drainage systems of south-central Australia. In: Thiry, M., & Simon-Coincon, S., (eds.), *Palaeo-Weathering, Palaeo-Surfaces and Related Continental Deposits* (Vol. 27, pp. 337–366). International Association of Sedimentologists Special Publication, Blackwell Science, Oxford, UK.
- Al-Snafi, A. E., (2015). Therapeutic properties of medicinal plants: A review of their antiviral activity. *International Journal of Pharmacological Screening Methods*, 5(2), 72–79.
- Al-Snafi, A. E., (2017). The pharmacological and therapeutic importance of *Eucalyptus* species grown in Iraq. *IOSR Journal of Pharmacy*, 7(3), 72–91.
- Ashraf, M., Ali, Q., Anwar, F., & Jussain, A. I., (2010). Composition of leaf essential oil of *Eucalyptus camaldulensis*. *Asian Journal of Chemistry*, 22(3), 1779–1786.
- Atta, A. H., & Alkofahi, A., (1998). Anti-nociceptive and anti-inflammatory effects of some Jordanian medicinal plant extracts. *Journal of Ethnopharmacology*, 60(2), 117–124.
- Bachir, R. G., & Benali, M., (2014). Antibacterial activity of essential oil of north-west Algerian *Eucalyptus camaldulensis* against *Escherichia coli* and *Staphylococcus aureus*. *Journal of Coastal Life Medicine*, 2(10), 799–804.
- Ball, J. B., (1995). Development of *Eucalyptus* plantations: An overview. *Proceedings of the Regional Expert Consultation on Eucalyptus* (Vol. 1, pp. 15–27). Bangkok, Thailand.
- Barazandeh, M. M., (2005). The effect of the method and duration of distillation on the essential oil yield and composition of *Eucalyptus globulus*. *Iranian Journal of Medicinal and Aromatic Plants Research*, 21, 75–93.
- Barra, A., Coroneo, V., Dessi, S., Cabras, P., & Angioni, A., (2010). Chemical variability, antifungal and antioxidant activity of *Eucalyptus camaldulensis* essential oil from Sardinia. *Natural Product Communications*, 5(2), 329–335.
- Basma, A., Majeed, A., Asrar, A. H., & Kurji, B. M., (2013). Extraction of oil from *Eucalyptus camadulensis* using water distillation method. *Iraqi Journal of Chemical and Petroleum Engineering*, 14(2), 7–12.
- Batisha, D. R., Singhb, H. B., Kohlia, R. K., & Kaura, S., (2008). *Eucalyptus* essential oil as a natural pesticide. *Forest Ecology and Management*, 256(12), 2166–2174.
- Begossi, A., (1996). Use of ecological methods in ethnobotany: Diversity indices. *Economic Botany*, 50(3), 280–289. doi: <http://dx.doi.org/10.1007/BF02907333>.
- Begum, S., Sultana, I., Siddiqui, B. S., Shaheen, F., & Gilani, A. H., (2002). Structure and apasmolytic activity of eucalyptanoic acid from *Eucalyptus camaldulensis* var. 'Obtusa' and synthesis of its active derivative from oleanolic acid. *Journal of Natural Products*, 65(12), 1939–1941.
- Begum, S., Sultana, I., Siddiqui, B. S., Shaheen, F., & Gilani, A. H., (2000). Spasmolytic constituents from *Eucalyptus camaldulensis* var. 'Obtusa' leaves. *Journal of Natural Products*, 63(9), 1265–1268.
- Ben, J. J. M., Haouel, S., Bouaziz, M., & Khouja, M. L., (2012). Seasonal variations in chemical composition and fumigant activity of five *Eucalyptus* essential oils against three moth pests of stored dates in Tunisia. *Journal of Stored Product Research*, 48, 61–67. doi: 10.1016/j.jspr.2011.10.001.
- Benbow, M. C., Callen, R. A., BourmaN, R. P., & Alley, N. F., (1995). Deep weathering, ferricrete and silcrete. In: Drexel, J. F., & Preiss, W. V., (eds.), *The Geology of South Australia* (Vol. 2, pp. 201–207). The Phanerozoic, Newstyle Printing Pty Ltd., Australia.
- Berry, E. W., (1916). *The Lower Eocene Floras of South-Eastern North America* (Vol. 91, pp. 1–481). U.S. Geological Survey Professional Paper.

- Bhatia, C. L., (1984). *Eucalyptus* in India – its status and research need. *Indian Forester*, 110(2), 91–96.
- Bignell, C. M., Dunlop, P. J., & Brophy, J. J., (1997). Volatile leaf oils of some south-western and southern Australian species of the genus *Eucalyptus*. *Flavor and Fragrance Journal*, 12, 423–432.
- Bignell, C. M., Dunlop, P. J., Brophy, J. J., & Jackson, J. F., (1994). Volatile leaf oils of some south-western and southern Australian species of the genus *Eucalyptus*, subgenus symphyomyrtus, section Dumaria, series incrassatae. *Journal of Flavor and Fragrance*, 9(3), 113–117.
- Blake, S. T., (1953). Studies on northern Australian species of eucalypts. *Australian Journal of Botany*, 1(2), 185–352.
- Blakely, W. F., (1934). *A Key to the Eucalyptus*. Sydney, Govt. Printer.
- Bonaldo, S. M., Schwan-Estrada, K. R. F., Stangarlin, J. R., Cruz, M. E. S., & Fiori-tutida, A. C. G., (2007). Contribution for the study of antifungal and phytoalexins elicitors in sorghum and soybean activities by eucalyptus (*Eucalyptus citriodora*). *Summa Phytopathologica*, 33, 383–387.
- Bortoloto, T. M., (2006). *Construction Aode Mapa Molecular deuma Populac , ~ Aode Eucalyptus Grandis Segregante parao Car'ater Florescimento Precoce Utilizando Marcadores RAPD* (p. 89). M.S. Dissertation, Instituto de Biociências–UNESP, Botucatu, Brazil.
- Brondani, R. P. V., Brondani, C., Tarchini, R., & Grattapaglia, D., (1998). Development and mapping of microsatellite-based markers in *Eucalyptus*. *Theoretical and Applied Genetics*, 97, 816–829.
- Brooker, I., (2002). Botany of the *Eucalyptus*. In: Coppen, J. J. W., (ed.), *Eucalyptus: The Genus Eucalyptus, Medicinal and Aromatic Plants Industrial Profiles* (Vol. 22, pp. 3–35). London, Taylor, and Francis.
- Brooker, M. I. H., (2000). A new classification of the genus *Eucalyptus* (Myrtaceae). *Australian Systematic Botany*, 13(1), 79–148.
- Brooks, P. M., (2002). Impact of osteoarthritis on individuals and society: How much disability? Social consequences and health economic implications. *Current Opinion in Rheumatology*, 14(5), 573–577.
- Caixeta, R. P., Carvalho, D., Rosado, S. C. S., & Trugilho, P. F., (2003). Variac , ~ oes gen'eticas em populac , ~ aoes de *Eucalyptus* spp. detectadas por meio de marcadores moleculares. *Revista 'Arvore*, 27, 357–363.
- Callen, R. A., & Cowley, W. M., (1995). Billa Kalina basin. In: Drexel, J. F., & Preiss, W. V., (eds.), *The Geology of South Australia* (Vol. 2, pp. 195–198). The Phanerozoic, Newstyle Printing, Mill End, Australia.
- Camargo, M. L. P., (2001). *An'alise Utilizando Marcadores Microsat'Elites da Paternidade de Indiv'idos Seleccionados em Fam'lias de Meios Irm~aos de Eucalyptus Grandis* (p. 56). M.S. Dissertation, Instituto de Biociências—UNESP, Botucatu, Brazil.
- Campinhos, E., (1993). *Sustainable Management of Plantation Forest in the Tropics and Subtropics*. In: The challenge of sustainable forest management: Technical papers. FAO, Rome.
- Carr, A. J., Robertsson, O., & Gravesetal, S., (2012). Knee replacement. *The Lancet*, 379(9823), 1331–1340.

- Chalchat, J. C., Cabard, J. L., Gorunović, M. S., Đermanović, V., & Bulatović, V., (1995). Chemical composition of *Eucalyptus globulus* oils from the Montenegro coast and east coast of Spain. *Journal of Essential Oil Research*, 7, 147–152.
- Cheng, S. S., Huang, C. G., Chen, Y. J., Yu, J. J., Chen, W. J., & Chang, S. T., (2009). Chemical compositions and larvicidal activities of leaf essential oils from two *Eucalyptus* species. *Bioresource Technology*, 100(1), 452–456.
- Chippendale, G. M., & Johnson, R. D., (1983). *Eucalypts* (p. 368). New York, Van Nostrand Reinhold.
- Chippendale, G. M., (1968). *Eucalyptus Buds and Fruits* (p. 96). Canberra, Forestry and Timber Bureau.
- Chippendale, G. M., (1988). Flora of Australia. In: *Myrtaceae-Eucalyptus, Angophora. Canberra* (Vol. 19, p. 542). Australian Govt. Publ. Service.
- Damjanović-Vratnica, B., Đakov, T., Šuković, D., & Damjanović, J., (2011). Antimicrobial effect of essential oil isolated from *Eucalyptus globulus* Labill. from Montenegro. *Czech Journal of Food Science*, 3, 277–284.
- Dawoud, A. D. H., (2015). Effects of ethanolic leaf extract of *Eucalyptus camaldulensis* on oral glucose tolerance test in type-2 model diabetic rats. *Journal of Network Communications and Emerging Technologies*, 2(2), 6–8.
- Delwaulle, J. C., Laplace, Y., & Quillet, G., (1983). Production massive deboutures d'eucalyptusen r'épublique Populaire du Congo. *Silvicultura*, 8(32), 779–781.
- Dey, B., & Mitra, A., (2013). Chemo-profiling of *Eucalyptus* and study of its hypoglycemic potential. *World Journal of Diabetes*, 4(5), 170–176.
- Dhifi, W., Bellili, S., Jazi, S., Bahloul, N., & Mnif, W., (2016). Essential oils' chemical characterization and investigation of some biological activities: A critical review. *Medicines*, 3(4), 25.
- Dixit, A., Rohilla, A., & Singh, V., (2012). *Eucalyptus globulus*: A new perspective in therapeutics. *International Journal of Pharmacy and Chemistry: Science*, 1(4), 1678–1683.
- Dreger, M., & Wielgus, K., (2013). Application of essential oils as natural cosmetic preservatives. *Herba Polonica*, 59(4), 142–156. doi: 10.2478/hepo-2013-0030.
- Durand-Cresswell, R., Boulay, M., & Franclet, A., (1985). Vegetative propagation of *Eucalyptus*. In: Bonga, J. M., & Durzan, D. J., (eds.), *Tissue Culture in Forestry* (pp. 150–181). Martinus Nijhoff, Dordrecht, The Netherlands.
- Elaissi, A., Hadj, S. K., Mabrouk, S., Khouja, M. L., Chemli, R., & Harzallah-Skhiri, F., (2011). Antibacterial activity and chemical composition of 20 *Eucalyptus* species essential oils. *Food Chemistry*, 129, 1427–1434. doi: 10.1016/j.foodchem.2011.05.100.
- El-Baz, F. K., Mahmoud, K., El-Senousy, W. M., Darwesh, O. M., & ElGohary, A. E., Antiviral, antimicrobial and schistosomicidal activities of *Eucalyptus camaldulensis* essential oils. *International Journal of Pharmaceutical Sciences Reviews and Research*, 31(1), 262–268.
- Eldridge, K. G., Davidson, J., Harwood, C., & Van, W. G., (1994). *Eucalypt Domestication and Breeding* (p. 288). Oxford Science, Oxford.
- El-Mahmoud, M. A., (2010). Antibacterial potential of crude leaf extracts of *Eucalyptus camaldulensis* against some pathogenic bacteria. *African Journal of Plant Science*, 4(6), 202–209.
- Erler, F., Ulug, I., & Yalcinkaya, B., (2006). Repellent activity of five essential oils against *Culex pipiens*. *Fitoterapia*, 77(7, 8), 491–494.
- Ernest, G., (1948). *The Essential Oils* (Vol. 1, p. 427). Dr. Van Nostrand publishing company.

- Eyles, A., Pinkard, E. A., O'grady, A. P., Worledge, D., & Warren, C. R., (2009). Role of cortical photosynthesis following defoliation in *Eucalyptus globulus*. *Plant, Cell & Environment*, 32(8), 1004–1014. doi: 10.1111/j.1365-3040.2009.01984.x.
- Fact.MR (2022) Eucalyptus Oil Market Forecast, Trend Analysis and Competition Tracking: Global Market insights 2017 to 2022. Retrieved from: <https://www.factmr.com/report/92/eucalyptus-oil-market>.
- Falahati, M., Tabrizib, N. O., & Jahaniani, (2005). Anti dermatophyte activities of *Eucalyptus camaldulensis* in comparison with griseofulvin. *Iranian Journal of Pharmacology & Therapeutics*, 4(2), 80–83.
- FAO Website, (2000). *Global Forest Resources Assessment*. Retrieved from: <http://fao.org/forestry/fo/fra/index.jsp> (accessed on 31 August 2023).
- Gaiotto, F. A., & Grattapaglia, D., (1997). Estimation of genetic variability in a breeding population of *Eucalyptus urophylla* using AFLP markers. In: *Proceedings of the IUFRO Conference on Silviculture and Improvement of Eucalypts* (pp. 46–49). Salvador, Brazil.
- Gauthier, J. J., (1991). *Plantation Wood in International Trade*. Paper to the issues dialogue on tree plantations – benefits and drawbacks. Centre in Applied Studies in International Negotiations, Geneva.
- Ghaffar, A., Yameen, M., Kiran, S., Kamal, S., Jalal, F., Munir, B., Saleem, S., et al., (2015). Chemical composition and *in vitro* evaluation of the antimicrobial and antioxidant activities of essential oils extracted from seven *Eucalyptus* species. *Molecules*, 20, 20487–20498.
- Gion, J. M., Boudet, C., Grima-Pettenati, J., Ham, P. F., Plomion, C., Baillères, H., & Verhaegen, D., (2001). A candidate genes approach identifies CCR, Pal and C4H as loci for syringyl/guaiacyl ratio in an interspecific hybrid between *Eucalyptus urophylla* and *E. grandis*. In: *Developing the Eucalypt of the Future—IUFRO International Symposium* (p. 125). Valdivia, Chile.
- Gobel, H., Schmidt, G., & Soyka, D., (1994). Effect of peppermint and eucalyptus oil preparations on neurophysiological and experimental algometric headache parameters. *Cephalalgia*, 14(3), 228–234.
- González, E. R., Andrade, A. A., Bertolo, A. L., Lacerda, G. C., Carneiro, R. T., Defavari, V. A. P., Labate, M. T. V., & Labate, C. A., (2002). Production of transgenic *Eucalyptus grandis* × *E. urophylla* using the sonication-assisted *Agrobacterium* transformation (SAAT) system. *Functional Plant Biology*, 29, 97–102.
- Grattapaglia, D., & Sederoff, R. R., (1994). Genetic linkage maps of *Eucalyptus grandis* and *Eucalyptus urophylla* using a pseudo-testcross: Mapping strategy and RAPD markers. *Genetics*, 137, 1121–1137.
- Handa, S. S., Khanuja, S. P., Longo, G., & Rakesh, D. D., (2008). *Extraction Technologies for Medicinal and Aromatic Plants* (p. 260). United Nations Industrial Development Organization and the International Centre for Science and High Technology.
- Hassani, S., Asghari, G., Yousefi, H., Kazemian, A., Rafieian, M., & Darani, H. Y., (2013). Effects of different extracts of *Eucalyptus camaldulensis* on *Trichomonas vaginalis* parasite in culture medium. *Advance Biomedical Research*, 2, 47.
- Hermesen, E. J., Gandolfo, M. A., & Zamaloa, M. D. C., (2012). The fossil record of *Eucalyptus* in patagonia. *American Journal of Botany*, 99(8), 1356–1374.
- Herrero, M., Cifuentes, A., & Ibanez, E., (2006). Sub and supercritical fluid extraction of functional ingredients from different natural sources: Plants, food-by-products, algae, and microalgae. *Food Chemistry*, 98, 136–148.

- Hill, K. D., & Johnson, L. A. S., (1995). Systematic studies in the *Eucalyptus*. In: A revision of the bloodwoods, genus *Corymbia* (*Myrtaceae*). *Telopea*, 6(2, 3), 185–504.
- Hill, K., (1991). *PlantNet, Eucalyptus largiflorens* F. Muell. (Vol. 2). Taxon concept: Flora of NSW. Retrieved from: <http://plantnet.rbgsyd.nsw.gov.au/cgi-bin/NSWfl.pl?page=nswfl&lvl=sp&name=Eucalyptus~largiflorens> (accessed on 31 August 2023).
- Hochberg, M. C., Altman, R. D., & April, K. T., (2012). American college of rheumatology 2012 recommendations for the use of non-pharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. *Arthritis Care and Research*, 64(4), 465–474.
- Islam, F., Khanam, J. A., Khatun, M., Zuberi, N., Khatun, L., Kabir, S. R., Ali, M. M., et al., (2015). A p-Menth-1-ene-4, 7-diol (EC-1) from *Eucalyptus camaldulensis* Dnh. Triggers apoptosis and cell cycle changes in Ehrlich ascites carcinoma cells. *Phytotherapy Research*, 29(4), 573–581.
- Islam, F., Khatun, H., Khatun, M., Ali, S. M., & Khanam, J. A., (2014). Growth inhibition and apoptosis of Ehrlich ascites carcinoma cells by the methanol extract of *Eucalyptus camaldulensis*. *Pharmaceutical Biology*, 52(3), 281–290.
- Jelena, D., (2012). *Myrtus communis* and *Eucalyptus camaldulensis* cytotoxicity on breast cancer cells. *Matica Srpska Journal for Natural Sciences*, 123, 65–73.
- Jimenez-Carmona, M. M., & Luque De, C. M. D., (1999). Isolation of *Eucalyptus* essential oil for GC-MS analysis by extraction with subcritical water. *Chromatographia*, 50, 578–582.
- Juergens, U. R., Engelen, T., Racké, K., Stöber, M., Gillissen, A., & Vetter, H., (2004). Inhibitory activity of 1, 8-cineol (eucalyptol) on cytokine production in cultured human lymphocytes and monocytes. *Pulmonary Pharmacology and Therapeutics*, 17(5), 281–287.
- Juergens, U. R., Engelen, T., Racké, K., Stöber, M., Gillissen, A., & Vetter, H., (2004). Inhibitory activity of 1,8-cineol (eucalyptol) on cytokine production in cultured human lymphocytes and monocytes. *Pulmonary Pharmacology and Therapeutics*, 17(5), 281–287.
- Juergens, U. R., Stöber, M., & Vetter, H., (1998b). Inhibition of cytokine production and arachidonic acid metabolism by eucalyptol (1,8-cineole) in human blood monocytes *in vitro*. *European Journal of Medical Research*, 3(11), 508–510.
- Juergens, U. R., Stöber, M., Schmidt-Schilling, L., Kleuver, T., & Vetter, H., (1998a). Anti-inflammatory effects of eucalyptol (1,8-cineole) in bronchial asthma: Inhibition of arachidonic acid metabolism in human blood monocytes *ex vivo*. *European Journal of Medical Research*, 3(9), 407–412.
- Jun, Y. S., Kang, P., Min, S. S., Lee, J. M., Kim, H. K., & Seol, G. H., (2013). Effect of *Eucalyptus* oil inhalation on pain and inflammatory responses after total knee replacement: A randomized clinical trial. *Evidence-Based Complementary and Alternative Medicine*, 2013(502727), <http://dx.doi.org/10.1155/2013/5027271-7>.
- Junghans, D. T., Alfenas, A. C., Brommonschenkel, S. H., Maffia, L. A., Oda, S., Mello, E. J., & Grattapaglia, D., (2001). *Eucalyptus* rust: Rating scale, inheritance of resistance and identification of RAPD markers linked to resistance. In: *Eucalyptus Grandis* (p. 123). Developing the Eucalypt of the future—IUFRO International Symposium, Valdivia, Chile.
- Kabiru, Y. A., Ogbadoyi, E. O., Okogun, J. I., Gbodi, T. A., & Makun, H. A., (2013). Antitrypanosomal potential of *Eucalyptus camaldulensis*. *British Journal of Pharmacology and Toxicology*, 4(2), 25–32.
- Kabuba, J., & Huberts, R., (2009). Steam extraction of essential oils: Investigation of process parameters. *The Canadian Journal of Chemical Engineering*, 87, 915–920.
- Kadambi, K., (1944). *A Working Plan for the Devarayadurga Group of Forests*, Tumkur District, 1942–51, Printed by the Superintendent, Government Press, Bangalore.

- Knezevic, P., Aleksic, V., Simin, N., Svircev, E., Petrovic, A., & Mimica-Dukic, N., (2016). Antimicrobial activity of *Eucalyptus camaldulensis* essential oils and their interactions with conventional antimicrobial agents against multi-drug resistant *Acinetobacter baumannii*. *Journal of Ethnopharmacology*, 178, 125–136.
- Kumar, H. D., & Laxmidhar, S., (2011). A review on phytochemical and pharmacological of *Eucalyptus globulus*: A multipurpose tree. *International Journal of Research in Ayurveda & Pharmacy*, 2(5), 1527–1530.
- Labate, C. A., De Assis, T. F., Oda, S., De Mello, E. J., Mori, E. S., Moraes, M. L. T., Cid, L. P. B., et al., (2008). Forest tree species. In: *Eucalyptus* (pp. 1–9).
- Lawal, T. O., Adeniyi, B. A., & Olaleye, S. B., (2014). Ulcer-healing promoting activities of methanol extracts of *Eucalyptus camaldulensis* Dehnh. and *Eucalyptus torelliana* F. Muell in rat. *Archives of Basic and Applied Medicines*, 2, 147–152.
- Lawal, T. O., Adeniyi, B. A., Adegoke, A. O., Franzblau, S. G., & Mahady, G. B., (2012). *In vitro* susceptibility of *Mycobacterium tuberculosis* to extracts of *Eucalyptus camaldulensis* and *Eucalyptus torelliana* and isolated compounds. *Pharmaceutical Biology*, 50(2): 92–98. doi: 10.3109/13880209.2011.625953.
- Lee, S. C., Yoon, J. Y., Jung, K. A., Nam, C. H., & Jung, S. H., (2009). Perioperative changes in C-reactive protein levels after unilateral and simultaneous bilateral total knee replacement. *The Journal of the Korean Orthopaedic Association*, 44(4), 442–448.
- Liapi, C., Anifandis, G., Chinou, I., Kourounakis, A. P., Theodosopoulos, S., & Galanopoulou, P., (2007). Antinociceptive properties of 1,8-cineole and beta-pinene, from the essential oil of *Eucalyptus camaldulensis* leaves, in rodents. *Planta Medica*, 73(12), 1247–1254.
- Lo Cantore, P., Shanmugaiah, V., & Iacobellis, N. S., (2009). Antibacterial activity of essential oil components and their potential use in seed disinfection. *Journal of Agricultural Food Chemistry*, 57(20), 9454–9461. doi: <http://dx.doi.org/10.1021/jf902333g>.
- Lucia, A., Licastro, S., Zerba, E., Gonzalez, A. P., & Masuh, H., (2009). Sensitivity of *Aedes aegypti* adults (*Diptera: Culicidae*) to the vapors of *Eucalyptus* essential oils. *Bioresource Technology*, 100(23), 6083–6087.
- Maghsoodlou, M. T., Kazemipoor, N., Valizadeh, J., Seifi, M. F. N., & Rahnesan, N., (2015). Essential oil composition of *Eucalyptus microtheca* and *Eucalyptus viminalis*. *Avicenna Journal of Phytomedicine*, 5(6), 540–552.
- Mahmoud, S. N., (2012). Antifungal activity of *Cinnamomum zeylanicum* and *Eucalyptus microtheca* crude extracts against food spoilage fungi. *Euphrates Journal of Agriculture Science*, 4(3), 26–39.
- Mamada, A., Ishihama, M., Fukuda, R., & Inoue, S., (2008). Changes in hair properties by *Eucalyptus* extract. *Journal of Cosmetic Science*, 59(6), 481–496.
- Marques, C., Brondani, R. P. V., Grattapaglia, D., & Sederoff, R., (2002). Conservation of microsatellite loci and QTL for vegetative propagation in *Eucalyptus tereticornis*, *E. globulus*, *E. grandis* and *E. urophylla*. *Theoretical and Applied Genetics*, 105, 474–478.
- Martin, B., & Cossalter, C., (1975). *Eucalyptus* in the Sunda isles. In: *Les Eucalyptus Des Iles de la Sonde* (pp. 1–25). (Retrieved from: [https://uses.plantnet-project.org/e/index.php?title=Eucalyptus\\_urophylla\\_\(PROSEA\)&mobileaction=toggle\\_view\\_desktop](https://uses.plantnet-project.org/e/index.php?title=Eucalyptus_urophylla_(PROSEA)&mobileaction=toggle_view_desktop) (accessed on 30 September 2023)).
- Menck, A. L. M., (1996). *Crescimento e Atividade da Fosfatase 'Acida de Plântulas de Progenies de Eucalyptus Grandis Hill ex Maiden em Diferentes Doses de Fósforo in Vitro* (p. 88). M. S. Dissertation, Escola Superior de Agricultura “Luiz de Queiroz”—USP, Piracicaba, Brazil.

- Mori, E. S., & Kageyama, P. Y., (2001). Genetic variability in selected subpopulations of *Eucalyptus grandis* Hill ex. Maiden by isoenzymes. In: *Developing the Eucalypt of the Future—IUFRO International Symposium* (p. 124). Valdivia, Chile.
- Mori, E. S., (1993). *Variabilidade Genética Isoenzimática em uma População de Eucalyptus grandis Hill ex Maiden Submetida a Diferentes Intensidades de Seleção*, ao (p. 119). PhD Thesis, Escola Superior de Agricultura “Luiz de Queiroz”—USP, Piracicaba, Brazil.
- Mori, E. S., Valle, C. F., Golvêca, C. F., & Martins-Corder, M. P., (1996). Isoenzymatic characterization of *Eucalyptus urophylla*, *E. grandis* and *E. saligna* for inter-specific hybrid production. In: *Proceedings of the Tree Improvement for Sustainable Tropical Forestry—QFRI-IUFRO Conference* (pp. 524, 525). Caloundra, Australia.
- Mubarak, E. E., Zeenelabdin, A. L., Ahmed, I. F. A., Ahmed, A. B. A., & Taha, R. M., (2015). Essential oil compositions and cytotoxicity from various organs of *Eucalyptus camaldulensis*. *International Journal of Agricultural Biology*, 17, 320–326.
- Murata, S., Shiragami, R., & Kosugi, C., (2013). Antitumor effect of 1, 8-cineole against colon cancer. *Oncology Report*, 30(6), 2647–2652. doi: <https://doi.org/10.3892/or.2013.2763>.
- Muro-Abad, J. I., Rocha, R. B., Cruz, C. D., & Araújo, E. F., (2005). Obtainment of *Eucalyptus* spp. hybrids aided by molecular markers—SSR analysis. *Scientia Forestalis*, 67, 53–63.
- Nagata, H., Inagaki, Y., Tanaka, M., Ojima, M., Kataoka, K., Kuboniwa, M., Nishida, N., et al., (2008). Effect of *Eucalyptus* extract chewing gum on periodontal health: A double-masked, randomized trial. *Journal of Periodontology*, 79(8), 1378–1385.
- Naithan, H. B., (2016). ENVIS report on forestry and forest related livelihoods. Botany of genus *Eucalyptus*. *ENVIS Forestry Bulletin*, 12(2). Retrieved from: <https://frienvis.nic.in/WriteReadData/UserFiles/file/Content-Page/Books/Eucalypts/Botany-of-Genus-Eucalypts.pdf> (accessed on 30 September 2023).
- Nakhoda, M., & Jain, S. M., (2016). A review of *Eucalyptus* propagation and conservation. *Propagation of Ornamental Plants*, 16(4), 101–119.
- Neaylon, K., Delaporte, K. L., Sedgley, M., Collins, G. G., & Conran, J. G., (2001). Molecular analysis of hybrids among the ornamental eucalypts *Eucalyptus macrocarpa*, *E. pyriformes*, and *E. youngiana*. *Journal of the American Society for Horticultural Science*, 126, 336–339.
- Nosratabadi, S. J., Sharifi, I., Sharififar, F., Bamorovat, M., Daneshvar, H., & Mirzaie, M., (2015). *In vitro* antileishmanial activity of methanolic and aqueous extracts of *Eucalyptus camaldulensis* against *Leishmania major*. *Journal of Parasitic Disease*, 39(1), 18–21.
- Olayinka, A. J., Olawumi, O. O., Olalekan, A. M., Abimbola, A. S., Idowu, D. I., & Theophilus, O. A., (2012). Chemical composition, antioxidant, and cytotoxic effects of *Eucalyptus globulus* grown in north-central Nigeria. *Journal of Natural Product and Plant Research*, 2(1), 1–8.
- Pain, G., (2007). *Eucalyptus Oil Applications and Markets*. Technical Report, Verve Energy Eucalyptus Oil Markets. Retrieved from: [https://www.researchgate.net/publication/272355780\\_Eucalyptus\\_oil\\_applications\\_and\\_markets](https://www.researchgate.net/publication/272355780_Eucalyptus_oil_applications_and_markets) (accessed on 31 August 2023).
- Palanna, R. M., (n.d.). *Eucalyptus in India*. Retrieved from: <http://www.fao.org/3/ac772e/ac772e06.htm> (accessed on 31 August 2023).
- Pandey, B., & Singh, S., Evaluation of antimicrobial potential of *Eucalyptus camaldulensis* L. *Journal of Pharmaceutical Chemical and Biological Sciences*, 2(3), 166–171.

- Pigato, S. M. P., & Lopes, C. R., (2001). The evaluation of genetic variability in four generations of *Eucalyptus urophylla* S.T. Blake by RAPD marker. *Scientia Forestalis*, 60, 119–133.
- Pimenta, D., Campinhos, E. N., Augusto, F., & Brun, F. L., (2001). Molecular characterization of the main International Paper eucalypt clones with operational purposes in Brazil. In: *Developing the Eucalypt of the Future—IUFRO International Symposium* (p. 135). Valdivia, Chile.
- Potts, B. M., (2004). Genetic improvements of eucalypts. In: Burley, J., Evans, J., & Youngquist, J. A., (eds.), *Encyclopedia of Forest Sciences* (pp. 1480–1490). Elsevier Academic Press, Oxford.
- Pryor, L. D., (1995). *Eucalyptus for Planting* (Vol. 11). FAO Forestry Series. ISBN 92-5-100570-2.
- Pryor, L. D., Williams, E. R., & Gunn, B. V., (1995). A morphometric analysis of *Eucalyptus urophylla* and related taxa with descriptions of 2 new species. *Australian Systematic Botany*, 8(1), 57–70.
- Qanbar, F. H., & Al-Mizraqchi, A. S., (2009). The antimicrobial effect of aqueous & alcoholic extracts of *Eucalyptus* leaves on oral *Mutans streptococci*, *Lactobacilli* & *Candida albicans* (an *in vitro* study). *Journal of Bagh Coll Dentistry*, 21(4), 109–112.
- Rahimi-Nasrabadi, M., Nazarian, S., Farahani, H., Koohbijari, G. R. F., Ahmadi, F., & Batooli, H., (2013). Chemical composition, antioxidant, and antibacterial activities of the essential oil and methanol extracts of *Eucalyptus largiflorens* F. Muell. *International Journal of Food Properties*, 16(2), 369–381.
- Rasooli, I., Shayegh, S., & Astaneh, S., (2009). The effect of *Mentha spicata* and *Eucalyptus camaldulensis* essential oils on dental biofilm. *International Journal of Dental Hygiene*, 7(3), 196–203.
- Reddy, J., (2015). *Eucalyptus Farming Information Guide*. Retrieved from: <https://www.agrifarming.in/eucalyptus-farming> (accessed on 31 August 2023).
- Rocha, R. B., Abad, J. I. M., Pires, I. E., & Ara'ujo, E. F., (2002). Fingerprint and genetic diversity analysis of *Eucalyptus* spp. genotypes using RAPD and SSR markers. *Scientia Forestalis*, 62, 24–31.
- Rockwood, D. L., (2012). History and status of *Eucalyptus* improvement in Florida. *International Journal of Forestry Research*, 2012, 1–10. doi: 10.1155/2012/607879.
- Rozzi, N. L., Phippen, W., Simon, J. E., & Singh, R. K., (2002). Supercritical fluid extraction of essential oil components from lemon-scented botanicals. *Lebensmittel-Wissenschaft und –Technologie*, 35, 319–324.
- Sadlon, A. E., & Lamson, D. W., (2010). Immune-modifying and anti-microbial effects of *Eucalyptus* oil and simple inhalation devices. *Alternative Medicine Review*, 15(1), 33–47.
- Safaei-Ghomi, J., & Ahd, A. A., (2010). Antimicrobial and antifungal properties of the essential oil and methanol extracts of *Eucalyptus largiflorens* and *Eucalyptus intertexta*. *Pharmacognosy Magazine*, 6(23), 172–175.
- Salaffi, F., De Angelis, R., & Grassi, W., (2005). Prevalence of musculoskeletal conditions in an Italian population sample: Results of a regional community-based study – the mapping study. *Clinical and Experimental Rheumatology*, 23(6), 819–828.
- Saleh, T. A., Abid, T. M., & Thaker, A. A., (2010). The accumulative and non-accumulative effects of water and some organic extracts of *Eucalyptus microtheca* and *Datura innoxia* on the larvae of *Culex quinquefasciatus*. *Anbar Journal of Agriculture Sciences*, 8(4), 321–333.



- Salem, M. Z., Ashmawy, N. A., Elansary, H. O., & El-Settawy, A. A., (2015). Chemotyping of diverse *Eucalyptus* species grown in Egypt and antioxidant and antibacterial activities of its respective essential oils. *Natural Product Research*, 29(7), 681–685.
- Salman, E. D., Al-Saedi, A. J. H., Al-Kazzaz, A. G. M., & Yahya, S. S., (2014). The effect of aqueous extract and essential oils of the leaves of *Eucalyptus incrassate* on  $\beta$ -lactam resistant *Staphylococcus aureus*. *Journal for Pure and Applied Science*, 17(1), 76–82.
- Santos, F. A., & Rao, V. S., (2000). Anti-inflammatory and antinociceptive effects of 1, 8-cineole a terpenoid oxide present in many plant essential oils. *Phytotherapy Research*, 14(4), 240–244.
- Saveyn, A., Steppe, K., Ubierna, N., & Dawson, T. E., (2010). Woody tissue photosynthesis and its contribution to trunk growth and bud development in young plants. *Plant Cell and Environment*, 33(11), 1949–1958. doi: 10.1111/j.1365-3040.2010.02197.x.
- Sebei, K., Sakouhi, F., Herchi, W., Khouja, M. L., & Boukhchina, S., (2015). Chemical composition and antibacterial activities of seven *Eucalyptus* species essential oils leaves. *Biological Research*, 48(1), 1–7.
- Sedaghat, M. M., SaneAli, R., Khnavi, M., Abai, M. R., Hadjiakhoondi, A., Mohtarami, F., & Vatandoost, H., (2010). Phytochemistry and larvicidal activity of *Eucalyptus camaldulensis* against malaria vector, *Anopheles stephensi*. *Asian Pacific Journal of Tropical Medicine*, 3(1), 841–845.
- Sefidkon, F., Bahmanzadegan, A., & Assareh, M. H., (2008). Effect of distillation methods and harvesting times on the essential oil and cineole content of *Eucalyptus dealbata*. *Chemistry of Natural Compounds*, 44, 250–253.
- Serafino, A., Vallebona, P. S., Andreola, F., Zonfrillo, M., Mercuri, L., Federici, M., Rasi, G., et al., (2008). Stimulatory effect of *Eucalyptus* essential oil on innate cell-mediated immune response. *BMC Immunology*, 9, 1–17.
- Seyyednejad, S. M., Motamedi, H., Najvani, F. D., & Hassannejad, Z., (2014). Antibacterial effect of *Eucalyptus microtheca*. *International Journal of Enteric Pathog.*, 2(2), 1–5.
- Sharma, G. K., Naiar, C. T. S., Kedarnath, S., & Kundan, S., (1986). *Eucalyptus* in India. Past, present, and future. *Proceedings of National Seminar on Eucalyptus*. KFRI, Pecchi, Kerala–India.
- Shepherd, M., Chaparro, J., Dale, G., Jefferson, L., Duong, H., Vogel, H., Walsh, J., et al., (1995). Mapping in sect resistance and essential oil traits in a tropical *Eucalyptus* hybrid. In: *Proceeding of the Eucalyptus Plantations: Improving Fiber Yield and Quality, CRCTHFIUFRO Conference* (pp. 420–423). Hobart, Australia.
- Silva, J., Abebe, W., Sousa, S. M., Duarte, V. G., Machado, M. I. L., & Matos, F. J. A., (2003). Analgesic and anti-inflammatory effects of essential oils of *Eucalyptus*. *Journal of Ethnopharmacology*, 89(2, 3), 277–283.
- Singab, A., Ayoub, N., Al-Sayed, E., Martiskainen, O., Sinkkonen, J., & Pihlaja, K., (2011). Phenolic constituents of *Eucalyptus camaldulensis* Dehnh. with potential antioxidant and cytotoxic activities. *Records of Natural Products*, 5(4), 271–280.
- Singh, H. P., Mittal, S., Kaur, S., Batish, D. R., & Kohli, R. K., (2009). Characterization, and antioxidant activity of essential oils from fresh and decaying leaves of *Eucalyptus tereticornis*. *Journal of Agricultural and Food Chemistry*, 57(15), 6962–6966.
- Singla, N., Thind, R. K., & Mahal, A. K., (2013). Potential of *Eucalyptus* oil as repellent against house rat, *Rattus rattus*. *The Scientific World Journal*, 2014, 1–7. <http://dx.doi.org/10.1155/2014/249284>.

- Siramon, P., & Ohtani, Y., (2007). Antioxidative and antiradical activities of *Eucalyptus camaldulensis* leaf oils from Thailand. *Journal of Wood Science*, 53, 498–504.
- Squillassi, M. G., & Grattapaglia, D., (1998). A preliminary assessment of the efficiency of marker assisted selection and phenotypic selection in *Eucalyptus*. In: *Proceedings of the IUFRO Conference on Silviculture and Improvement of Eucalypts* (pp. 14–18). Salvador, Brazil.
- Sudhoff, H., Klenke, C., Greiner, J. F., Müller, J., Brotzmann, V., Ebmeyer, J., Kaltschmidt, B., & Kaltschmidt, C., (2015). 1, 8-Cineol reduces mucus-production in a novel human *ex vivo* model of late rhinosinusitis. *PLoS One*, 10(7), 133–140.
- Suliman, K. D., & Al-Dulimi, F. I., (2008). The synergistic inhibitory effect *Ulmus rubra* and *Eucalyptus microtheca* against *Staphylococcus aureus* and *Salmonella typhimurium* isolated from food poisoning. *Journal of Education and Science*, 21(3), 28–52.
- Takasaki, M., Konoshima, T., Kozuka, M., Haruna, M., Ito, K., Crow, W. D., & Paton, D. M., (1994). Euglobal-In-1, a new euglobal from *Eucalyptus incrassata*. *Chemical Pharmaceutical Bulletin*, 42(10), 2113–2116.
- Takeuchi, H., Moriya, N., & Kurahashi, T., (2003). Response induced by the essential oil in single olfactory receptor cells. *Aroma Research*, 4, 336–343.
- Tisserand, R., & Balacs, T., (1995). *Essential Oil Safety: A Guide for Health Professionals*. Churchill Livingstone, Edinburgh.
- Trivedi, N. A., & Hotchandani, S. C., (2004). A study of the antimicrobial activity of oil of *Eucalyptus*. *Indian Journal of Pharmacology*, 36(2), 93–95.
- Tysyar, A. A., (1997). The effect of hot and cold water extracteous of *Eucalyptus microtheca* on some survival of the mosquito *Culex pipiens* L. (*Diptera: Culicidae*) at different stages. *Journal of Al-Qadisiyah for Pure Science*, 15(3), 1–5.
- Vecchio, M. L., & Clara, C. M., (2016). Beneficial and healthy properties of *Eucalyptus* plants: A great potential use. *The Open Agriculture Journal*, 10, 52–57.
- Verhaegen, D., Plomion, C., Gion, J. M., Poitel, M., Costa, P., & Kremer, A., (1997). Quantitative trait dissection analysis in *Eucalyptus* using RAPD markers, Detection of QTL in interspecific hybrid progeny, stability of QTL expression across different ages. *Theoretical and Applied Genetics*, 95, 597–608.
- Wallace, A. R., (1913). *The Malay Archipelago, the Land of the Orang-Utan, and the Bird of 1913 Paradise: A Narrative of Travel with Studies of Man and Nature*. London, Macmillan. Retrieved from: <https://www.biodiversitylibrary.org/bibliography/49461#/summary> (accessed on 31 August 2023).
- Zang, C., & Fu, S., (2009). Allelopathic effects of eucalyptus and the establishment of mixed stands of *Eucalyptus* and native species. *Forest Ecology and Management*, 258(7), 1391–1396. doi: 10.1016/j.foreco.2009.06.045.
- Zhang, J., An, M., Wu, H., Stanton, R., & Lemerle, D., (2010). Chemistry and bioactivity of *Eucalyptus* essential oils. *Allelopathy Journal*, 25(2), 313–330.
- Zhao, Q., Bowles, E. J., & Zhang, H., (2008). Antioxidant activities of eleven Australian essential oils. *Natural Product Communications*, 3, 837–842.

## CHAPTER 6

---

# *Commiphora* spp. (Guggul): A Wonder Ayurvedic Drug

JAI MALIK<sup>1</sup> and SUBASH C. MANDAL<sup>2</sup>

<sup>1</sup>*University Institute of Pharmaceutical Sciences, Center of Advanced Study, Panjab University, Chandigarh, India*

<sup>2</sup>*Department of Pharmaceutical Technology, Jadavpur University, Kolkata, West Bengal, India*

---

### ABSTRACT

Guggul is a famous Ayurvedic oleo-gum resin drug which is obtained after injury from the stems and branches of *Commiphora wightii* (Arnott) Bhandari [syn. *Commiphora mukul* (Hook. Ex Stocks) Engl; *Balsamodendron mukul* (Hook. Ex Stocks); Family, Burseraceae]. Since time immemorial, it has been used in one form or other to treat various disorders such as rheumatism, inflammation, gout, hyperlipidemia, etc. Guggul is known for its terpenoidal (mono-, di-, sesqui-, and triterpenoids), steroidal, flavonoidal, and lignan compounds that have been found responsible for its multi-facet biological activity. The dry regions of Gujarat and Rajasthan States of India, and the bordering regions of Pakistan are the natural habitat of guggul. It is used as one of the major ingredients in more than 50 Ayurvedic formulations in India. In US and other Western countries, it is used as an OTC medicine or a dietary supplement. Its unchecked commercial exploitation over the last several decades, has significantly affected its wild population. Due to this, *C. wightii* has been enlisted as “Critically Endangered” in the IUCN red list of threatened species. The present chapter provides an update on the pharmacology and phytochemistry of guggul along with its historical aspects, traditional uses and agro-technical methods.

## 6.1 INTRODUCTION

Therapeutical use of plants is perhaps as old as the history of man. Almost all the traditional systems of medicine around the world are based on the usage of plants as medicines. Indian Traditional system of medicine, “Ayurveda,” is one such system and perhaps the oldest systems of medicine known to mankind. “Ayurveda” has been derived from two words “Ayur,” i.e., life and “veda,” i.e., science and therefore Ayurveda is “science of life.” It is believed that Ayurveda has developed from “Atharavaveda” and “Rigveda.” Atharavaveda has description of medicinal properties of more than 100 plants. “Guggul” or “Guggulu” is one such plant that has its mention in Atharavaveda and according to it “wherever there is fragrance of guggul, the people will remain free from diseases” (Sastry, 1976). Guggul has also been mentioned in the main treatise of Ayurveda, i.e., “Charak and Shusrut Samhitas,” for its medicinal properties. Later, Vagbhata mentioned guggul as remedy for lipid disorders in “Ashtanga Sangraha and Ashtanga Hridaya.” Shusruta and Vagbhata also provided a detailed description of the physical properties and therapeutic qualities of guggul. It has also been mentioned as a “Rasayana” (preparations having immunomodulatory and rejuvenating properties) in some of the Ayurvedic texts (Sastry, 1976).

Guggul is an oleo-gum resin that is obtained after tapping the stem and branches of *Commiphora wightii* (Arnott) Bhandari of family Burseraceae. *C. mukul* (Hook. Ex Stocks) Engl. and *Balsamodendron mukul* (Hook. Ex Stocks) are the two synonyms used for *C. wightii* (Anonymous, 1986). Earlier, the ‘guggul’ plant was known as *C. mukul* (Hook. ex-Stocks) Engl. or *B. mukul* (Hook. ex-Stocks). Later in 1962, Santapau renamed it as *C. roxburghii*. The present name, *C. wightii* was the name given by Bhandari, as according to him the name ‘wightii’ was used prior to ‘roxburghi’ since 1839 (Dalal, 1995). The plant is found in the dry regions of South Asia mainly in India, Pakistan, and Bangladesh. In our country, guggul plant is found in Gujarat, Rajasthan, Karnataka, Madhya Pradesh and Assam. *C. wightii* is a bushy plant and it requires growth of minimum 5–10 years before it can be tapped to obtain the resin (Bhatt, Nair, & Ram, 1989). Commercially, the resin is available in irregular yellowish-brown pieces or mass with an aromatic odor and an astringent or bitter taste. Ayurveda recommends purification of guggul before it can be used for therapeutic purpose. The process of purification is known as “Shodhana Vidhi” and according to Ayurvedic texts, it can be done by using different fluids, known as “dravayas.” Different dravayas used for purification are cow urine, cow milk, triphala kasaya, vasa-patras kasaya, vasapatra svaras, etc. (Anonymous, 2007).

## 6.2 PHYTOCHEMISTRY OF GUGGUL

Since guggul is an oleo-gum resin, it primarily has essential oil, gum, and resin which are composed of wide array of chemical constituents belonging to different phytochemical classes with terpenoids (mono-, di-, and tri-terpenoids) and steroids being the most prominent ones. It also contains lignans, carbohydrates, aliphatic alcohols (known as tetrols), flavonoids, and amino acids.

### 6.2.1 STEROIDS

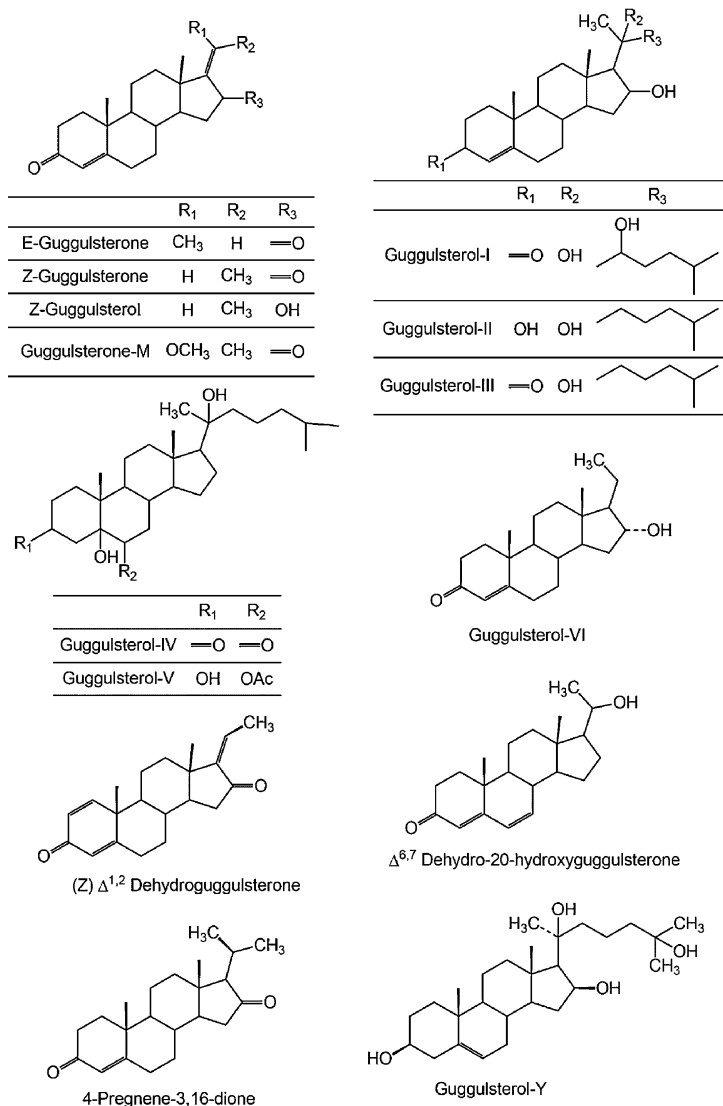
Oleo-gum resin of guggul is known for its steroidal constituents that are also considered as its major bioactive constituents. *E*-guggulsterone and *Z*-guggulsterone (Figure 6.1), two isomers, are the major bioactive steroids reported from guggul (Jain, 2006). Various biological activities of guggul have been attributed to these steroidal constituents. Besides these two, guggulsterone-M, and dihydroguggulsterone-M, (*Z*)- $\Delta$  1,2-dehydroguggulsterone and  $\Delta$  6,7-dehydro-20-hydroxyguggulsterone (El-Mekkawy, Meselhy, Nkobole, & Lall, 2013) have also been isolated from guggul. It also contains sterols like guggulsterol I-VI (Purushothaman & Chandrasekharan, 1976), guggulsterol-Y (Figure 6.1), progesterone like steroids (4-pregnene-3,16-dione, (20*R*)-20-acetoxy-4-pregnene-3,16-dione, 16 $\beta$ -acetyloxypregn-4,17(20)-*trans*-diene-3-one, 3 $\alpha$ -acetyloxy-5 $\alpha$ -pregnan-16-one, cholesterol, and its derivatives (Bajaj & Dev, 1982).

### 6.2.2 TERPENOIDS

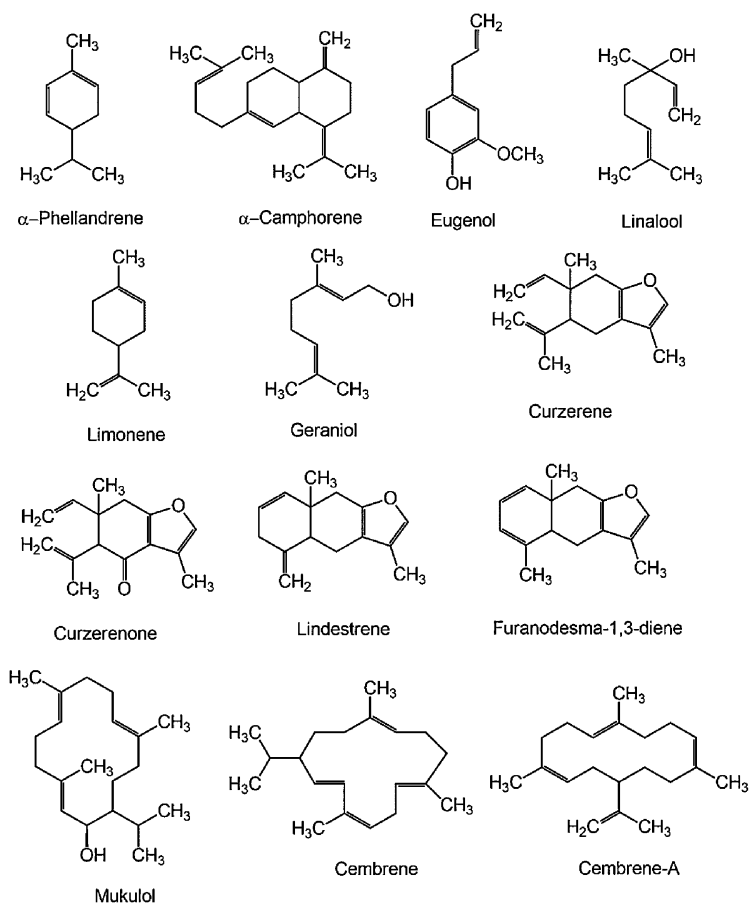
Guggul contains large number of terpenoidal constituents which are present in its volatile oil and resin part (Figure 6.2):

1. **Monoterpenoids:** These are present mainly in the volatile oil of the guggul. Various monoterpenoids present are – myrcene and camphorene or dimyrcene as major monoterpenoids (Patil, Nayak, & Dev, 1972) along with polymyrcene, linalool,  $\alpha$ -phellandrene, eugenol, limonene, geraniol, methyl heptanone, cineol, and bornyl acetate (Saxena & Sharma, 1998).
2. **Sesquiterpenoids:** Guggul contains various sesquiterpenoids namely, curzerenone, curzerene, cadinene, lindestrene, furanoeudesma-1,3-diene, and furanodien-6-one, 3-methoxy-10-methylene-furano-germacr-1-en-6-one and 2-methoxy-4,5-dihydrofuranodien-6-one (Saeed & Sabir, 2004).
3. **Diterpenoids:** Numerous diterpenoids namely, mukulol, cembrene-A (Patil, Nayak, & Dev, 1973; Prasad & Dev, 1976) and  $\alpha$ -camphorene

have been reported from guggul resin. Besides these guggul also contain isocembrol, (4*Z*, 6*E*)-4,7,12,15,15-pentamethylbicyclo [9.3.1] pentadeca-4,6-diene-12-ol and (2*E*, 12*E*)-2,7,13-trimethyl-9-(1-methylethyl)-15-oxabicyclo [12.1.0] pentadeca-2,12-diene-7-ol (Francis, Raja, & Nair, 2004).



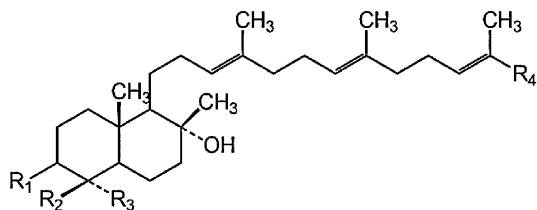
**FIGURE 6.1** Steroidal constituents of guggul.



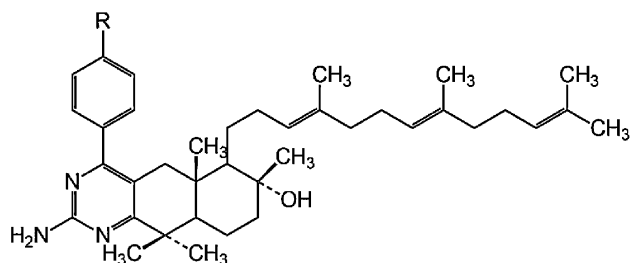
**FIGURE 6.2** Terpenoidal constituents of guggul.

- 4. Triterpenoids:** Various triterpenes belonging to polypodane class have also been isolated from guggul (Figure 6.3). These include myrrhanol A-C, and myrrhanones A-B (Kimura et al., 2001). Myrrhanol B is an acid derivative of myrrhanol A whereas myrrhanones A, B, and C are the ketonic derivatives of myrrhanol A, B, and C (Figure 6.3), respectively (Kimura et al., 2001). Fused pyrimidine derivatives of myrrhanon C have been synthesized and exhibited potent anticancer activity. Among various derivatives, 4''chloro- and 4''bromo-pyrimidine hybrids were found to be most potent compounds. Isomers of myrrhanone A and B, namely commipherol and commipherin, respectively, have also been reported from guggul.

Various other triterpenoids viz., epimansumbinol, mansumbinone, and mansumbinoic acid have also been isolated from guggul.



	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>	R <sub>4</sub>
Myrrhanol A	OH	CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>2</sub> OH
Myrrhanol B	OH	CH <sub>3</sub>	CH <sub>3</sub>	COOH
Myrrhanol C	OH	CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>
Myrrhanone A	=O	CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>2</sub> OH
Myrrhanone B	=O	CH <sub>3</sub>	CH <sub>3</sub>	COOH
Myrrhanone C	=O	CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>
Commipherol	=O	---CH <sub>3</sub>	—CH <sub>3</sub>	CH <sub>2</sub> OH
Commipherin	=O	---CH <sub>3</sub>	—CH <sub>3</sub>	COOH



	R
4 <sup>o</sup> Chloro pyrimidine hybrid	Cl
4 <sup>o</sup> Bromo pyrimidine hybrid	Br

**FIGURE 6.3** Triterpenoidal constituents of guggul.

### 6.2.3 LIGNANS

Lignans are the potent biologically active molecules found in nature. Lignans namely, Epi-mukulin, diasartemin, (+)-*epi*-magnolin, (+)-diayangambin



(El-Mekkawy, Meselhy, Nkobile, & Lall, 2013) have been found in guggul (Figure 6.4).

### 6.2.4 FLAVONOIDS

Various flavonoids, mainly from the stem and flowers, found in guggul are muscanone (a nringin derivative) (Fatope et al., 2003), naringenin, quercetin, and its glycosides namely quercetin-3-*O*- $\beta$ -D-glucuronide, quercetin-3-*O*--L-rhamnoside and pelargonidin-3,5, di-*O*-glucoside (Kakrani, 1981).

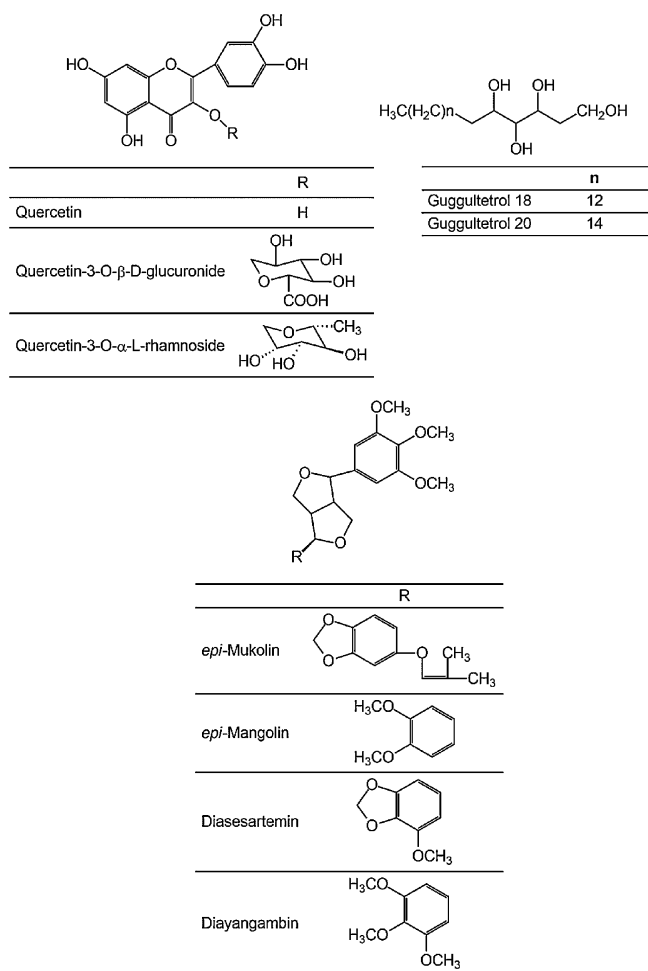


FIGURE 6.4 Flavonoids and lignans of guggul.

### **6.2.5 LIPIDS**

A new class of lipidic compounds, collectively known as guggultetrols (have four hydroxyl groups at C-1 to C-4) namely octadecane-1,2,3,4-tetrol, nonadecane-1,2,3,4-tetrol and eicosane-1,2,3,4-tetrol, have been isolated from the saponified guggul resin. Besides these guggultetrol-18 (a C-18 compound) and guggultetrol-20 (a C-20 compound) have also been isolated from the guggul (Kumar & Dev, 1987).

### **6.3 TRADITIONAL USES**

Since ages, guggul has been used as an incense to worship gods. The word “Bhutahara” has also been given to guggul as it was believed that its smoke and incense protects humans from evil spirits. Synonyms of guggul like “Rukshagandha, Palankasha, Rakshohan,” etc., describes its medicinal properties which protects the body from different disorders and thus prolongs the age (Sastry, 1976). It was believed that one cannot afflict with any disease if he is exposed to the odor of guggul. Ample therapeutic properties of guggul have been documented in various Ayurvedic treatises and lexicons. Charak and Shustruta Samhitas described guggul for its protective effects in diseases of the head, irregular fevers, nasal, heart, and skin diseases. It has also been mentioned as a digestive, laxative, an emulsive, an aphrodisiac, tonic, and for reducing fat (in obesity). Its fumigation has been prescribed for destroying the reptiles, mice, worms, and various parasites. In early Christian era, Vagbhata included guggul as “Rasayna Dravya” and also described its types and doses (Sastry, 1976). He mentioned guggul for diseases of lipid metabolism (obesity and hyperlipidemia), teeth, ear, head, and throat, dyspnea, hernia, internal tumors, leukoderma, and other skin infections, urinary complaints (as diuretic and bladder stones), ulcers, fistula, arthritis, seminal, and menstrual disorders, and as antidote for snake, spider, and arsenic poisoning. Keeping in mind the wide array of therapeutic activities of guggul, various Ayurvedic formulations of guggul alone or as a major component in combination with other herbs have been prepared for different disorders. All the traditional therapeutic claims formed the basis for the pharmacological studies on modern guidelines that led to discovery of its newer uses and validation of its traditional therapeutic claims.

### **6.4 PHARMACOLOGICAL ACTIVITIES**

#### **6.4.1 ANTIARTHRITIC AND ANTI-INFLAMMATORY ACTIVITY**

These activities of gum guggul were first reported somewhat six decades ago (Gujral, Sareen, Tangri, Amma, & Roy, 1960). Since then, copious

reports have highlighted and established these activities of guggul and its formulations (Singh, Mishra, Aquilina, & Kohlbeck, 2001; Singh, Mishra, Vinjamury, Aquilina, & Shepard, 2003; Bagul, Srinivasa, Kanaki, & Rajani, 2005; Shah, Gulati, & Palombo, 2012; Patel & Pundarikakshudu, 2016; Ahmad et al., 2020). Guggulsterones, by virtue of their action on various molecular markers involved in arthritis and inflammations, have been found to be the active against such disorders. Gum resin reduces the joint swelling, leucocytes concentration in affected area and represses the pro-inflammatory mediators like IFN- $\gamma$ , IL-1 $\beta$ , TNF- $\alpha$ , and IL-12 (Kunnumakkara et al., 2018). Guggulsterones and ethyl acetate fraction of gum guggul suppresses NF $\kappa$ -B and also down regulate the cyclooxygenase-2 (COX-2) controlling genes expression (Shishodia & Aggarwal, 2004). Guggulsterones alters the Toll like receptors (TLRs) signaling causing inhibition of both the downstream pathways viz., the myeloid differential factor 88 (MyD88)-dependent pathway and the toll-interleukin-1 receptor domain-containing adapter inducing interferon- $\beta$  (TRIF)-dependent pathway. This further prevents activation of NF $\kappa$ B causing downregulation of cytokine gene expression which eventually prevents the inflammatory responses (Youn, Ahn, & Lee, 2009) (Figure 6.5).



**FIGURE 6.5** Pharmacological activities of guggul.

Guggulsterones by suppressing NF $\kappa$ B, also lowers the mRNA levels of nitric oxide synthase (iNOS) and COX-2 that led to the protective effect against inflammation induced by NO and COX-2 (Lv, Song, Kim, Park, Kwon, & Park, 2008). In addition to the suppressing effect on NF $\kappa$ B, guggulsterones also modulate receptor activator of NF- $\kappa$ B ligand (RANKL) signaling and prevents osteoclastogenesis (Ichikawa & Aggarwal, 2006). Besides, guggulsterones, triterpenoidal compounds of guggul especially, myrrhanol A and myrrhanone A have also exhibited anti-inflammatory activity when studied on adjuvant-induced air-pouch granuloma model in mice (Kimura et al., 2001). Further, myrrhanol A was found to be more potent than myrrhanone A and methanol extract of guggul. In addition to triterpenoids, diterpenes cembrene and cembrene A have also exhibited anti-inflammatory effects by attenuating COX-1 and COX-2 enzymes (Francis, Raja, & Nair, 2004).

#### **6.4.2 HYPOLIPIDEMIC ACTIVITY**

Guggul is known for its beneficial effect in lipid metabolism disorders and has been used for lowering the lipid levels and in the treatment of obesity (Das et al., 2016; Singh, Niaz, & Ghosh, 1994). Numerous studies have shown the lipid lowering effect of guggul in different experimental animals (Satyavati, Dwarakanath, & Tripathi, 1969; Khanna, Agarwal, Gupta, & Arora, 1969; Dixit, Joshi, Sinha, Bharvava, & Varma, 1980; Baldwa, Bhasin, Ranka, & Mathur, 1981). Various clinical trials have also validated the pronounced hypolipidemic effect (Ulbricht et al., 2005). In 1987, guggul was approved for its cholesterol lowering effects in India. In 1988, Central Drug Research Institute (CDRI), Lucknow developed and marketed a standardized and guggulsterone rich ethyl acetate fraction named as “Guggulipid” (Satyavati, 1991). It exhibited significant antihyperlipidemic activity in both pre-clinical and clinical studies and guggulsterones were found responsible for this activity (Satyavati, 1991; Deng, 2007). In a short study, guggulsterones lowered the levels of cholesterol and triglycerides but detailed studies were warranted (Singh, Kaul, Chander, & Kapoor, 1990). Later in 1996, Chander et al. confirmed guggulsterones to be active constituents responsible for lipid lowering effects of guggul (Chander, Khanna, & Kapoor, 1996). According to their study, guggulsterones also enhance the activity of lipolytic enzyme and receptor-mediated metabolism of LDL. Besides this, several other mechanisms have also been reported for hypolipidemic activity of guggulsterones.

Guggul and guggulsterones have also shown to decrease the hepatic steroid production which increases the lipid metabolism and its clearance. It has also been suggested that the major pathway of removing excess of cholesterol is by converting it to bile acids and then subsequently excreting it through the enterohepatic circulation (Russell, 2003). Further, an enzyme, cholesterol 7 $\alpha$ -hydroxylase (CYP7A1) is responsible for bile acids synthesis from cholesterol (Davis, Miyake, Hui, & Spann, 2002). Excess bile acid concentration activates the bile acid sensor, farnesoid X receptor (FXR), which leads to myriad of changes causing repression of CYP7A1 genes resulting in inhibition of bile acid production from cholesterol (Urizar et al., 2002). Guggulsterones have been found to be FXR antagonist and their antagonist action leads to increased expression of CYP7A1 genes which further enhances the metabolism of cholesterol to bile acids (Urizar & Moore, 2003; Wu, Xia, Meier, Li, Hu, & Lala, 2002). The increased bile acid concentration further activates bile salt export pump (BSEP) which finally causes excretion of bile acids. Guggulsterones have also been reported to directly activate BSEP thereby exhibiting a synergistic effect with its FXR antagonist activity (Deng, Yang, Radke, Yang, & Yan, 2007).

### **6.4.3 ANTICANCER ACTIVITY**

Guggul and its constituents, especially guggulsterones, have been extensively studied for their anticancer activity (Saeidnia, Rahimi, Rezaeizadeh, & Taheripanah, 2015). Guggulsterones have exhibited anticancer activity by virtue of their multiple mechanisms (apoptosis, preventing proliferation, metastasis, and angiogenesis) and effect on molecular markers. Guggulsterones have shown apoptotic action against different cancer cell lines such as HL60 and U937 cell lines, primary leukemic blasts in culture, Barrett's esophagus (a risk factor for esophageal adenocarcinoma), PC-3 cells, human prostate cancer cells, etc. (Singh, Choi, Zeng, Hahm, & Xiao, 2007). Apoptotic action of these compounds is through both, mitochondria dependent and independent pathways. Besides this, guggulsterones also repress I $\kappa$ B $\alpha$  activation and down regulate antiapoptotic genes like IAP1, Bfl-1/A1, cFLIP, Bcl-2, Bax, and Bak, by inhibiting NF $\kappa$ B, thereby enhancing the apoptotic action in cancer cells (Shishodia & Aggarwal, 2004). Guggulsterones also exhibit apoptotic action by stimulating c-Jun NH<sub>2</sub>-terminal kinase (JNK) and p38 mitogen-activated protein kinase (p38 MAPK) (Shishodia, Sethi, Ahn, & Aggarwal, 2007). It is a known fact that FXR regulates metabolism of bile

acids, cholesterol, lipids, and glucose (Urizar et al., 2002; Stayrook et al., 2005). FXR is over expressed in Barrett's esophagus and guggulsterones being FXR antagonist, exhibit apoptotic action in these cancer cells (De Gottardi et al., 2006).

Guggulsterones also exhibit antiproliferation activity against various cancers including carcinoma of head, neck, lung, breast, and ovaries (Shishodia, Harikumar, Dass, Ramawat, & Aggarwal, 2008). They have shown anticancer activity by affecting the cell cycle proteins. These compounds inhibited cyclin D1 expression (a protein which is over expressed in cancer cells) by attenuating the activity of cyclin or cyclin-dependent kinase (CDK)-2 complexes and concomitantly augment CDK inhibitors (p21 and p27) level (Shishodia, Sethi, Ahn, & Aggarwal, 2007). Inhibition of cyclin D1 expression has also been found responsible for antiproliferative action of guggulsterones. These changes inhibit DNA synthesis of these cells causing cell cycle arrest in S-phase, eventually preventing proliferation of cancer cells. Matrix metalloproteinase 9 (MMP-9) is a proteinase responsible for the invasion (into normal cells) and metastasis of cancer cells. Guggulsterones inhibit MMP-9 (by inhibiting NF- $\kappa$ B) thereby preventing the invasion and metastasis of cancer cells. FXR antagonism by guggulsterones also prevents the metastasis of these cells (Shishodia, Harikumar, Dass, Ramawat, & Aggarwal, 2008).

#### **6.4.4 ANTIDIABETIC ACTIVITY**

Diabetes is a metabolic and hormonal disorder which occurs largely due to irregular insulin secretion from the islets of Langerhans in pancreas that leads to improper glucose metabolism. Alcoholic and aqueous extracts of guggul have shown to reduce and control the streptozotocin-induced increase in glucose levels in diabetic rats (Al-Bishri & Al-Attas, 2013; Bellamkonda et al., 2018). Guggulsterones, the active constituents of guggul, increase the activity of peroxisome proliferator-activated receptor (PPAR)- $\gamma$  which is responsible for the glucose metabolism. In addition to this, increased PPAR- $\gamma$  activity also increases the insulin sensitivity that further helps in keeping a check on glucose levels in blood (Sharma, Salunke, Srivastava, Majumder, & Roy, 2009). Irregular lipid metabolism also spikes the blood-glucose levels and PPAR- $\gamma$  also being responsible for lipid metabolism, their activation by guggulsterones improves the lipid metabolism thereby keeping check on the blood glucose levels. Furthermore, guggulsterones also inhibit glucose-6-phosphate enzyme in order to control glucose levels (Sharma, Salunke, Srivastava, Majumder, & Roy, 2009).

#### 6.4.5 ANTI-OBESITY ACTIVITY

Guggul has been known for its hypolipidemic and cholesterol lowering activities. Guggulipid, a standardized ethylacetate fraction of guggul resin has shown lipid lowering activity in various studies (Satyavati, 1991; Singh, Kaul, Chander, & Kapoor, 1990; Bhutani, Birari, & Kapat, 2007). It reduces LDL cholesterol by about 15–18% and triglyceride by about 25%–30%. Clinically also guggulipid has shown its beneficial effects in reducing cholesterol and triglyceride levels (Ulbricht et al., 2005; Bhatt et al., 1995). Guggulsterones were found to be the major antiobesity compounds of guggul. Though both *cis*- and *trans*-isomers of guggulsterone were effective in lowering lipid levels, former was found to be more active than latter. *cis*-Guggulsterone increased basal lipolysis of mature adipocytes to reduce the deposition of lipids. Guggulsterones also exhibited their antiobesity effect by increasing caspase-3 activity which further increases apoptosis of adipocytes (*cis*-isomer was found more effective). Intriguingly, these compounds also decrease the expression of PPAR $\gamma$ 2 and C/EBP- $\alpha$  and - $\beta$  (CCAT-enhancer binding protein) which leads to maturation of adipocytes (Yang, Dellaâ-Fera, & Baile, 2008). These results further supported the FXR antagonist action of guggulsterones as FXR agonist increase the expression of PPAR $\gamma$ 2, C/EBP $\alpha$  and  $\beta$  mRNAs. Thus, it can also be said that guggul exhibit its antiobesity action by increasing the apoptosis of adipocytes and by preventing the maturation of adipocytes.

#### 6.4.6 CARDIOPROTECTIVE ACTIVITY

Guggul and guggulsterones have been extensively studied for their cardioprotective activity (Deng, 2007). Their potent hypolipidemic activity was the major motivation and basis to study their cardioprotective effects. Guggul has shown cardioprotective effects against dl-isoproterenol hydrochloride (85 mg/kg, i.p.) injection induced cardiac necrosis and myocardial damage (Kaul & Kapoor, 1989; Ojha et al., 2008). Structural integrity of myocardium was also maintained by treatment of guggul and guggulsterones. In addition, it also mitigated the alteration in oxidative stress induced parameters (Chander, Rizvi, Khanna, & Pratap, 2003). Further, guggul has also shown to increase the serum fibrinolytic activity and has been proposed for its beneficial action in coronary artery diseases (Bordia & Chuttani, 1979). Hypolipidemic and antioxidant activity of guggul and guggulsterones are considered to be the mainstay in their cardioprotective activity.

Guggul and guggulsterones have also shown various other activities (summarized in Table 6.1) by virtue of their multifarious mechanism of actions and their effect of various molecular markers.

**TABLE 6.1** Other Pharmacological Activities of Guggul

Activity	Mechanism	References
Hepatoprotective	Decrease NF-kB, p-JNK, TLR-3, -4, and MyD88	Kim et al. (2013)
Neuroprotective and memory enhancement	AChEI activity; antioxidant, increase CREB-BDNF signaling	Chen, Huang, & Ding (2016); Saxena, Singh, Pal, Singh, Pratap, & Nath (2007)
Thyroid dysfunction	Increase iodine uptake	Tripathi, Malhotra, & Tripathi (1984)
Gastroprotective	Decrease NF-kB and leukotrienes Increase Nrf2 and prostaglandin	Zhang, Shangguan, Chen, Zhang, & Lin (2016)
Antimicrobial	–	Goyal, Chauhan, & Kaushik (2010); Ishnava, Mahida, & Mohan (2010)
Antiacne	–	Thappa & Dogra (1994)
Antifertility	Decrease weight of ovaries, uterus, and cervix.	Amma, Malhotra, Suri, Arya, Dani, & Sareen (1978)

*Abbreviations:* JNK: c-Jun N-terminal kinase; NF-kB: nuclear factor kappa B; Nrf-2: nuclear factor erythroid 2 (NFE2)-related factor 2; TLR-3: toll-like receptor-3; TLR-4: toll-like receptor-4; BDNF: brain-derived neurotrophic factor; CREB: cyclic adenosine monophosphate (cAMP) response element binding protein.

## 6.5 CURRENT STATUS AND CULTIVATION OF GUGGUL

Guggul, due to its potential therapeutic activities, has always been in demand across the globe. India exports more than 200 tons/year of processed guggul to more than 40 countries like UK, France, Belgium, Netherlands, etc. (Cunningham, Brinckmann, Kulloli, & Schippmann, 2018). This huge demand has led to overexploitation of this wonderful drug. Extensive and improper tapping, looping, and chopping of the guggul tree (to obtain gum-resin), which eventually leads to ‘tree death,’ is the major cause of decrease in guggul tree population. In 2002, guggul was declared as ‘Low risk’ plant and it was proposed to increase or maintain its population by conservation. But now, it has been declared as ‘Critically endangered’ as per International Union for Conservation of Nature (IUCN) “Red List” and has been incorporated in Convention on International Trade in Endangered Species (CITES) Appendix II based on Art. IV 2(a) of the CITES (Kumar, 2013). Some of



the states like Rajasthan and Madhya Pradesh have banned tapping of wild guggul trees. In order to protect this important plant, various *ex-situ* and *in-situ* conservation programs have been started. Rajasthan government-initiated cultivation of around 500,000 guggul saplings over an area of 1,700 hectares across different districts of Rajasthan. They also started “Guggal Bachao Abhiyan” as a part of “community-based management and planting of guggul.” Under this initiative, Regional Research Ayurveda Institute, Jaipur, started a ‘Guggul Herbal Farm’ at Mangaliyawas at Ajmer, Rajasthan.

### 6.5.1 CULTIVATION OF GUGGUL

Guggul being an endangered species, ample work is being done to conserve it, to improve its cultivation methods and to develop high yielding varieties. ‘Marusudha’ a high oleo-gum resin yielding cultivar has been developed by Central Institute of Medicinal and Aromatic Plants (CIMAP), Lucknow. National Medicinal Plant Board, India has also given cultivation method for guggul (National Medicinal Plants Board, 2008). The plant grows well in arid, sandy, and rocky tracts of tropical India. Sandy or sandy loam soils are best for its cultivation. Propagation can be done in nursery beds using seeds, stem cuttings or air layering of 5–8-year-old mother plants. Black-colored seeds are considered suitable for propagation (yellowish-white seeds are non-viable). Due to their polyembryonic nature, one seed can give rise to more than one seedling. Seeds have poor germination rate and they germinate within 7–10 days after sowing in the rainy season. Propagation with stem cuttings and air layering is normally done in May and rainy season (July–August), respectively followed by root development during next 15–20 days. Once the plantlets are developed, they are shifted into field pits (45 cm x 45 cm x 45 cm) filled with sand, soil, and FYM (1:1:1). The plantlets transplanted in field pits should have a spacing of 2 m x 2 m between them. Application of growth hormones like IBA (10 mg/liter) along with organic manures like hexameal (100 g/plant) every month or NPK (nitrogen, phosphorus, potassium: 75:130:30 g/plant) after every three months up to a period of one year has shown improved survival of plant. Irrigation, with sufficient amount of water (8 ltr/plant), every 15 days is required for better growth. Plant is allowed to grow for 5–6 years before tapping which is normally done during November–February. A 7–10 cm incision (horizontal incision have shown better yield) is made on the stem near the base and the resin exudate is collected every week for one month after which exudation stops. After collecting the resin, it should be packed in air tight plastic containers.

## 6.6 CONCLUSION

Guggul has been used since antiquity for its multifarious pharmacological activities. It possesses a special place in Ayurvedic System of Medicine. Guggul has well-established hypolipidemic, anti-inflammatory, and anti-arthritic activities and is clinically used for related disorders. Guggulsterones have been found to be the major biologically active constituents of guggul and are responsible for majority of its pharmacological or therapeutic activities. Studies using modern methodologies have revealed the molecular targets of guggul and guggulsterones and this has opened new avenues of research on guggul. Action of guggulsterones on different molecular biomarkers has also unveiled newer pharmacological activities of guggul like anticancer, neuro-protective, antidiabetic, etc. But detailed pre-clinical and clinical studies are warranted to validate these claims. Besides therapeutical use, guggul is now also used extensively in cosmetic industry. Extensive commercial usage of guggul had a detrimental effect on the population of guggul trees and its bio-distribution making it a critically endangered species. Lot of efforts are put in by government and local people to save this precious gift of Mother Nature. Still lot of hard work and commitment is required to save this incredible plant.

## KEYWORDS

- anticancer
- antiobesity activity
- *C. mukul*
- cardioprotective activity
- *Commiphora wightii*
- guggul
- guggulsterones
- pharmacological activities

## REFERENCES

- Ahmad, M. A., Mujeeb, M., Akhtar, M., Khushtar, M., Arif, M., & Haque, M. R., (2020). Guggulipid: A promising multi-purpose herbal medicinal agent. *Drug Res.*, 70, 123–130.
- Al-Bishri, W. M., & Al-Attas, O. S., (2013). Guggul resin extract improve hyperglycemia and lipid profile in streptozotocin induced diabetes mellitus in rats. *Life Sci. J.*, 10, 2735–2741.

- Amma, M. K., Malhotra, N., Suri, R. K., Arya, O. P., Dani, H. M., & Sareen, K., (1978). Effect of oleoresin of gum guggul (*Commiphora mukul*) on the reproductive organs of female rat. *Indian J. Exp. Biol.*, *16*, 1021–1023.
- Anonymus, (1986). *Ayurvedic Pharmacopoeia of India*. Pharmacopoeia Commission for Indian Medicine and Homeopathy, Ministry of AYUSH, Government of India New Delhi.
- Anonymus, (2007). *Ayurvedic Pharmacopoeia of India*. Pharmacopoeia Commission for Indian Medicine and Homeopathy, Ministry of AYUSH, Government of India.
- Bagul, M. S., Srinivasa, H., Kanaki, N. S., & Rajani, M., (2005). Anti-inflammatory activity of two Ayurvedic formulations containing guggul. *Indian J. Pharmacol.*, *37*, 399.
- Bajaj, A. G., & Dev, S., (1982). Chemistry of ayurvedic crude drugs-V: Guggulu (resin from *Commiphora mukul*)-5 some new steroidal components and, stereochemistry of guggulsterol-I at C-20 and C-22. *Tetrahedron*, *38*, 2949–2954.
- Baldwa, V. S., Bhasin, V., Ranka, P. C., & Mathur, K. M., (1981). Effects of *Commiphora mukul* (guggul) in experimentally induced hyperlipemia and atherosclerosis. *The J. Assoc. Phy. India*, *29*, 13–17.
- Bellamkonda, R., Karuna, R., Rao, B. S. B., Haritha, K., Manjunatha, B., Silpa, S., & Saralakumari, D., (2018). Beneficiary effect of *Commiphora mukul* ethanolic extract against high fructose diet induced abnormalities in carbohydrate and lipid metabolism in Wistar rats. *J. Trad. Compl. Med.*, *8*, 203–211.
- Bhatt, A. D., Dalal, D. G., Shah, S. J., Joshi, B. A., Gajjar, M. N., Vaidya, R. A., Vaidya, A. B., & Antarkar, D. S., (1995). Conceptual and methodologic challenges of assessing the short-term efficacy of guggulu in obesity: Data emergent from a naturalistic clinical trial. *J. Postgrad Med.*, *41*, 5.
- Bhatt, J. R., Nair, M. N. B., & Ram, H. Y. M., (1989). Enhancement of oleo-gum resin production in *Commiphora wightii* by improved tapping technique. *Curr. Sci.*, 349–357.
- Bhutani, K. K., Birari, R., & Kapat, K., (2007). Potential antiobesity and lipid lowering natural products: A review. *Nat. Prod. Com.*, *2*, 331–348.
- Bordia, A., & Chuttani, S. K., (1979). Effect of gum guggulu on fibrinolysis and platelet adhesiveness in coronary heart disease. *Indian J. Med. Res.*, *70*, 992–996.
- Chander, R., Khanna, A. K., & Kapoor, N. K., (1996). Lipid lowering activity of guggulsterone from *Commiphora mukul* in hyperlipaemic rats. *Phytother. Res.*, *10*, 508–511.
- Chander, R., Rizvi, F., Khanna, A. K., & Pratap, R., (2003). Cardioprotective activity of synthetic guggulsterone (E and Z-isomers) in isoproterenol induced myocardial ischemia in rats: A comparative study. *Indian J. Clin. Biochem.*, *18*, 71–79.
- Chen, Z., Huang, C., & Ding, W., (2016). Z-guggulsterone improves the scopolamine-induced memory impairments through enhancement of the BDNF signal in C57BL/6J mice. *Neurochem. Res.*, *41*, 3322–3332.
- Cunningham, A. B., Brinckmann, J. A., Kulloli, R. N., & Schippmann, U., (2018). Rising trade, declining stocks: The global guggul (*Commiphora wightii*) trade. *J. Ethnopharmacol.*, *223*, 22–32.
- Dalal, K. C., (1995). *All About Guggulu*. The Medplan Conservatory Society, Bengaluru.
- Das, S., Datta, A., Bagchi, C., Chakraborty, S., Mitra, A., & Tripathi, S. K., (2016). A comparative study of lipid-lowering effects of guggul and atorvastatin monotherapy in comparison to their combination in high cholesterol diet-induced hyperlipidemia in rabbits. *J. Dietary Supp.*, *13*, 495–504.
- Davis, R. A., Miyake, J. H., Hui, T. Y., & Spann, N. J., (2002). Regulation of cholesterol-7 $\alpha$ -hydroxylase: BAREly missing a SHP. *J. Lipid Res.*, *43*, 533–543.

- De Gottardi, A., Dumonceau, J. M., Bruttin, F., Vonlaufen, A., Morard, I., Spahr, L., Rubbia-Brandt, L., et al., (2006). Expression of the bile acid receptor FXR in Barrett's esophagus and enhancement of apoptosis by guggulsterone *in vitro*. *Mol. Cancer*, 5, 48.
- Deng, R., (2007). Therapeutic effects of guggul and its constituent guggulsterone: Cardiovascular benefits. *Cardiovas Drug Rev.*, 25, 375–390.
- Deng, R., Yang, D., Radke, A., Yang, J., & Yan, B., (2007). The hypolipidemic agent guggulsterone regulates the expression of human bile salt export pump: Dominance of transactivation over farnesoid X receptor-mediated antagonism. *J. Pharmacol. Exp. Therap.*, 320, 1153–1162.
- Dixit, V. P., Joshi, S., Sinha, R., Bharvava, S. K., & Varma, M., (1980). Hypolipidemic activity of guggul resin (*Commiphora mukul*) and garlic (*Alium sativum* Linn.) in dogs (*Canis familiaris*) and monkeys (*Presbytis entellus entellus* Dufresne). *Biochem. Exp. Biol.*, 16, 421–424.
- El-Mekkawy, S., Meselhy, M. R., Nkobile, N., & Lall, N., (2013). Three new alpha-glucosidase inhibitors from guggul, the oleogum resin of *Commiphora wightii*. *Nat. Prod. Res.*, 27, 146–154.
- Fatope, M. O., Al-Burtomani, S. K., Ochei, J. O., Abdulnour, A. O., Al-Kindy, S. M., & Takeda, Y., (2003). Muscanone: A 3-O-(1", 8", 14"-trimethylhexadecanyl) naringenin from *Commiphora wightii*. *Phytochem.*, 62, 1251–1255.
- Francis, J. A., Raja, S. N., & Nair, M. G., (2004). Bioactive terpenoids and guggulsteroids from *Commiphora mukul* gum resin of potential anti-inflammatory interest. *Chem Biodiv.*, 1, 1842–1853.
- Goyal, P., Chauhan, A., & Kaushik, P., (2010). Assessment of *Commiphora wightii* (Arn.) Bhandari (Guggul) as potential source for antibacterial agent. *J. Med. Med. Sci.*, 1, 71–75.
- Gujral, M. L., Sareen, K., Tangri, K. K., Amma, M. K., & Roy, A. K., (1960). Antiarthritic and anti-inflammatory activity of gum guggul (*Balsamodendron mukul* Hook). *Indian J. Physiol. Pharmacol.*, 4, 267–273.
- Ichikawa, H., & Aggarwal, B. B., (2006). Guggulsterone inhibits osteoclastogenesis induced by receptor activator of nuclear factor-kappaB ligand and by tumor cells by suppressing nuclear factor-kappaB activation. *Clin. Cancer Res.*, 12, 662–668.
- Ishnava, K. B., Mahida, Y. N., & Mohan, J. S. S., (2010). *In vitro* assessments of antibacterial potential of *Commiphora wightii* (Arn.) Bhandari. gum extract. *J. Pharmacog. Phytother.*, 2, 91–96.
- Jain, A., (2006). Chemistry and pharmacological profile of guggul: A review. *Indian J. Trad. Knowl.*, 5, 478–483.
- Kakrani, H. K., (1981). Flavonoids from the flowers of *Commiphora mukul*. *Fitoterapia*, 52, 221–223.
- Kaul, S., & Kapoor, N. K., (1989). Reversal of changes of lipid peroxide, xanthine oxidase and superoxide dismutase by cardio-protective drugs in isoproterenol induced myocardial necrosis in rats. *Indian J. Exp. Biol.*, 27, 625–627.
- Khanna, D. S., Agarwal, O. P., Gupta, S. K., & Arora, R. B., (1969). A biochemical approach to anti-atherosclerotic action of *Commiphora mukul*: An Indian indigenous drug in Indian domestic pigs (*Sus scrofa*). *Indian J. Med. Res.*, 57, 900–906.
- Kim, B. H., Yoon, J. H., Yang, J. I., Myung, S. J., Lee, J. H., Jung, E. U., Yu, S. J., et al., (2013). Guggulsterone attenuates activation and survival of hepatic stellate cell by inhibiting nuclear factor kappa B activation and inducing apoptosis. *J. Gastro. Hep.*, 28, 1859–1868.

- Kimura, I., Yoshikawa, M., Kobayashi, S., Sugihara, Y., Suzuki, M., Oominami, H., Murakami, T., et al., (2001). New triterpenes, myrrhanol A and myrrhanone A, from guggul-gum resins, and their potent anti-inflammatory effect on adjuvant-induced air-pouch granuloma of mice. *Bioorg. Med. Chem. Lett.*, *11*, 985–989.
- Kumar, R., (2013). Distribution and abundance of *Commiphora wightii* (Arn) Bhandari, in the forest of north Gujarat region (NGR) Gujarat. India. *Ind. J. Pl. Sci.*, *2*, 43–51.
- Kumar, V., & Dev, S., (1987). Chemistry of ayurvedic crude drugs-VII guggulu (resin from *Commiphora mukul*)-6: Absolute stereochemistry of guggultetrols. *Tetrahedron*, *43*, 5933–5948.
- Kunnumakkara, A. B., Banik, K., Bordoloi, D., Harsha, C., Sailo, B. L., Padmavathi, G., Roy, N. K., et al., (2018). Googling the guggul (*Commiphora* and *Boswellia*) for prevention of chronic diseases. *Front Pharmacol.*, *9*, 686.
- Ly, N., Song, M. Y., Kim, E. K., Park, J. W., Kwon, K. B., & Park, B. H., (2008). Guggulsterone, a plant sterol, inhibits NF-kappaB activation and protects pancreatic beta cells from cytokine toxicity. *Mol. Cell Endocrinol.*, *289*, 49–59.
- National Medicinal Plants Board, (2008). *Department of AYUSH and Ministry of Health and Family Welfare, G. O. I, Agro-Techniques of Selected Medicinal Plants*. TERI Press, The Energy and Resources Institute, New Delhi.
- Ojha, S. K., Nandave, M., Arora, S., Mehra, R. D., Joshi, S., Narang, R., & Arya, D. S., (2008). Effect of *Commiphora mukul* extract on cardiac dysfunction and ventricular function in isoproterenol-induced myocardial infarction. *Indian J. Exp. Biol.*, *46*, 646–652.
- Patel, M. G., & Pundarikakshudu, K., (2016). Anti-arthritis activity of a classical Ayurvedic formulation Vatari guggulu in rats. *J. Trad. Compl. Med.*, *6*, 389–394.
- Patil, V. D., Nayak, U. R., & Dev, S., (1972). Chemistry of ayurvedic crude drugs-I: Guggulu (resin from *Commiphora mukul*)-I: Steroidal constituents. *Tetrahedron*, *28*, 2341–2352.
- Patil, V. D., Nayak, U. R., & Dev, S., (1973). Chemistry of ayurvedic crude drugs-II: Guggulu (resin from *Commiphora mukul*)-2: Diterpenoid constituents. *Tetrahedron*, *29*, 341–348.
- Prasad, R. S., & Dev, S., (1976). Chemistry of ayurvedic crude drugs-IV: Guggulu (resin from *Commiphora mukul*)-4 absolute stereochemistry of mukulol. *Tetrahedron*, *32*, 1437–1441.
- Purushothaman, K. K., & Chandrasekharan, S., (1976). Guggulsterols from *Commiphora mukul* (*Burseraceae*). *Indian J. Chem, Section B*, *14*, 802–804.
- Russell, D. W., (2003). The enzymes, regulation, and genetics of bile acid synthesis. *Ann. Rev. Biochem.*, *72*, 137–174.
- Saeed, M. A., & Sabir, A. W., (2004). Antibacterial activities of some constituents from oleo-gum-resin of *Commiphora mukul*. *Fitoterapia*, *75*, 204–208.
- Saeidnia, S., Rahimi, R., Rezaeizadeh, H., & Taheripanah, T., (2015). *An Evidence-Based Approach to Traditional Herbal Remedies for the Management of Cancer*. Springer Briefs in Pharmaceutical Science & Drug Development, Springer Publications, New York, USA.
- Sastry, V. V. S., (1976). History of guggulu based on Ayurvedic literature. *Bulletin Ind. Inst. Hist Med.*, *6*, 102–116.
- Satyavati, G. V., (1991). Guggulipid: A promising hypolipidemic agent from gum guggul (*Commiphora wightii*). *Eco. Med. Plant Res.*, *5*, 47–82.
- Satyavati, G. V., Dwarakanath, C., & Tripathi, S. N., (1969). Experimental studies on the hypocholesterolemic effect of *Commiphora mukul*. Engl. (Guggul). *Indian J. Med. Res.*, *57*, 1950–1962.
- Saxena, G., Singh, S. P., Pal, R., Singh, S., Pratap, R., & Nath, C., (2007). Guggulipid, an extract of *Commiphora whightii* with lipid-lowering properties, has protective effects

- against streptozotocin-induced memory deficits in mice. *Pharmacol. Biochem. Behav.*, *86*, 797–805.
- Saxena, V. K., & Sharma, R. N., (1998). Constituents of the essential oil from *Commiphora mukul* gum resin. *JMAPs*, *20*, 55–56.
- Shah, R., Gulati, V., & Palombo, E. A., (2012). Pharmacological properties of guggulsterones, the major active components of gum guggul. *Phytother. Res.*, *26*, 1594–1605.
- Sharma, B., Salunke, R., Srivastava, S., Majumder, C., & Roy, P., (2009). Effects of guggulsterone isolated from *Commiphora mukul* in high at diet induced diabetic rats. *Food Chem. Toxicol.*, *47*, 2631–2639.
- Shishodia, S., & Aggarwal, B. B., (2004). Guggulsterone inhibits NF-kB and I $\kappa$ B $\alpha$  kinase activation, suppresses expression of anti-apoptotic gene products, and enhances apoptosis. *J. Bio. Chem.*, *279*, 47148–47158.
- Shishodia, S., Harikumar, K. B., Dass, S., Ramawat, K. G., & Aggarwal, B. B., (2008). The guggul for chronic diseases: Ancient medicine, modern targets. *Anticancer Res.*, *28*, 3647–3664.
- Shishodia, S., Sethi, G., Ahn, K. S., & Aggarwal, B. B., (2007). Guggulsterone inhibits tumor cell proliferation, induces S-phase arrest, and promotes apoptosis through activation of c-Jun N-terminal kinase, suppression of Akt pathway, and downregulation of antiapoptotic gene products. *Biochem. Pharmacol.*, *74*, 118–130.
- Singh, B. B., Mishra, L. C., Vinjamury, S. P., Aquilina, N., & Shepard, N., (2003). The effectiveness of *Commiphora mukul* for osteoarthritis of the knee: An outcomes study. *Alt. Ther. Health Med.*, *9*, 74–79.
- Singh, B. B., Mishra, L., Aquilina, N., & Kohlbeck, F., (2001). Usefulness of guggul (*Commiphora mukul*) for osteoarthritis of the knee: An experimental case study. *Alt. Ther. Health Med.*, *7*, 112.
- Singh, R. B., Niaz, M. A., & Ghosh, S., (1994). Hypolipidemic and antioxidant effects of *Commiphora mukul* as an adjunct to dietary therapy in patients with hypercholesterolemia. *Card Drugs Ther.*, *8*, 659–664.
- Singh, S. V., Choi, S., Zeng, Y., Hahm, E. R., & Xiao, D., (2007). Guggulsterone-Induced Apoptosis in human prostate cancer cells is caused by reactive oxygen intermediate-dependent activation of c-Jun NH<sub>2</sub>-terminal kinase. *Cancer Res.*, *67*, 7439–7449.
- Singh, V., Kaul, S., Chander, R., & Kapoor, N. K., (1990). Stimulation of low-density lipoprotein receptor activity in liver membrane of guggulsterone treated rats. *Pharmacol. Res.*, *22*, 37–44.
- Stayrook, K. R., Bramlett, K. S., Savkur, R. S., Ficorilli, J., Cook, T., Christe, M. E., Michael, L. F., & Burris, T. P., (2005). Regulation of carbohydrate metabolism by the farnesoid X receptor. *Endocrinol.*, *146*, 984–991.
- Thappa, D. M., & Dogra, J., (1994). Nodulocystic acne: Oral Gugu lipid versus tetracycline. *J. Derm.*, *21*, 729–731.
- Tripathi, Y. B., Malhotra, O. P., & Tripathi, S. N., (1984). Thyroid stimulating action of Z-guggulsterone obtained from *Commiphora mukul*. *Planta Med.*, *50*, 78–80.
- Ulbricht, C., Basch, E., Szapary, P., Hammerness, P., Axentsev, S., Boon, H., Kroll, D., et al., (2005). Guggul for hyperlipidemia: A review by the natural standard research collaboration. *Comp. Ther. Med.*, *13*, 279–290.
- Urizar, N. L., & Moore, D. D., (2003). GUGULIPID: A natural cholesterol-lowering agent. *Ann. Rev. Nutri.*, *23*, 303–313.

- Urizar, N. L., Liverman, A. B., D'Nette, T. D., Silva, F. V., Ordentlich, P., Yan, Y., Gonzalez, F. J., et al., (2002). A natural product that lowers cholesterol as an antagonist ligand for FXR. *Science*, *296*, 1703–1706.
- Wu, J., Xia, C., Meier, J., Li, S., Hu, X., & Lala, D. S., (2002). The hypolipidemic natural product guggulsterone acts as an antagonist of the bile acid receptor. *Mol. Endocrinol.*, *16*, 1590–1597.
- Yang, J. Y., Dellaâ-Fera, M. A., & Baile, C. A., (2008). Guggulsterone inhibits adipocyte differentiation and induces apoptosis in 3T3–L1 cells. *Obesity*, *16*, 16–22.
- Youn, H. S., Ahn, S. I., & Lee, B. Y., (2009). Guggulsterone suppresses the activation of transcription factor IRF3 induced by TLR3 or TLR4 agonists. *Int. Immunopharmacol.*, *9*, 108–112.
- Zhang, J. H., Shangguan, Z. S., Chen, C., Zhang, H. J., & Lin, Y., (2016). Anti-inflammatory effects of guggulsterone on murine macrophage by inhibiting LPS-induced inflammatory cytokines in NF- $\kappa$ B signaling pathway. *Drug Des. Dev. Ther.*, *10*, 1829.



# Taylor & Francis

Taylor & Francis Group

<http://taylorandfrancis.com>



## CHAPTER 7

---

# *Kaempferia galanga* L. (Aromatic Ginger): A High Potential Zingiberaceae Species

LILLY ZEITLER

*Sustainable International Agriculture Student,*

*Georg-August University of Göttingen and University of Kassel, Germany*

---

### ABSTRACT

*Kaempferia galanga* is an aromatic, medicinal herb of the Zingiberaceae family. *K. galanga* is found primarily in India, China, and Southeast Asia. These regions are rich in ethnomedical traditions involving *K. galanga*. Phytochemical screenings show that *K. galanga* contains pharmacologically active phyto-constituents, such as ethyl-p-methoxy-cinnamate, ethyl cinnamate, and kaempferol. These display a range of valuable characteristics, including sedative, antibacterial, antifungal, anti-inflammatory, anti-insecticidal, antinociceptive, antihypertensive, and anticarcinogenic properties. Hundreds of patents for *K. galanga* have been granted for medicinal, culinary, cosmetic, or other industrial uses and applications. Though *K. galanga* shows great promise for further development, it remains relatively under-utilized in the western world.

### 7.1 GENERAL INTRODUCTION

*Kaempferia galanga* L. is an aromatic and medicinal herb of the Zingiberaceae family. The *Kaempferia* genus is named after Engelbert Kaempfer, a German naturalist and physician. Vernacular names for *Kaempferia galanga* include

resurrection lily, sand ginger and aromatic ginger, among others. *Kaempferia galanga* ranges across tropical and subtropical Asia and medicinal uses in the region extend back to ancient Ayurvedic and Chinese traditions. The first pharmacological investigation of *Kaempferia galanga* was on its inhibition of monoamine oxidase enzyme (Noro, Miyase, Kuroyanagi, Ueno, & Fukushima, 1983). Since then, a multitude of studies on the pharmacological activities and applications of *Kaempferia galanga* have been conducted. Though *Kaempferia galanga* shows great potential for further development, it remains relatively under-utilized in the western world.

## 7.2 AREA AND PRODUCTION

Global statistics on the production area of *Kaempferia galanga* are lacking. On the national level, India is a key source of both supply and demand for *K. galanga*. In northern India, *K. galanga* production benefits from subsidies, which support the cultivation of 32 key medicinal species over an area of 35,000 hectares in 4,250 projects, implemented by the National Medicinal Plants Board (2007). In terms of consumption, it is estimated that 109 metric tons of *K. galanga* are consumed ‘industrially’ each year in India (National Medicinal Plants Board, 2007). National-level data, statistics, and estimates for production and consumption of *K. galanga* are lacking for most countries.

## 7.3 MARKETING AND TRADE

*Kaempferia galanga* is one of the most industrially and medicinally important plants of the Zingiberaceae family; (Munda, Saikia, & Lal, 2018) yet its potential remains under-utilized. The essential oils of *K. galanga* hold great market potential, particularly in India, but also throughout the world (Munda, Saikia, & Lal, 2018). The international market price of *K. galanga* essential oils ranges between US \$600–700 per kilogram (Munda, Saikia, & Lal, 2018). Although market analyses and global statistics on the international marketing and trade of the species are lacking, some national-level data is available. For instance, India is a major producer and supplier of *K. galanga*, and annual trade of *K. galanga* is estimated at 100–200 metric tons (National Medicinal Plants Board, 2007). With rhizomes fetching a price of approximately 250 Rupees per kilogram (Chandana, 2011). The area of production in Central Java and West Sumatra, Indonesia in 1999, was 2,000 hectares, yielding 20,000 tons of fresh rhizomes annually (Ibrahim,

1999). At the time of writing, dried *K. galanga* rhizomes are available to order online from Chinese and Indian suppliers. Dried *K. galanga* rhizomes fetched a price of US \$3,700–4,700 per metric ton on the Chinese website, Alibaba (n.d.). In terms of sustainable production, marketing, and trade, the *Sisaket Fairtrade Farmer Group* in Thailand produces, markets, and trades *K. galanga* and is certified by the FLO Fairtrade Organization (International Trade Center, 2016).

## 7.4 COMPOSITION AND USES

### 7.4.1 COMPOSITION

*Kaempferia galanga* holds a wealth of pharmacological activity and applications (Munda, Saikia, & Lal, 2018). Rhizomes contain approximately 2.5–4% essential oils (He, Yue, Lau, Ge, & But, 2012). Of the essential oils obtained by hydro-distillation, 31.77% were constituted of ethyl-p cinnamate, 23.23% methyl cinnamate, 11.13% carvone, 9.59% eucalyptol and 6.41% pentadecane (Tewtrakul, Yuenyongsawad, Kummee, & Atsawajaruan, 2005). Ethyl-p methoxy cinnamate and ethyl-cinnamate are the most important active compounds in *K. galanga* rhizome oil with pharmacological properties (Umar, Asmawi, Sadikun, Altaf, & Iqbal, 2011). Other important compounds are 1,8-cineole, borneol, camphene, linoleoyl, methyl-cinnamate, and pentadecane (Munda, Saikia, & Lal, 2018). Another biochemical assay found that six major compounds were responsible for 96.9–97.81% of total oil contents (Sahoo, Parida, Singh, Padhy, & Nayak, 2014), and ethyl p-methoxy cinnamate constituted 72 to 82% of rhizome oil (Sahoo, Parida, Singh, Padhy, & Nayak, 2014). This compound has numerous pharmacological properties to treat various ailments.

### 7.4.2 ETHNOBOTANICAL USES

With its potent active compounds, *Kaempferia galanga* is valued for culinary, medicinal, and other purposes (Ibrahim, 1999; Umar, Asmawi, Sadikun, Altaf, & Iqbal, 2011). *K. galanga* is used as a spice and for incense (Vincent, Bejoy, Hariharan, & Mathew, 1991), perfume (Ibemhal, Laishram, Singh, & Toijam, 2012), skin protection (Babitha, Shin, & Kim, 2009), animal feed (Muhammad & Nataamijaya, 2006), cloth preservation from insects (Ibrahim, 1999), fermentation (Ibrahim, 1999), ‘kretek’ cigarettes

(Ibrahim, 1999) and a wide variety of other applications (see Section 20 on patents). *K. galanga* aromas and flavoring are also used in the production of foodstuffs, beverages, perfumes, and cosmetics (Ibrahim, 1999; Rahman, Amin, Ahamed, Ali, & Habib, 2004).

*Kaemperia galanga* is a popular medicinal spice in India, China, and Southeast Asia. Pickled *K. galanga* rhizomes feature in the national and regional cuisines of these countries with numerous health benefits (Srivastava et al., 2019). Ethnobotanical culinary-health uses are confirmed by nutritional assays, which have determined nutraceutical properties, namely potassium, phosphorus, magnesium, iron, manganese, zinc, cobalt, and nickel (Srivastava et al., 2019). *K. galanga* has high calorific value and carbohydrate content, comparable to some cereals, and higher than some leguminous and other Zingiberaceae species, with the exception of *C. zedoaria* (Srivastava et al., 2019). *K. galanga* demonstrates high energy value, as well as a nutrient and mineral composition that is promising for the development of a flavored, phytoceutical health food product (Srivastava et al., 2019). Moreover, ethyl-p-methoxy-cinnamate is a key flavoring agent in *K. galanga* and inhibits the production of reactive oxygen species (Srivastava et al., 2019). Consumption of *K. galanga* may thereby prevent oxidative damage and therewith cancer (Srivastava et al., 2019).

### **7.4.3 MEDICINAL USES**

#### **7.4.3.1 ETHNOPHARMACOLOGICAL AND ETHNOMEDICAL USES**

The rhizomes of *Kaemferia galanga* are an important ingredient in traditional medicine and used as an expectorant, stimulant, diuretic, and carminative (Ibrahim, 1999; Rahman, Amin, Ahamed, Ali, & Habib, 2004; Kumar, Kader, Rangaswami, & Irulappan, 1997; Sirirugsa, 1997). The fragrance of the rhizomes is camphor-like and suitable for aromatherapy. A decoction of the rhizome is used for dyspepsia, headaches, and malaria. Rhizome extract is used to treat skin and spleen disorders, wounds, and injuries, coughs, and pectoral ailments. The rhizomes are also used in indigenous medicine to treat ascariasis, bacterial infections, tumors, as well as topically for swelling, rheumatism, and abdominal pain in women (Ibemhal, Laishram, Singh, & Toijam, 2012; Sirirugsa, 1997; Hirschhorn, 1983). *K. galanga* rhizomes are also used as an anti-tussive, expectorant, anti-pyretic, diuretic, anabolic, cicatrizant, and carminative, as well as in treatments to counter gastrointestinal ailments, asthma, wounds, rheumatism, epilepsy, and skin disorders

(Ibrahim, 1999; Elshamy et al., 2019; Sivarajan & Balachandran, 1994). Rhizome extracts are also used to cure nasal blocks, nose bleeds, asthma, and hypertension (Ibrahim, 1999; Bhattacharya & Sen, 2013).

In traditional Chinese medicine, *Kaempferia galanga* is used as a stomachic (Vincent, Bejoy, Hariharan, & Mathew, 1991) and in cholera, contusion, and constipation treatments (Srivastava et al., 2019). Rhizomes and tubers are also used in traditional Chinese medicine to treat toothache or in a wash against dandruff or head scabs (Ibrahim, 1999; Sirirugsa, 1997). In India, *K. galanga* is an important ingredient in Ayurvedic preparations, such as *Dasamularista*, *Valiyarasnadikasaya*, *Kaccoradichurna*, *Asanaeladitaila*, *Valiyanarayana-taila*, among others (Joy, Thomas, Mathew, & Skaria, 1998; Kumar, Asish, Sabu, & Balachandran, 2013), *K. galanga* is also used in traditional Tibetan medicine and is a key ingredient of one of the most important Tibetan medicinal formulas, Gabur-25, from the Aginsky monastery in Buryatia (Schwabl & Vennos, 2015). This formula was used to treat ‘heat’ related disorders, such as agitation and infectious diseases, poisoning, gout, arthritis, and other inflammations, as well as for pus drainage (Schwabl & Vennos, 2015).

Another traditional recipe is a juice mixture of *K. galanga*, *Curcuma montana* and *Curcuma aromatica* to facilitate delivery and childbirth (Ling, Hoon, & Kian, 2009). *K. galanga* rhizomes are also a common ingredient in Malaysian and Indonesian health tonics, known as ‘Jamus’ (Ibrahim, 1999; Chan et al., 2009). They are also mixed with rice flour to make ‘*beras kencur*,’ a refreshing and sudorific drink used in Indonesia (Ibrahim, 1999). *K. galanga* rhizomes are often an ingredient in children’s medicinal tonics (Ibrahim, 1999). Rhizome extracts are also used to relieve irritation from caterpillar stings (Chithra, Martin, Sunandakumari, & Madhusoodanan, 2004). In addition, *K. galanga* rhizome oil serves as a cicatrizant (Chithra, Martin, Sunandakumari, & Madhusoodanan, 2004).

Leaf infusions are given to pregnant women for prenatal health (Rahman, Amin, Ahamed, Ali, & Habib, 2004; Sulaiman et al., 2008). The ashes of *K. galanga* leaves are rubbed on swollen breasts after childbirth (Sulaiman et al., 2008). In Malaysia and Indonesia, fresh leaves are chewed as an expectorant to relieve coughs (Ibrahim, 1999; Ling, Hoon, & Kian, 2009; Sulaiman et al., 2008). Leaf poultices and teas are used for curing sore throats, rheumatism, swellings, and eye infections (Parida, Mohanty, Kuanar, & Nayak, 2010). Leaf extracts are also used for sore eyes, sore throat, rheumatism, swellings, and fevers (Bhattacharya & Sen, 2013). *K. galanga* leaves hold antioxidant, antinociceptive, and anti-inflammatory properties that facilitate mouth ulcer healing and headache treatments (Chan et al., 2009; Sulaiman et al., 2008).

### 7.4.3.2 PHARMACOLOGICAL ACTIVITIES

Rhizome extracts contain a wide range of active compounds with pharmacological properties, including ethyl-p-methoxy-cinnamate, n-pentadecane, ethyl cinnamate, L-D3-carene, camphene, borneol, cineol, p-methoxy styrene, kaempferol, and kaempferide. The total phenolic content, radical-scavenging activity, and metal ion-chelating properties were significantly higher in *K. galanga* leaves than in the rhizomes (Chan et al., 2008).

### 7.4.3.3 SEDATIVE PROPERTIES

*K. galanga* is traditionally used to treat restlessness, stress, anxiety, depression, and other conditions of nervousness in tropical and subtropical Asia (Ali, Dash, & Nasrin, 2015). Studies on mice corroborate these traditional uses, in that acetone, petroleum ether fraction, chloroform fraction and methanol fraction extracts of *K. galanga* exhibit sedative properties in sleeping time tests, righting reflexes and locomotor activity suppression (Ali, Dash, & Nasrin, 2015). Other studies on mice considered the potential of *K. galanga* for aromatherapy treatments. Hexane extracts of ethyl trans-p-methoxycinnamate and ethyl cinnamate have shown sedative and relaxant effects when inhaled by mice, suggesting a promising application of *K. galanga* in aromatherapy (Huang, Yagura, & Chen, 2008).

### 7.4.3.4 ANTIMICROBIAL AND ANTIFUNGAL

The major active compounds of *Kaempferia galanga* exhibit various antimicrobial activities (Munda, Saikia, & Lal, 2018). Methanol and petroleum-based extracts of *Kaempferia galanga* exhibit inhibitory effects on *E. coli*, *Salmonella* sp., *Shigella* sp., *Bacillus* sp. and *Pseudomonas* sp. (2–16 µg/ml concentrations) (Parvez, Khan, Islam, & Hasan, 2005). Other studies confirm the antimicrobial and antifungal properties of *Kaempferia galanga*, by inhibiting the bacterial pathogens *Staphylococcus aureus*, *Streptococcus faecalis*, *Bacillus cereus*, *Bacillus subtilis*, *Enterobacter aerogenes*, *Salmonella typhi*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Vibrio cholerae*, as well as the fungal species *Aspergillus niger*, *A. flavus*, *A. fumigatus* and *Candida albicans* (Kochuthressia, Britto, & Jaseentha, 2012). The strongest inhibitory effects were exhibited against *Staphylococcus aureus* using ethanol extracts (Kochuthressia, Britto, & Jaseentha, 2012). Samples of *V. cholerae* were extracted from an outbreak in Sarawak and tested with methanol extracts of *K. galanga* rhizome. These

extracts eradicated 90% of the biofilm of *V. cholerae* at a concentration of 500 mg/ml (Nillian et al., 2018). The antimicrobial properties of *K. galanga* have proved to be suitable for dental plaque prevention against *Streptococcus mutans* (Hertiani, Pratiwi, Irianto, & Febriana, 2010).

#### 7.4.3.5 INSECTICIDAL AND REPELLENT

The hexane fraction of *Kaempferia galanga* exhibits larvicidal properties, as well as repellent properties against *Aedes aegypti* for a three-hour period in a laboratory setting (ED<sub>50</sub> value of 30.73 µg/cm<sup>2</sup>) (Choochote et al., 1999). In field experiments, the mosquito species *Armigeres subalbatus*, *Anopheles barbirostris*, *An. Aconitus*, *Mansonia uniformis*, *Cx. Quinquefasciatus*, *Cx. Gelidus*, *Cx. Tritaeniorhynchus* and *Aedes Aegypti*, were repelled by *Kaempferia galanga* hexane extracts (Choochote et al., 1999). Other studies also found the larvicidal impacts of *K. galanga* on *A. aegypti*; however, they also indicate that extraction needs to be improved to increase mortality rates (RMUS, BMAC, WTPSK, & GC, 2017).

#### 7.4.3.6 NEMATOCIDAL USES

*Kaempferia galanga* exhibits nematocidal properties. *K. galanga* extracts at a concentration of 1,000 mg per liter resulted in 100% mortality of *Bursaphelenchus xylophilus* and *Meloidotyne incognita* after a 24-hour period (TianZhu, Yong, FuWei, MeiYing, & QunFang, 2010). *Ditylenchus destructor*, *M. eloidogyne hainensis* and *M. enterolobii* were also inhibited by *K. galanga* compounds, including ethyl cinnamate and ethyl-p-methoxyl cinnamate (TianZhu, Yong, FuWei, MeiYing, & QunFang, 2010). Another study found that *K. galanga* significantly inhibited the root-knot nematode, *M. incognita*, indicating the applicability of *K. galanga* to control plant nematode diseases (YueYe, QunFang, TianZhu, MeiYing, & FuWei, 2011). The nematocidal effect of *K. galanga* extract has shown to be stronger than Carbofuran and metham sodium (Hong et al., 2010).

#### 7.4.3.7 ANTI-INFLAMMATORY, ANTINOCICEPTIVE, AND WOUND HEALING

*Kaempferia galanga* has long been included in folk pharmacopeias as an anti-inflammatory, which have been supported by numerous studies. For instance, a study of air-dried *K. galanga* leaf extracts demonstrated antinociceptive and anti-inflammatory properties on rats, which supports

traditional medicinal uses in Malaysia for mouth ulcer, headache, and sore throat treatments (Sulaiman et al., 2008). Studies on Wistar rats found that the application of alcoholic extracts of *K. galanga* with dexamethasone led to a significant reduction in wound breaking strength, increased percentage of wound contraction, and reduced epithelialization time as compared to control groups (Shanbhag et al., 2006). Another study on rats found that the compound, ethyl p-methoxyl cinnamate from *K. galanga* extracts, is an effective anti-inhibitory agent (Umar et al., 2012). Other studies found that *K. galanga* extracts possessed both anti-inflammatory and analgesic properties on rats (Vittalrao, Shanbhag, Meena, Bairy, & Shenoy, 2011). *K. galanga* is combined with *Quercus infectoria*, *Coptis chinensis* and *Glycyrrhiza uralensis* in traditional Thai medicine to treat aphthous ulcers due to its anti-inflammatory properties; these have been further confirmed by *in vitro* tests (Aroonrerk & Kamkaen, 2009). The antinociceptive effect of *K. galanga* is found to be similar to aspirin (Umar, Asmawi, Sadikun, Altaf, & Iqbal, 2011; Ridtitid, Sae-Wong, Reanmongkol, & Wongnawa, 2008).

#### 7.4.3.8 CIRCULATORY DISORDERS

Ethyl cinnamate isolated from *Kaempferia galanga* had a vaso-relaxant effect on the aortas of rats, indicating the antihypertensive activities of this isolated compound (Othman et al., 2002). Oral administration of *K. galanga* extracts significantly lowered total cholesterol, triglyceride, phospholipid, and high-density lipoproteins (HDL) in Wistar rats fed on a high cholesterol diet, indicating the efficacy of *K. galanga* in treating lipid disorders, particularly atherosclerosis (Achuthan & Padikkala, 1997).

#### 7.4.3.9 NEOPLASMS

Methanolic extracts of *Kaempferia galanga* rhizomes have cytotoxic effects on HeLa cells (Kosuge et al., 1985). The bioactive compound of ethyl-p-methoxycinnamate from *K. galanga* extracts also exhibit moderate cytotoxic activity in mice against the human CCA tumor (CL-6) line (Amuamuta, Plengsuriyakarn, & Na-Bangchang, 2017). Jagadish et al. found that extracts and fractions of *Kaempferia galanga* exhibited selective cytotoxic activities, acting against four different cancerous lines (DU145, PA1, SW620, B16F10); however, not against normal Vero cell cultures (Jagadish, Raghu, Vinod, & Latha, 2010). Studies on mice found that both -cis and -trans ethyl-p-methoxycinnamate from *K. galanga* demonstrated a relatively



strong anticarcinogenic potential (Xue & Chen, 2002). Other phytochemical screenings found that the presence of flavonoids in *K. galanga*, in addition to demonstrated tumor inhibition, showed that *K. galanga* is a promising candidate for anticancer treatments and pharmacological development (Bagya, Rajashree, & Sam, 2011). A cytotoxicity assay found that *K. galanga* inhibited early activation of the Epstein-Barr virus (Vimala, Norhanom, & Yadav, 1999). The authors propose that *Kaempferia galanga*, alongside several other rhizobia used in traditional Malaysian medicine, could contribute to the development of cancer treatment at tumor-promoting stages (Vimala, Norhanom, & Yadav, 1999).

The active compounds, trans-ethyl-p-methoxycinnamate and kaempferol, showed potent antiangiogenic effects on wildtype zebrafish (He, Yue, Lau, Ge, & But, 2012). Of the two compounds, trans-ethyl-p-methoxycinnamate exhibited much stronger effects and was therefore, further investigated for identifying action mechanisms (He, Yue, Lau, Ge, & But, 2012). *In vitro*, trans-ethyl-p-methoxycinnamate inhibited the migration and tube formation of human umbilical cells; *in vivo*, it could block bFGF-induced vessel formation (He, Yue, Lau, Ge, & But, 2012).

## 7.5 ORIGIN AND DISTRIBUTION

*Kaempferia galanga* is native to tropical Asia, and its range extends across southern China, Vietnam, Laos, Cambodia, Thailand, Malaysia, India, and Taiwan (Umar, Asmawi, Sadikun, Altaf, & Iqbal, 2011; Ling, Hoon, & Kian, 2009). It is also found in Assam, Bangladesh, south-central, and southeast China, Lesser Sundarban Islands, Maluku, Philippines, and Sri Lanka (Naturalis Biodiversity Center, n.d.). It is mainly cultivated in Southeast Asia and China, and in the Indian provinces of Kerala, Karnataka, Tamil Nadu and West Bengal (Preetha, Sudarsanan, & Krishnan, 2016). In China, it is cultivated in the southern and north-western provinces of Guangdong, Guangxi, Guizhou, Yunnan, and Sichuan (Li, Zhao, & Liu, 2019). *K. galanga* is believed to have originated in East Asia, probably in Myanmar (Preetha, Sudarsanan, & Krishnan, 2016; Wood, 1991).

## 7.6 BOTANY AND TAXONOMY

### 7.6.1 BOTANY

*Kaempferia galanga* is a small, short-stemmed, monocotyledonous perennial herb (Ibrahim, 1999; Umar, Asmawi, Sadikun, Altaf, & Iqbal, 2011). The

rhizomes are strongly aromatic with either pale green or greenish white internal coloration. The rhizomes are either sympodial, tuberous or cylindrical and often bear smaller tubers and fibrous roots (Ibrahim, 1999). The leaves are few, distichous, simple, subsessile, and spread flat on the ground. The leaf form is orbicular with a mucronate or acute apex. Leaf texture is glabrous on both the upper and lower leaf surfaces or villous abaxially. Leaf margins are typically white, while the rest of the leaf is adaxially deep green and abaxially pale green. Petioles are short and channeled. Ligules are small or absent (Ibrahim, 1999). Bracteoles are small with 1 to 2 presents (Ibrahim, 1999). Lower leaves and sheaths have auriculate apices (Ibrahim, 1999). The inflorescence is terminal with the peduncle usually enclosed by an imbricate sheath (Ibrahim, 1999). Flowers are monoecious, zygomorphic, and spirally arranged on a discoid receptacle (Ibrahim, 1999). The corolla is white with purple spots in the axillary fascicles or base of the labellum. The corolla tube is approximately 2.5 cm long. Calyx is tubular and shorter than the corolla tube (Ibrahim, 1999). Stamen are fertile (1) with a short or absent filament (Ibrahim, 1999). Ovary is inferior with 3 locules (Ibrahim, 1999). Ovules are few to many, filiform, with one style and funnel-shaped stigma (Ibrahim, 1999). Fruits are oblong, dehiscent, 3-celled and -valved capsules. The seeds are few to many, ellipsoidal to nearly globular and lacerate arillate (Ibrahim, 1999).

### 7.6.2 TAXONOMY

*Kaempferia galanga* is a species in the Zingiberaceae family, one of four families in the monophyletic ‘ginger group’ present in the eight-family large order of Zingiberales (Sass, Iles, Barrett, Smith, & Specht, 2016). The *Kaempferia* genus consists of approximately 50 species (Li, Zhao, & Liu, 2019). Taxonomically, species within the *Kaempferia* genus are difficult to differentiate due to morphological similarities (Techaprasan, Klinbunga, Ngamriabsakul, & Jenjittikul, 2010). Molecular profiling and genome sequencing show that *K. galanga* and *K. elegans* form a cluster within the *Kaempferia* genus (Labrooy, Abdullah, & Stanslas, 2018).

### 7.7 VARIETIES AND CULTIVARS

Raina et al. (2015) found substantial genetic variation within the *Kaempferia galanga* species in India, while Rajasekharan et al. (2017) found little genetic diversity (Raina, Abraham, & Sivaraj, 2015; Rajasekharan, Abdul, Ravish, &

Mini, 2017). Few studies have considered intra-specific genetic variation within a given cultivar, as has been done for the local Indian cultivar, 'Vellanikkara' (Kanakamanay, 2008). Approximately 10 varieties are present in Indonesia, of which 'Cileungsi Besar' is the most high-yielding (Ibrahim, 1999).

In India, 'Kasturi' and 'Rajani' are two common, locally registered varieties (Raina, Abraham, & Sivaraj, 2015; Indrayan, Kurian, Tyagi, Shatru, & Rathi, 2007). Both varieties were developed using clonal selection by Kerala Agricultural University (Preetha, Sudarsanan, & Krishnan, 2016). The two varieties differ both morphologically and biochemically. The rhizomes of 'Kasturi' are large and light brown, while those of 'Rajani' are medium size and cream colored (Preetha, Sudarsanan, & Krishnan, 2016). A chemical analysis of the essential oils of these varieties revealed that 'Kasturi' contained 13 compounds not found in 'Rajani,' while the latter had 11 compounds not found in the former (Indrayan, Kurian, Tyagi, Shatru, & Rathi, 2007). The composition of their shared 45 compounds also differ (Indrayan, Kurian, Tyagi, Shatru, & Rathi, 2007). In terms of production, 'Kasturi' yields 2.52 tons of dry rhizomes per hectare with a dry recovery rate of 32.78% (Preetha, Sudarsanan, & Krishnan, 2016). It has high volatile oil content with 34% extractable (Preetha, Sudarsanan, & Krishnan, 2016). 'Rajani,' on the other hand, yields 2.55 tons of dry rhizomes per hectare (Preetha, Sudarsanan, & Krishnan, 2016). Its volatile content is 1% with high total extractives at 7.68% (Preetha, Sudarsanan, & Krishnan, 2016).

Other Indian cultivars have been recognized for particular traits and compounds. An analysis of eight cultivars from Manipur in northeast India found that the 'Tamenglong' cultivar contained the highest Vitamin C levels, the 'Ukhrul' cultivar had the highest phenol content, and the 'Imphal-east' cultivar was highest in kaempferol (Sunitibala, Devala, Brojendro, Samarjit, & Punyarani, 2015). There are also other promising germplasm ascensions, which could be further developed (Raina, Abraham, & Sivaraj, 2015). For instance, the Bharamputra-1 (IC0610826; INGR17081) germplasm exhibits high essential oil content and dry rhizome recovery, as well as yields as high as 10 tons per hectare (Lal, 2019).

A promising variety of *Kaempferia galanga* is the newly registered Jor Lab K-1 variety, which is high yielding in both oil content and rhizome mass (Lal, Munda, Dutta, Baruah, & Pandey, 2017). This variety exhibited 35% superiority over the standard varieties of 'Kasturi' and 'Rajani' with an herbage yield of 7.156 tons per hectare (Lal, Munda, Dutta, Baruah, & Pandey, 2017). Dry matter recovery from fresh rhizomes was 25% (Lal, Munda, Dutta, Baruah, & Pandey, 2017). Average essential oil content was

2.38% (Lal, Munda, Dutta, Baruah, & Pandey, 2017). Of these, 31.12% was ethyl trans-cinnamate, 14.3% was ethyl trans-p-methoxycinnamate, 10.57% was 1,8-cineole and 4.8% was n-pentadecane (Lal, Munda, Dutta, Baruah, & Pandey, 2017).

## 7.8 SOIL AND CLIMATE

*Kaempferia galanga* grows in the humid tropics and subtropics. It can remain dormant during the dry seasons of the subtropics. It grows best in warm climates with an average annual temperature of 25 to 30°C (Riptanti, Qonita, & Fajarningsih, 2018). The agro-climates most suitable for *K. galanga* growth are Type A, B, and C (Schmidt-Ferguson). *K. galanga* thrives in altitudes up to 1,000 meters above sea level (asl) with annual precipitation levels of 2,000 to 4,000 mm (Ibrahim, 1999) or preferably at 50 to 600 meters asl with 2,500 to 4,000 mm annual precipitation (Riptanti, Qonita, & Fajarningsih, 2018). A slope of less than 3% inclination is preferable (Riptanti, Qonita, & Fajarningsih, 2018). *K. galanga* can grow with full light intensity (100%) or in shade (25–30%). Overall, *Kaempferia galanga* prefers rich, moist, and partially shaded microclimates. Although *Kaempferia galanga* can grow on a diverse range of soil types from vertisols and latosols to andosols with clay to silt-loam textures, it grows best on humus-rich soils with good texture and drainage (Ibrahim, 1999; Riptanti, Qonita, & Fajarningsih, 2018; Kamaruddin, 2006). Waterlogged soils damage *K. galanga*, while acidic soils hinder development and growth (Ibrahim, 1999). Optimum growth occurs with a soil pH of 5.5 to 6.5, which can be achieved by adding dolomite to more acidic soils (Riptanti, Qonita, & Fajarningsih, 2018). Ecologically, *K. galanga* grows naturally in open and teak forest and alongside forest margins (Ibrahim, 1999). The plant may spread from cultivated areas into grasses, lawns, and abandoned areas (Ibrahim, 1999).

A study considering *K. galanga* yields in the Indian state of Kerala found that vegetative growth and nutrient uptake vary greatly according to ecotype (Gangadharan & Menon, 2003). The authors found that less shade appeared to promote rhizome yield, while increased shade appeared to increase the proportion of active compounds. Shade appeared to affect the compounds present in the rhizome and leaf. Although shade did not appear to affect nitrogen availability and absorption, it was linked to calcium, magnesium, manganese, and zinc uptake in the leaves and rhizome. In contrast, phosphorus and potassium uptake increased with greater light

exposure. Rhizome yield was correlated to nitrogen, potassium, phosphorus, and calcium nutrient uptake from the soil, while magnesium, sulfur, manganese, and zinc related to oleoresin and essential oil content. Phosphorus and potassium were linked to initial crop development, while magnesium and sulfur were important for development of active components. This indicates that phasic soil management is likely to optimize production, characterized by the addition of potassium and phosphorus at early growth stages. The field studies show that this initial treatment can improve vegetative growth and rhizome yield two months after planting. During the rhizome formation stages four months after planting, application of MgSO<sub>4</sub> can enhance the qualitative components of the rhizomes. Application of animal manure (20 tons per hectare) can fulfill crop nitrogen requirements. Soil surface dressings of sulfur and magnesium were shown to improve rhizome yields (Kavitha & Menon, 2013). In terms of soil preparation, shallow soil loosening of 10 cm appeared to optimize yields, while deeper soil loosening of 20 cm resulted in nutrient leaching and lower yields (Gangadharan & Menon, 2003).

## 7.9 PROPAGATION AND ROOTSTOCK

The natural regeneration from the rhizomes or seeds is poor, to the extent that the species is on the brink of being endangered in the wild (Ibemhal, Laishram, Singh, & Toijam, 2012; Shirin, Kumar, & Mishra, 2000). The traditional propagation method is clonal using rhizome cuttings and plantings, as is commonly practiced with plants of the Zingiberaceae family (Bhattacharya & Sen, 2013). Studies of *K. galanga* populations in southern India found little genetic variation, but showed high genetic differentiation, attributable to traditional clonal propagation methods (Rajasekharan, Abdul, Ravish, & Mini, 2017). Habitat fragmentation contributes to high genetic differentiation between populations and reduces the potential for genetic drift (Rajasekharan, Abdul, Ravish, & Mini, 2017). Although traditional propagation methods potentially preserve ancient clonal lines with highly desirable traits, they also raise conservation concerns for the species due to reduced genetic variability (Rajasekharan, Abdul, Ravish, & Mini, 2017).

Similarly, in conventional commercial production, *K. galanga* is propagated using rhizome rootstocks (Rahman, Amin, Ahamed, Ali, & Habib, 2004). However, this method tends to lower the rate of multiplication

(Vincent, Bejoy, Hariharan, & Mathew, 1991; Ibemhal, Laishram, Singh, & Toijam, 2012; Parida, Mohanty, & Nayak, 2019). Moreover, high disease susceptibility and cost of production has led to the development and application of alternative *in vitro* propagation methods. These facilitate further commercial development and address conservation concerns regarding the species (Ibemhal, Laishram, Singh, & Toijam, 2012; Parida, Mohanty, Kuanar, & Nayak, 2010; Swapna, Binitha, & Manju, 2004). *In vitro* clonal propagation has been successful using rhizome buds (Vincent, Bejoy, Hariharan, & Mathew, 1991; Chirangini, Sinha, & Sharma, 2005; Kalpana & Anbazhagan, 2009; Keng & Hing, 2004; Rahman et al., 2005; Vincent, Mathew, & Hariharan, 1992; Lakshmi & Mythili, 2003; Geetha et al., 1997), rhizome pieces (Kochuthressia, Britto, & Jaseentha, 2012; Shirin, Kumar, & Mishra, 2000), terminal buds (Prathanturarug, Apichartbutra, Chuakul, & Saralamp, 2007) and leaf materials (see Table 7.1) (Rahman, Amin, Ahamed, Ali, & Habib, 2004; Parida, Mohanty, Kuanar, & Nayak, 2010; Wijekoon & Senarath, 2006). Biochemical and molecular profiling of micro-propagated rhizome clones have shown that *in vitro* propagation methods can produce true-to-type *K. galanga* for a stable supply of medicinal compounds for commercial production (Mohanty et al., 2011). Genetic profiling of *in vitro* micro-propagated *K. galanga* leaf biomass from tissue culture showed that this propagation method is also suitable for commercial utilization and rapid production of genetically stable *K. galanga* leaf material (Parida, Mohanty, Kuanar, & Nayak, 2010). Moreover, *in vitro* micro-propagation of leaf shoot extracts found that this propagation method produced pathogen free *Kampferia galanga* plants efficiently and effectively (Bhattacharya & Sen, 2013). A bioassay comparing the larvicidal activity and phytochemical identities in naturally grown and cultured plants found that cultured plants had higher larvicidal activity, while the phytochemical properties were 90% similar with the exception of Cyclopentane (58% similar) and p-Hydroxycinnamic acid ethyl ester (78%) (RMUS, BMAC, WTPSK, & GC, 2017). Other comparative studies found that *in vitro* propagated plants obtained higher oil yields than naturally grown plants, while the composition remained constant (Sahoo, Parida, Singh, Padhy, & Nayak, 2014). To optimize the regeneration and plant growth during micro-propagation, sucrose concentrations and light exposure act as key variables (Bhatt, Kean, & Keng, 2012). Silver nitrate has also been shown to optimize micro-propagation outcomes (Chithra, Martin, Sunandakumari, & Madhusoodanan, 2005).

**TABLE 7.1** Chronologically Organized Literature of Kampferia Galangal Micro-Propagation

Plant Organ	Results	References
Vegetative bud (excised from rhizome)	80–85% survival rate	Vincent et al. (1991)
Rhizome bud	90% survival	Vincent et al. (1992)
Rhizome bud	–	Geetha (1997)
Rhizome pieces	–	Shirin et al. (2000)
Rhizome bud	–	Lakshmi (2003)
Rhizome bud	~ 76% survival	Keng et al. (2004)
Leaf and rhizome extracts	–	Swapna et al. (2004)
Leaf base-derived callus	–	Rahman et al. (2004)
Rhizome tip and lateral bud	100% culturation success; 85% planting success.	Rahman et al. (2005)
Rhizome buds	80–90% survival	Chirangini et al. (2005)
Rhizome	12.1 shoots per explant with silver nitrate 95% survival. <i>In vitro</i> developed rhizome and naturally grown rhizome exhibited no difference in rhizome growth.	Chithra et al. (2005)
Leaf discs and axillary buds	100% survival	Wijekoon & Senarath (2006)
Terminal buds	20,000 successful regenerants	Prathanturug (2007)
Rhizome tip and lateral bud	81% survival rate	Kalpna & Anbazhagan (2009)
Sprouting rhizome bud	> 90% survival	Rajasekharan et al. (2009)
Leaf	–	Parida et al. (2010)
Rhizome	–	Mohanty et al. (2011)
–	Shoot height and proliferation affected by sucrose concentration and photoperiod.	Bhatt et al. (2012)
Rhizome explant	95% survival	Ibemhal et al. (2012)
Rhizome segment explants	100% regeneration	Kochuthressia et al. (2012)
Leaf shoot extract	Survival Rate: 94% in greenhouse; 95% in field. Pathogen free	Bhattacharya & Sen (2013)
Rhizome bud	No difference in composition between <i>in vitro</i> and naturally propagated plants, but higher oil yield in <i>in vitro</i> plants.	Sahoo et al. (2014)
Shooting rhizome bud	100% regeneration. Higher larvicidal activity in cultured that naturally grown plants (max. 10% mortality of <i>A. aegypti</i> ). Mostly 90% similarity in phytochemical constituents between naturally grown and cultured plants.	Senarath et al. (2017)

## 7.10 PLANTING, IRRIGATION, AND NUTRIENT MANAGEMENT

Planting materials by conventional methods typically involve 2.5 to 4 cm long rhizome pieces with 2 to 3 buds (Ibrahim, 1999). These can be kept 1 to 2 weeks in dry, shaded conditions before planting at the beginning of the rainy season (Ibrahim, 1999). In Central Java, *K. galanga* rhizome planting material is planted in furrows 7.5 to 10 cm deep with spacing of 10 to 15 cm between planting materials (Ibrahim, 1999). In West Sumatra, rhizome planting materials are planted in separate holes 5 to 7.5 cm deep and 25 to 60 cm apart (Ibrahim, 1999). Approximately 840–1,700 kg of rhizome planting material are needed per hectare (Riptanti, Qonita, & Fajarningsih, 2018). Chitra et al. recommend 1,500 kg of rhizome planting material per hectare (Chithra, Martin, Sunandakumari, & Madhusoodanan, 2004).

Intercropping has been shown to be an effective planting strategy for *K. galanga*. These systems typically provide 30–50% shade (Thakur, Attar, & Chauhan, 2017). Nair et al. (1989) found no reduction in yield for *K. galanga* grown in intercrop systems, even at later stages of canopy growth with reduced light intensities (Nair, Sudhadevi, & 1989). Mahaswarappa et al. (1998) found higher yields for *K. galanga* grown in a 30-year-old coconut plantation (6.1 tons per hectare), rather than as a monocrop (4.8 tons per hectare) (Maheswarappa, Hegde, & Nanjappa, 1998). Mixed multistoried coconut-based agroforestry systems have also been successful in the production systems of other *Kaempferia* species, for instance *Kaempferia augustifolia* (Bari & Rahim, 2012). In Java, *K. galanga* is commonly intercropped with groundnut and rice (Ibrahim, 1999). Competition in intercrop systems with *K. galanga* is responsible for modestly reducing soil nitrogen levels (Kumar, Kumar, & Fisher, 2005).

A field experiment at the Kerala Agricultural University planted *K. galanga* as an understory crop in a coconut garden within a randomized block control trial. Chlorophyll, carotenoid, oil, and oleoresin levels did not significantly differ when mother or finger rhizomes were used as planting material (Maheswarappa, Nanjappa, & Hegde, 2000a, b; Maheswarappa, Nanjappa, Hegde, & Biddappa, 2000). These contents also did not significantly differ with respect to planting intensities (333,000 and 500,000 plants per hectare). However, in terms of yield, finger rhizome planting was 2.1% less than mother rhizome plantings. Moreover, planting intensities with plant population levels of 500,000 plants per hectare (10 x 20 cm) produced 6.7% more rhizome yield than at lower intensity planting densities (333,000 plants per hectare). Lower planting intensities and mother rhizome planting



materials exhibited a significantly higher harvest index (Maheswarappa, Nanjappa, & Hegde, 1999).

Soil nutrient applications, such as farmyard manure, vermi-compost, and combined manure and NPK treatments, significantly increased dry matter production, as compared to composted coir pith, NPK, and control treatment. The farmyard manure, vermi-compost, NPK, and combined manure and NPK treatments improved the harvest index, as compared to composted coir pith. Combined organic farmyard manure and NPK treatments resulted in the highest growth and yield levels, followed by manure and vermi-compost treatments. The oil and oleoresin contents were significantly higher with combined manure and NPK treatments, followed by manure and vermi-compost treatments, in contrast to the composted coir pith and control treatments.

The study from Kerala Agricultural University recommends application of combined farmyard manure and NPK treatments at high planting intensities (500,000 plants per hectare; 10 x 20 cm spacing) using mother rhizomes as planting materials for the highest yields (6.3 tons per hectare, as compared to 4.8 tons per hectare), active compound and oil contents (Maheswarappa, Nanjappa, Hegde, & Biddappa, 2000). However, mother rhizome planting materials and higher planting intensities deplete soil nutrients at higher rates; thus, this planting method must be combined with soil additive measures, preferably combined farmyard manure and NPK treatments, to ensure high productivity and yields. Recommendations in Indonesia advise supplementary irrigation to optimize crop production with sprinklers, if possible, particularly during the dry seasons (Kamaruddin, 2006). However, further studies on specific irrigation regimes and their interactions with different production systems still need to be conducted for *K. galanga*.

### 7.11 TRAINING AND PRUNING

The Kerala Agricultural University conducted an experimental planting of *Kaempferia galanga* under different shade intensities and canopy covers in a randomized block control trial (Kumar, Kumar, & Fisher, 2005). *K. galanga* was planted with no shade cover as a control, while *Cocos nucifera* provided a solitary canopy (Kumar, Kumar, & Fisher, 2005). For the multi-strata test environment, dicot trees, *Vateria indica*, *Ailanthus triphysa* or *Grevillea robusta* were grown in single and double rows (Kumar, Kumar, & Fisher, 2005). These treatments did not appear to influence rhizome yield (Kumar, Kumar, & Fisher, 2005). However, foliar phosphorus and potassium

concentrations were significantly higher under canopy cover (Kumar, Kumar, & Fisher, 2005). Since these nutrient concentrations are linked to the development of active compounds for essential oil production, planting a canopy cover is advisable for the production of active compounds for essential oils. It is also recommended that the associated dicot species in *Kaempferia spp.* intercropped production systems be pruned, so as to limit competition and enhance management for the temporal continuity of resources in the production system (Kumar, 2007).

## 7.12 PEST AND DISEASE MANAGEMENT

Commonly transferred pathogens using conventional rhizome clonal propagation methods include the bacterial *Pseudomonas spp.* and fungal *Pythium spp.* (Bhattacharya & Sen, 2013). In Indonesia, *Pythium spp.* has been observed to cause root rot, particularly in soils with poor drainage (Ibrahim, 1999). *In vitro* propagation methods are a means of overcoming contamination, although *in vitro* planting cultures may become bacterially and fungal contaminated; however, these are effectively treated with mercuric chloride and ethanol treatments (Bhattacharya & Sen, 2013). Other major diseases and pathogens of *K. galanga* include *Ralstonia solanacearum* (Smith), *Colletotrichum gloeosporioides* (Penz.) Sacc, and *Colletotrichum capsici* (Syd.) Butler and Bisby (Priya, 2005). *Pseudomonas solanacearum* is the major pathogen causing bacterial wilt of *Kaempferia galanga* (Dake & Manoj, 1995). A common pest is *Erionata thrax*, which can be controlled with acephate spray. Mitex can be used for mite control under canopy cover.

Two genotypes are immune to bacterial wilt, while nine are highly resistant to leaf spot disease (Priya, 2005). In terms of biotechnology, significant developments have been made to identify the candidate disease resistant genes in *K. galanga* L. (Joshi, Kar, Mohanty, Subudhi, & Nayak, 2012). In an *in vitro* evaluation and in field studies, *Trichoderma viride* proved to be a highly efficient fungal antagonist with an inhibitory effect (Priya, 2005). The antagonists, *P. fluorescens* and *A. niger*, were also effective (Priya, 2005). Among other tested fungicides, Bordeaux mixture was most effective against fungal pathogens, while Kocide, followed by the application of Bordeaux mixture, was effective against bacterial pathogens. In addition, the soil microbial population impacts disease susceptibility and yield (Priya, 2005). Thus, soil additives, such as farmyard manure play a key role in disease management (Priya, 2005).

## 7.13 HARVESTING AND YIELD

### 7.13.1 HARVESTING

For culinary purposes, the leaves and rhizomes are harvested at vegetative stages. For medicinal purposes, mature rhizomes are harvested approximately 10 to 11 months after planting, characterized by drying and yellowing leaves as a marker. However, harvesting times may vary according to geographic locations. For instance, in Central Java, *K. galanga* rhizomes are harvested 6 to 18 months after planting, whereas in West Sumatra, they are harvested 18 to 24 months after planting (Ibrahim, 1999). In the former, yields are approximately 6 to 15 tons per hectare, while in the latter, yields range from 12 to 20 tons per hectare (Ibrahim, 1999). Harvesting by digging up the rhizomes at this stage helps to prevent fungal decay (Ibrahim, 1999). Potential fresh harvest yield is approximately 7–10 tons per hectare. However, some reports from Indonesia have indicated yields as low as 1.2 tons per hectare (Ibrahim, 1999). Harvesting and collection may be undertaken by specialist collectors and herbalists, particularly if collected from the wild. *K. galanga* is also harvested in home gardens manually. Detailed reports of mechanized harvesting techniques for *K. galanga* were not found under this review.

### 7.13.2 YIELDS

Yields vary, depending on production systems, treatments, varieties, and other variables. However, intercropping has been shown to increase *K. galanga* yields from 4.8 tons per hectare to 6.1 tons per hectare (Maheswarappa, Hegde, & Nanjappa, 1998). In a field experiment in Kerala, the highest yields of 6.3 tons per hectare, were obtained in intensive planting systems with 500,000 plants per hectare (10 x 20 cm spacing) with mother rhizome planting materials and with the application of farmyard manure and NPK (Maheswarappa, Nanjappa, & Hedge, 2000b). In terms of the yields of different varieties, the common Indian varieties of 'Kasthuri' and 'Rajani' yield 2.52 and 2.55 tons of dry rhizomes per hectare, respectively (Preetha, Sudarsanan, & Krishnan, 2016). A promising registered variety is Jor Lab K-1 with an herbage yield of 7.16 tons per hectare, an improvement of 35% on the herbage yields of 'Kasthuri' and 'Rajani' (Lal, Munda, Dutta, Baruah, & Pandey, 2017). The highest yielding genome documented in the scientific literature appears to be that of the germplasm of Bharamputra-1 (IC0610826; INGR17081), which delivers yields as high as 10 tons per hectare (Lal, 2019).

In Indonesia, the production cost per hectare, including land preparation, external inputs and labor is approximately US \$1.12 (RM 15,530), which varies depending on yields per hectare (Kamaruddin, 2006). In 2006, fresh rhizome production cost approximately US \$0.00012 (RM 1.60) per kilogram, based on a yield of 10 tons of fresh rhizome per hectare (Kamaruddin, 2006). With a yield of 7 tons of fresh rhizome per hectare, the production costs increased to US \$0.00016 (RM 2.20) (Kamaruddin, 2006).

## **7.14 POST-HARVEST HANDLING AND STORAGE**

### **7.14.1 POST-HARVEST HANDLING**

The post-harvest handling of *Kaempferia galanga* typically entails slicing rhizomes into circular pieces to be sun-dried, followed by storage for indeterminate time periods (Chandana, 2011; Ibrahim, 1999). For storage and medicinal purposes, *K. galanga* rhizomes are sliced and dried at 40°C, either in the sun or using a commercial dryer (Kamaruddin, 2006). For the sale of freshly prepared rhizomes, harvested rhizomes are first washed and air-dried at outdoor temperatures and sold fresh.

### **7.14.2 STORAGE**

*Kaempferia galanga* rhizomes can be stored for 6 months (Bhattacharya & Sen, 2013); in addition, they have the capacity to regrow 6 to 12 months after storage (Rajasekharan, Ambika, & Ganeshan, 2009). However, dried rhizomes are often stored in unhygienic, suboptimal conditions, and microbial contamination will deteriorate the quality (Chandana, 2011). Further research and development is needed to promote Good Agricultural Practice in post-harvest handling and storage of *K. galanga* (Chandana, 2011).

## **7.15 PROCESSING OF MEDICINAL/AROMATIC PLANTS**

Conventional processing of *Kaempferia galanga* for medicinal purposes entails hydro-distillation of its essential oils. Other common processing methods include drying and slicing the rhizomes for medicinal decoctions and culinary spices. Blanching at 80°C can increase the water content of *K. galanga* products (Setiarso, Rusijono, Samik, & Kusumawati, 2018). Drying and raw material reversal procedures can reduce metal and microbial contamination (Setiarso, Rusijono, Samik, & Kusumawati, 2018). Thermal and non-thermal drying processes may reduce the antioxidant properties of

*Kaempferia* sp. (Chan, Lye, Eng, & Tan, 2013; Atun, 2014). However, freeze drying will reduce the loss of antioxidants during processing (Atun, 2014). Literature on *Kaempferia galanga* processing remains limited and requires further research.

## 7.16 CHARACTERIZATION OF PHYTO-CONSTITUENTS

Our knowledge of the phyto-constituents of *Kaempferia galanga* is comprehensive and considerable work has been done on their characterization. As of 2010, 98.98% of essential oil constituents of *K. galanga* had been identified, and only 1.11% of its constituents remained unknown (Umar, Asmawi, Sadikun, Altaf, & Iqbal, 2011; Sutthanont et al., 2010). Ethyl-p-methoxycinnamate and ethyl-cinnamate are the most vital constituents and have been successfully isolated (Othman, Ibrahim, Mohd, Mustafa, & Awang, 2006; Raina & Abraham, 2016). In a chemical profile of *K. galanga* rhizome volatile oils, 38 compounds comprised 96.4 to 98.9% of total oil contents, including trans-ethyl-p-methoxycinnamate (28.4–70.0%), trans-ethyl cinnamate (11.5–26.6%), pentadecane (6.0–16.5%),  $\delta$ -3-carene (0.1–6.5%), 1,8-cineole (0.2–5.2%) and borneol (1.0–2.4%) (Raina & Abraham, 2016). Other constituents include undecanone, isopropyl cinnamate, dicyclohexylpropane-dinitrile, dipentene dioxide, 9-hydroxy, 2-nonanone, 2,7-octadiene-1-yl acetate, ethyl cyclohexyl acetate, cis-11-tetradecenyl acetate, 2-heptadecanone, 4-methyl isopulegone, camphidine, trans,trans-octa-2, 4-dienyl acetate, 10-undecyn-1-ol, 3,7-dimethoxycoumarin, alpha pinene, camphene, cymene, alpha terpineol, alpha gurjunene, germacrenes, cadinenes, caryophyllenes, luteolin, and apigenin (Ling, Hoon, & Kian, 2009; Sutthanont et al., 2010; Raina & Abraham, 2016).

### 7.16.1 TOXICITY

No studies have linked *Kaempferia galanga* to mortality (Umar, Asmawi, Sadikun, Altaf, & Iqbal, 2011). Studies found that ethanolic extracts of *K. galanga* administered to rats resulted in central nervous system depression, reduced motor activity and respiration, loss of screen grip and analgesia in rats (25, 50, 100, and 800 mg/kg, respectively) (Ling, Hoon, & Kian, 2009; Kanjanapothi et al., 2004). A treatment of 25, 50, and 100 mg/kg over a 28-day period resulted in a slightly significant decreased lymphocyte count in male rats. Hexane fractions were not found to cause dermatological irritations in rats (Shanbhag et al., 2006) and rabbits (Kanjanapothi et al., 2004).

### 7.16.2 RHIZOME

Methanolic extract of *Kaempferia galanga* rhizomes revealed the presence of triterpenoids, alkaloids, flavonoids, carbohydrates, resins, and proteins (Rajendra, Magadam, Nadaf, Yashoda, & Manjula, 2011). Water extract of *K. galanga* rhizome revealed saponins, carbohydrates, and proteins present (Rajendra, Magadam, Nadaf, Yashoda, & Manjula, 2011). Petroleum ether extract and chloroform extract identified sterols, triterpenoids, and resins (Rajendra, Magadam, Nadaf, Yashoda, & Manjula, 2011). Chloroform extract also revealed the presence of flavonoids (Rajendra, Magadam, Nadaf, Yashoda, & Manjula, 2011). Tannins were not identified in any of these rhizome extracts (Rajendra, Magadam, Nadaf, Yashoda, & Manjula, 2011). The nutrient composition of *K. galanga* varies depending on production methods and inputs (Kavitha & Menon, 2013). For instance, soil management with application of sulfur and magnesium resulted in higher rhizome yields, while sulfur application resulted in higher oleoresin and essential oil contents (Kavitha & Menon, 2013).

Gas chromatography and mass spectroscopy analysis of *K. galanga* rhizome oil revealed that 95.5% of the oil was composed of 10 major compounds (Mohanty et al., 2011). These include ethyl-p-methoxy-cinnamate accounted for 59.5% of the detected compounds, followed by ethyl cinnamate, 3-carene, pentadecane, borneol, bornyl acetate, delta-selinene, camphor, alpha-piene, and imidazole 5-carbonylvinyl-4-nitro (Mohanty et al., 2011). Other sources report that *K. galanga* rhizome contains 2.4 to 3.9% essential oil, which is composed of up to 30% methyl-p-methoxycinnamate and approximately 25% ethyl cinnamate (Ibrahim, 1999).

## 7.17 VALUE ADDITIONS OF MEDICINAL AND AROMATIC PLANTS

The value additions of *Kaempferia galanga* include further processing of essential oils in cosmetic, skin care and diverse other products. Studies with specific data on the supply chains and value additions of *K. galanga* are lacking at the time of this review.

## 7.18 BIO-PROSPECTION OF MEDICINAL AND AROMATIC PLANTS

*Kaempferia galanga* holds prospects as an antifungal (Kochuthressia, Britto, & Jaseentha, 2012), antibacterial (Parvez, Khan, Islam, & Hasan, 2005;

Kochuthressia, Britto, & Jaseentha, 2012; Nillian et al., 2018; Hertiani, Pratiwi, Irianto, & Febriana, 2010; Dash, Nasrin, & Ali, 2014), anticarcinogenic (Srivastava et al., 2019; Kosuge et al., 1985; Amuamuta, Plengsuriyakarn, & Na-Bangchang, 2017; Jagadish, Raghu, Vinod, & Latha, 2010; Xue & Chen, 2002; Bagya, Rajashree, & Sam, 2011; Vimala, Norhanom, & Yadav, 1999; Yang, Ji, Feng, Yu, & Liu, 2018), and antioxidant (Chan et al., 2009; Sunitibala, Devala, Brojendro, Samarjit, & Punyarani, 2015). *K. galanga* also has potential as a pesticidal agent, and some herbicides have been developed and patented. Published literature on the bio-prospection of *K. galanga* was not found under this review.

## 7.19 COMMERCIAL PRODUCTS AVAILABLE

The most commonly available products of *Kaempferia galanga* are dried and sliced rhizomes for consumption. Rhizomes may be processed further into essential oil products. However, the oils are not regularly produced and are seldom available outside their country of origin (Arctander, 2017). Oils may be consumed directly or processed further into bath soaps, cosmetics, and perfumes (Kumar, 2014). *K. galanga* oil is registered under the European Chemical Agency (ECHA Number: 296-200-2). In the United States, *K. galanga* is registered under Safety Class 1 and Interaction Class A. There have been hundreds of patented applications for uses and products with *K. galanga* rhizomes, leaves, and active compounds.

## 7.20 TECHNOLOGY TRANSFER/PATENTS

There is a long tradition of cosmetic and skin care use of *Kaempferia galanga* in *Ayurvedic* preparations. The traditional uses of *K. galanga* have been adapted and patented as sunscreens to enhance UV absorbance. The Chinese patent CN101756831A (2010) is for a sunscreen, which combines *K. galanga* extract with glycerin, stearic acid, stearyl alcohol, glycerin monostereate, vitamin E acetic ester, aethylparabenum, butyl p-hydroxybenzoate, propyl p-hydroxybenzoate, butanediol, propanediol, potassium dydroxide, essence, and refined water. A similar patent exists in the United States (U.S.) (US20030124070A1), assigned to Avon Products Inc. Another recent Chinese patent application was filed in 2018 for skin care using *K. galanga* in a face mask that sterilizes, moisturizes, and whitens the skin, and removes spots and acne, based on traditional Chinese medicine (CN108403603A).

Another U.S. patent utilizes the compound, ethyl p-methoxycinnamate, from *K. galanga* rhizomes against skin irritations and discoloration (US20040166132A1; US6719964B1). A Russian patent utilizes kaempferol and other compounds of *K. galanga* extracts to increase expression of redox factors in human epidermal cells (RU2606856C2).

For other medicinal purposes, a recent Chinese patent for the pharmaceutical use of *K. galanga* to treat muscle disease and to improve muscular function (CN104411310B) was approved in 2018. In addition, another Chinese patent utilizes *K. galanga* to promote blood circulation and prevent pain (CN105797100B). There is also a patent for a *K. galanga*-based blood-activating, analgesic plasters (CN104225550B). *K. galanga* is one ingredient in a medicinal mixture used to treat cervical and lumbar diseases, as well as osteoproliferation (CN104435947B). A culinary application for *K. galanga* as a health food to improve immune defense has also been patented (CN103652922B).

*K. galanga* has also been patented for incorporation into cotton fabrics to improve their durability (CN106946863B). A South Korean patent uses *K. galanga* to control the growth of nematodes (KR100764482B1). Pending patent applications include obtaining phenolic compounds of *K. galanga* from post-fermented tea sources (CN109863159A). A search on Google Patents found 667 granted patents and 4,721 patent applications using the search term “*Kaempferia galanga*,” with a wide variety of medicinal, culinary, and other industrial uses and applications.

## KEYWORDS

- aromatic plants
- ethyl cinnamate
- ethyl-p-methoxy-cinnamate
- *Kaempferia galanga*
- kaempferol
- rhizome
- value additions
- Zingiberaceae



## REFERENCES

- Achuthan, C. R., & Padikkala, J., (1997). Hypolipidemic effect of *Alpinia galanga* (Rasna) and *Kaempferia galanga* (Kachoori). *Indian J. Clin. Biochem.*, 12(1), 55–58. <https://doi.org/10.1007/BF02867956>.
- Ali, M. S., Dash, P. R., & Nasrin, M., (2015). Study of sedative activity of different extracts of *Kaempferia galanga* in Swiss albino mice. *BMC Complement. Altern. Med.*, 15(158), 1–5. <https://doi.org/10.1186/s12906-015-0670-z>.
- Alibaba, (n.d.). *Premium Quality 100 Pure and Well Dried Sand Ginger Kaempferia Galanga*. [https://e12x12.fm.alibaba.com/product/60419867911-10938157/Premium\\_Quality\\_100\\_Pure\\_and\\_well\\_dried\\_Sand\\_Ginger\\_Kaempferia\\_Galanga\\_Kaempferia\\_galanga.html](https://e12x12.fm.alibaba.com/product/60419867911-10938157/Premium_Quality_100_Pure_and_well_dried_Sand_Ginger_Kaempferia_Galanga_Kaempferia_galanga.html) (accessed on 31 August 2023).
- Amuamuta, A., Plengsuriyakarn, T., & Na-Bangchang, K., (2017). Anticholangiocarcinoma activity and toxicity of the *Kaempferia galanga* Linn. rhizome ethanolic extract. *BMC Complement. Altern. Med.*, 17(213), 1–11. <https://doi.org/10.1186/s12906-017-1713-4>.
- Arctander, S., (2017). *Perfume and Flavor Materials of Natural Origin*. Lulu.com.
- Aroonrerk, N., & Kamkaen, N., (2009). Anti-inflammatory activity of *Quercus infectoria*, *Glycyrrhiza uralensis*, *Kaempferia galanga* and *Coptis chinensis*, the main components of Thai herbal remedies for aphthous ulcer. *J. Heal. Res.*, 23(1), 17–22.
- Atun, S., (2014). Phytochemical of *Kaempferia* plant and bioprospecting for cancer treatment. In: *Proceeding of International Conference on Research, Implementation and Education of Mathematics and Sciences*. Yogyakarta State University: Yogyakarta.
- Babitha, S., Shin, J. H., & Kim, E. K., (2009). Potential skin whitening agents of natural origin from South Asian region. *J. Soc. Cosmet. Sci. Korea*, 35(1), 1–9.
- Bagya, S. K., Rajashree, P. V., & Sam, K. G., (2011). Preliminary anticancer screening and standardization of some indigenous medicinal plants using cell-biology and molecular biotechnology based models. *Res. J. Med. Plant*, 5(6), 728–737. <https://doi.org/10.3923/rjmp.2011.728.737>.
- Bari, M. S., & Rahim, M. A., (2012). Economic evaluation and yield performance of some medicinal plants in coconut based multistoried agroforestry systems. *Agric.*, 10(1), 71–80.
- Bhatt, A., Kean, O. B., & Keng, C. L., (2012). Sucrose, benzylaminopurine and photoperiod effects on *in vitro* culture of *Kaempferia Galanga* Linn. *Plant Biosyst.*, 900–905. <https://doi.org/10.1080/11263504.2012.706238>.
- Bhattacharya, M., & Sen, A., (2013). *In vitro* regeneration of pathogen free *Kaempferia galanga* L. – A rare medicinal plant. *Res. Plant Biol.*, 3(3), 24–30.
- Chan, E. W. C., Lim, Y. Y., Wong, L. F., Lianto, F. S., Wong, S. K., Lim, K. K., Joe, C. E., & Lim, T. Y., (2008). Antioxidant and tyrosinase inhibition properties of leaves and rhizomes of ginger species. *Food Chem.*, 109(3), 477–483. <https://doi.org/10.1016/j.foodchem.2008.02.016>.
- Chan, E. W. C., Lim, Y. Y., Wong, S. K., Lim, K. K., Tan, S. P., Lianto, F. S., & Yong, M. Y., (2009). Effects of different drying methods on the antioxidant properties of leaves and tea of ginger species. *Food Chem.*, 113(1), 166–172. <https://doi.org/10.1016/j.foodchem.2008.07.090>.
- Chan, E. W. C., Lye, P. Y., Eng, S. Y., & Tan, Y. P., (2013). Antioxidant properties of herbs with enhancement effects of drying treatments: A synopsis. *Free Radicals Antioxidants*, 3(1), 2–6. <https://doi.org/10.1016/j.fra.2013.02.001>.

- Chandana, R., (2011). *Standardization of Good Agricultural Practices (GAP) in Kacholam (Kaempferia Galanga L.) for Yield and Quality*. College of Horticulture, Vellanikkara.
- Chirangini, P., Sinha, S. K., & Sharma, G. J., (2005). *In vitro* propagation and microrhizome induction in *Kaempferia galanga* Linn. and *K. Rotunda* Linn. *Indian J. Biotechnol.*, 4.
- Chithra, M., Martin, K. P., Sunandakumari, C., & Madhusoodanan, P. V., (2004). Protocol for rapid propagation, and to overcome delayed rhizome formation in field established *in vitro* derived plantlets of *Kaempferia galanga* L. *Sci. Hortic. (Amsterdam)*, 104(1), 113–120. <https://doi.org/10.1016/j.scienta.2004.08.014>.
- Chithra, M., Martin, K. P., Sunandakumari, C., & Madhusoodanan, P. V., (2005). Protocol for rapid propagation, and to overcome delayed rhizome formation in field established *in vitro* derived plantlets of *Kaempferia galanga* L. *Sci. Hortic. (Amsterdam)*, 104(1), 113–120. <https://doi.org/10.1016/j.scienta.2004.08.014>.
- Choochote, W., Kanjanapothi, D., Panthong, A., Taesotikul, T., Jitpakdi, A., Chaithong, U., & Pitasawat, B., (1999). Larvicidal, adulticidal and repellent effects of *Kaempferia galanga*. *Southeast Asian J. Trop. Med. Public Health*, 30(3), 470–476.
- Dake, G. N., & Manoj, P. S., (1995). Bacterial wilt of *Kaempferia galanga* L. caused by *Pseudomonas solanacearum* (Smith) smith. *J. Spices Aromat. Crop.*, 4(2).
- Dash, P. R., Nasrin, M., & Ali, M. S., (2014). *In vivo* cytotoxic and *in vitro* antibacterial activities of *Kaempferia galanga*. *J. Pharmacogn. Phytochem.*, 3(1), 172–177.
- Elshamy, A., Mohamed, T., Essa, A., Abd-ElGawad, M. A., Alqahtani, A., Shahat, A., Yoneyama, T., Farrag, A. R., Noji, M., El-Seedi, H., et al., (2019). Recent advances in *Kaempferia* phytochemistry and biological activity: A comprehensive review. *Nutrients*, 11(10), 1–33. <https://doi.org/10.3390/nu11102396>.
- Gangadharan, H., & Menon, V., (2003). Performance of Kacholam (*Kaempferia galanga*) ecotypes as influenced by variations in shade and preparatory cultivation. *J. Med. Aromat. Plant Sci.*, 25(4), 976–980.
- Geetha, S., Manjula, C., John, C., Minoos, D., Babu, K., & Ravindran, P., (1997). Micropropagation of *Kaempferia* spp. (*K. galanga* L. and *K. rotunda* L.). *J. Spices Aromat. Crop.*, 6(2), 129–135.
- He, Z. H., Yue, G. G. L., Lau, C. B. S., Ge, W., & But, P. P. H., (2012). Antiangiogenic effects and mechanisms of trans-ethyl p-methoxycinnamate from *Kaempferia galanga* L. *J. Agric. Food Chem.*, 60(45), 11309–11317. <https://doi.org/10.1021/jf304169j>.
- Hertiani, T., Pratiwi, S. U. T., Irianto, I. D. K., & Febriana, A., (2010). *Kaempferia galanga* L. rhizome as a potential dental plaque preventive agent. *Indones. J. Cancer Chemoprevention*, 1(1), 19–25. <https://doi.org/10.14499/indonesianjcanchemoprevliss1pp19-25>.
- Hirschhorn, H. H., (1983). Botanical remedies of the former Dutch East Indies (Indonesia). Part I: Eumycetes, Pteridophyta, Gymnospermae, Angiospermae (Monocotyledones only). *J. Ethnopharmacol.*, 7(2), 123–156. [https://doi.org/10.1016/0378-8741\(83\)90016-8](https://doi.org/10.1016/0378-8741(83)90016-8).
- Hong, T. K., Lee, J. K., Heo, J. W., Kim, S. I., Choi, D. R., & Ahn, Y. J., (2010). Toxicity of *Kaempferia galanga* rhizome-derived extract and steam distillate to *Meloidogyne incognita* juveniles and eggs, and their effects on *Lycopersicon esculentum* germination and growth. *Nematology*, 12(5), 775–782. <https://doi.org/10.1163/138855410X12628646276203>.
- Huang, L., Yagura, T., & Chen, S., (2008). Sedative activity of hexane extract of *Kaempferia galanga* L. and its active compounds. *J. Ethnopharmacol.*, 120(1), 123–125. <https://doi.org/10.1016/j.jep.2008.07.045>.
- Ibenthal, A., Laishram, J., Singh, C. D., & Toijam, R., (2012). *In-vitro* induction of multiple shoot and root from the rhizome of *Kaempferia galanga* L. *NeBIO*, 3(3), 46–50.

- Ibrahim, H., (1999). *Kaempferia* L. In: De Padua, L. S., Bunyaphratsara, N., & Lemmens, R. H. M., (eds.), *Plant Resources of South-East Asia: Medicinal and Poisonous Plants 1* (pp. 331–334). Prosea Foundation: Bogor, Indonesia.
- Indrayan, A. K., Kurian, A., Tyagi, P. K., Shatru, A., & Rathi, A. K., (2007). Comparative chemical study of two varieties of attractive medicinal plant *Kaempferia galanga* Linn. *Nat. Prod. Radiance*, 6(4), 327–333.
- International Trade Center, (2016). *Sustainable Sourcing: Markets for Certified Chinese Medicinal and Aromatic Plants*. International Trade Centre: Geneva, Switzerland.
- Jagadish, P. C., Raghu, C. H., Vinod, K. S., & Latha, K. P., (2010). Potent selective cytotoxic activity of *Kaempferia galanga* L. rhizome against cancer cell cultures. *Int. J. Pharma Bio Sci.*, 1(2), 105.
- Joshi, R. K., Kar, B., Mohanty, S., Subudhi, E., & Nayak, S., (2012). Molecular cloning, characterization, and expression analysis of resistance gene candidates in *Kaempferia galanga* L. *Mol. Biotechnol.*, 50(3), 200–210. <https://doi.org/10.1007/s12033-011-9430-6>.
- Joy, P. P., Thomas, J., Mathew, S., & Skaria, B. P., (1998). *Zingiberaceous Aromatic and Medicinal Plants*. Aromatic and Medicinal Plants Research Station.
- Kalpana, M., & Anbazhagan, M., (2009). *In vitro* production of *Kaempferia galanga* (L.) – an endangered medicinal plant. *J. Phytol.*, 1(1), 56–61.
- Kamaruddin, H. C., (2006). *Kaempferia galanga* L. In: *Penanaman Tumbuhan Ubatan & Beraroma* (pp. 8–13). MARDI: Serdang, Selangor.
- Kanakamanay, M. T., (2008). Induction of genetic variability in kacholam, *Kaempferia galanga* L. *Plant Mutat. Reports*, 2(1), 4–6.
- Kanjanapothi, D., Panthong, A., Lertprasertsuke, N., Taesotikul, T., Rujjanawate, C., Kaewpinit, D., Sudthayakorn, R., Choochote, W., Chaitong, U., Jitpakdi, A., et al., (2004). Toxicity of crude rhizome extract of *Kaempferia galanga* L. (Proh Hom). *J. Ethnopharmacol.*, 90(2, 3), 359–365. <https://doi.org/10.1016/j.jep.2003.10.020>.
- Kavitha, P. R., & Menon, M. V., (2013). Effect of potassium and secondary nutrients on the essential oil and oleoresin contents in kacholam (*Kaempferia galanga* L.). *J. Trop. Agric.*, 51(1, 2), 105–110.
- Keng, C. L., & Hing, T. W., (2004). *In vitro* propagation of *Zingiberaceae* species with medicinal properties. *J. Plant Biotechnol.*, 6(3), 181–188.
- Kochuthressia, K. P., Britto, S. J., & Jaseentha, M. O., (2012). *In vitro* multiplication of *Kaempferia galanga* L. An endangered species. *Int. Res. J. Biotechnol.*, 3(2), 27–31.
- Kosuge, T., Yokota, M., Sugiyama, K., Saito, M., Iwata, Y., Nakura, M., & Yamamoto, T., (1985). Studies on anticancer principles in Chinese medicines. II. cytotoxic principles in *Biota orientalis* (L.) Endl. and *Kaempferia galanga* L. *Chem. Pharm. Bull.*, 33(2). <https://doi.org/10.1248/cpb.33.5565>.
- Kumar, A., (2014). Physico-chemical and natural products investigations of essential oil from the rhizomes of *Kaempferia galanga* L. *Der Chem. Sin.*, 5(2), 91–94.
- Kumar, B. M., (2007). Coconut-based agroforestry for productive and protective benefits. In: Thampan, P. K., & Vasu, K. I., (eds.), *Coconut for Rural Welfare* (pp. 87–98). In: International Coconut Summit 2007. Kochi, India.
- Kumar, B. M., Kumar, S. S., & Fisher, R. F., (2005). Galangal growth and productivity related to light transmission in single-strata, multi-strata and “no-over-canopy” systems. *J. New Seeds*, 7(2), 111–126. [https://doi.org/10.1300/J153v07n02\\_06](https://doi.org/10.1300/J153v07n02_06).

- Kumar, K. M. P., Asish, G. R., Sabu, M., & Balachandran, I., (2013). Significance of ginger (*Zingiberaceae*) in Indian system of medicine – Ayurveda: An overview. *Anc. Sci. Life*, 32(4). <https://doi.org/10.4103/0257-7941.131989>.
- Kumar, N., Kader, A., Rangaswami, P., & Irulappan, (1997). *Spices, Plantation Crops, Medicinal and Aromatic Plants*. Oxford & IBH Publishing Co. Pvt. Ltd.: New Delhi.
- Labrooy, C. D., Abdullah, T. L., & Stanslas, J., (2018). Identification of ethnomedicinally important *Kaempferia* L. (*Zingiberaceae*) species based on morphological traits and suitable DNA Region. *Curr. Plant Biol.*, 14, 50–55. <https://doi.org/10.1016/j.cpb.2018.09.004>.
- Lakshmi, M., & Mythili, S., (2003). Somatic embryogenesis and plant regeneration from callus cultures of *Kaempferia galanga*. *J. Med. Aromat. Plant Sci.*, 25, 947–951.
- Lal, M., (2019). Bharamputra-1(IC0610826; INGR17081), an aromatic ginger (*Kaempferia galanga*) germplasm with high rhizome yield (10 Tones/Ha) and dry rhizome recovery. high essential oil. *Indian J. Plant Genet. Resour.*, 32(2), 284–285.
- Lal, M., Munda, S., Dutta, S., Baruah, J., & Pandey, S. K., (2017). Identification of the new high oil and rhizome yielding variety of *Kaempferia galanga* (Jor Lab K-1): A highly important indigenous medicinal plants of North East India. *J. Essent. Oil-Bearing Plants*, 20(5), 1275–1282. <https://doi.org/10.1080/0972060X.2017.1400405>.
- Li, D. M., Zhao, C. Y., & Liu, X. F., (2019). Complete chloroplast genome sequences of *Kaempferia galanga* and *Kaempferia elegans*: Molecular structures and comparative analysis. *Molecules*, 24(474). <https://doi.org/10.3390/molecules24030474>.
- Ling, K. H., Hoon, T. C., & Kian, C. T., (2009). *Guide To Medicinal Plants, A: An Illustrated Scientific and Medicinal Approach*. World Scientific.
- Maheswarappa, H. P., Nanjappa, H. V., & Hegde, M. R., (2000b). Influence of agronomic practices on growth, productivity, and quality of galangal (*Kaempferia galanga* L.) grown as intercrop in coconut garden. *J. Plant. Crop.*, 28(1), 72–81.
- Maheswarappa, H. P., Nanjappa, H. V., & Hegde, M. R., (1999). Influence of planting material, plant population and organic manures on galangal (*Kaempferia galanga* L.) grown as intercrop in coconut (*Cocos nucifera* L.) garden. *J. Spices Aromat. Crop.*, 8(1), 35–40.
- Maheswarappa, H. P., Nanjappa, H. V., & Hegde, M. R., (2000a). Dry-matter production and accumulation in different parts of galangal (*Kaempferia galanga*) as influenced by agronomic practices when grown as an intercrop in coconut garden. *Indian J. Agron.*, 45(4), 698–706.
- Maheswarappa, H., Hegde, M. R., & Nanjappa, H., (1998). Kacholam (*Kaempferia galanga* L.) – a potential medicinal-cum-aromatic crop for coconut gardens. *Indian Coconut J.*, 29(5), 4–5.
- Maheswarappa, H., Nanjappa, H., Hegde, M., & Biddappa, C., (2000). Nutrient content and uptake by galangal (*Kaempferia galanga* L.) as influenced by agronomic practices as intercrop in coconut (*Cocos nucifera* L.) garden. *J. Spices Aromat. Crop.*, 9(1), 65–68.
- Mohanty, S., Parida, R., Singh, S., Joshi, R. K., Subudhi, E., & Nayak, S., (2011). Biochemical and molecular profiling of micropropagated and conventionally grown *Kaempferia galanga*. *Plant Cell. Tissue Organ Cult.*, 106(1), 39–46. <https://doi.org/10.1007/s11240-010-9891-5>.
- Muhammad, Z., & Nataamijaya, A. G., (2006). Ginger (*Kaempferia galanga* L) supplementation to shorten broiler production period. *Anim. Prod.*, 8(1).
- Munda, S., Saikia, P., & Lal, M., (2018). Chemical composition and biological activity of essential oil of *Kaempferia galanga*: A review. *J. Essent. Oil Res.*, 30(5), 303–308. <https://doi.org/10.1080/10412905.2018.1486240>.

- Nair, G. S., Sudhadevi, P. K., & Kurian, A., (1989). Introduction of medicinal and aromatic plants as intercrops in coconut plantations. In: Raychaudhuri, S. P., (ed.), *Advances in Medicinal, Aromatic and Spice Crops* (pp. 163–165). Today and Tomorrow's Printers and Publishers: New Delhi.
- National Medicinal Plants Board, (2007). Key findings and recommendations. In: Ved, D., & Goraya, G., (eds.), *Demand and Supply of Medicinal Plants in India* (pp. 101–134). National Medicinal Plants Board & Foundation for Revitalization of Local Health Traditions: New Delhi & Bangalore.
- National Medicinal Plants Board, (2007). Production and supply of botanicals. In: Ved, D., & Goraya, G., (eds.), *Demand and Supply of Medicinal Plants in India* (pp. 53–67) National Medicinal Plants Board and the Foundation for Revitalization of Local Health Traditions: New Delhi.
- Naturalis Biodiversity Center, (n.d.). *Species Details: Kaempferia Galanga L.* <http://www.catalogueoflife.org/col/details/species/id/7575edb2bef87146353528aa7f34e2f8> (accessed on 31 August 2023).
- Nillian, E., Mathialagan, M., Benjamin, P. G., Lihan, S., & Bebey, G., (2018). Antimicrobial activity of *Kaempferia galanga* rhizome against biofilm of vibrio cholerae outbreak from Limbang Sarawak. *J. Adv. Res. Appl. Sci. Eng. Technol.*, 12(1), 24–31.
- Noro, T., Miyase, T., Kuroyanagi, M., Ueno, A., & Fukushima, S., (1983). Monoamine oxidase inhibitor from the rhizomes of *Kaempferia galanga* L. *Chem. Pharm. Bull.*, 31, 2708–2711. <https://doi.org/10.1248/cpb.31.2708>.
- Othman, R., Ibrahim, H., Mohd, M. A., Awang, K., Gilani, A. U. H., & Mustafa, M. R., (2002). Vasorelaxant effects of ethyl cinnamate isolated from *Kaempferia galanga* on smooth muscles of the rat aorta. *Planta Med.*, 68(7), 655–657. <https://doi.org/10.1055/s-2002-32900>.
- Othman, R., Ibrahim, H., Mohd, M. A., Mustafa, M. R., & Awang, K., (2006). Bioassay-guided isolation of a vasorelaxant active compound from *Kaempferia galanga* L. *Phytomedicine*, 13(1, 2), 61–66. <https://doi.org/10.1016/j.phymed.2004.07.004>.
- Parida, R., Mohanty, S., & Nayak, S., (2019). Population structure of *Kaempferia galanga* L. from Eastern India. *Int. J. Pharm. Pharm. Sci.*, 11(3), 62–65. <https://doi.org/10.22159/ijpps.2019v11i3.31226>.
- Parida, R., Mohanty, S., Kuanar, A., & Nayak, S., (2010). Rapid multiplication and *in vitro* production of leaf biomass in *Kaempferia galanga* through tissue culture. *Electron. J. Biotechnol.*, 13(4). <https://doi.org/10.2225/vol13-issue4-fulltext-12>.
- Parvez, M. A., Khan, M. M. H., Islam, M. Z., & Hasan, S. M., (2005). Antimicrobial activities of the petroleum ether, methanol, and acetone extracts of *Kaempferia galanga* L. Rhizome. *J. Life Earth Sci.*, 1(1), 25–29.
- Prathanturug, S., Apichartbutra, T., Chuakul, W., & Saralamp, P., (2007). Mass propagation of *Kaempferia parviflora* wall. Ex baker by *in vitro* regeneration. *J. Hortic. Sci. Biotechnol.*, 82(2), 179–183. <https://doi.org/10.1080/14620316.2007.11512217>.
- Preetha, S. T., Sudarsanan, H. A., & Krishnan, P. N., (2016). A comprehensive review of *Kaempferia galanga* L. (*Zingiberaceae*): A high sought medicinal plant in tropical Asia. *J. Med. Plants Stud.*, 4(3), 270–276.
- Priya, K., (2005). *Major Diseases of Kacholam (Kaempferia galanga L.) and Their Management*. College of Horticulture, Vellanikkara.
- Rahman, M. M., Amin, M. N., Ahamed, T., Ahmad, S., Habib, A., Ahmed, R., Ahmed, M. B., & Ali, M. R., (2005). *In vitro* rapid propagation of black thorn (*Kaempferia galanga* L.): A

- rare medicinal and aromatic plant of Bangladesh. *J. Biol. Sci.*, 5(3), 300–304. <https://doi.org/10.3923/jbs.2005.300.304>.
- Rahman, M., Amin, M., Ahamed, T., Ali, M., & Habib, A., (2004). Efficient plant regeneration through somatic embryogenesis from leaf base-derived callus of *Kaempferia galanga* L. *Asian J. Plant Sci.*, 3(6), 675–678.
- Raina, A. P., & Abraham, Z., (2016). Chemical profiling of essential oil of *Kaempferia galanga* L. germplasm from India. *J. Essent. Oil Res.*, 28(1), 29–34. <https://doi.org/10.1080/10412905.2015.1077165>.
- Raina, A. P., Abraham, Z., & Sivaraj, N., (2015). Diversity analysis of *Kaempferia galanga* L. germplasm from South India using DIVA-GIS approach. *Ind. Crops Prod.*, 69, 433–439. <https://doi.org/10.1016/j.indcrop.2015.02.052>.
- Rajasekharan, P. E., Abdul, K. V. K., Ravish, B. S., & Mini, S., (2017). ISSR analysis reveals low genetic diversity and high genetic differentiation in *Kaempferia galanga* L. in South India populations. *Indian J. Biotechnol.*, 16(3), 341–345.
- Rajasekharan, P. E., Ambika, R., & Ganeshan, S., (2009). *In vitro* regeneration and conservation of *Kaempferia galanga*. *ICFAI J. Genet. Evol.*
- Rajendra, C. E., Magadum, G. S., Nadaf, M. A., Yashoda, S. V., & Manjula, M., (2011). Phytochemical screening of the rhizome of *Kaempferia galanga*. *Int. J. Pharmacogn. Phytochem. Res.*, 3(3), 61–63.
- Riditid, W., Sae-Wong, C., Reanmongkol, W., & Wongnawa, M., (2008). Antinociceptive activity of the methanolic extract of *Kaempferia galanga* Linn. in experimental animals. *J. Ethnopharmacol.*, 118(2), 225–230.
- Riptanti, E. W., Qonita, A., & Fajarningsih, R. U., (2018). Potentials of sustainable development of medicinal plants in wonogiri regency of central java province of Indonesia. *Bulg. J. Agric. Sci.*, 24(5), 742–749.
- RMUS, S., BMAC, K., WTPSK, S., & GC, J., (2017). *In vitro* propagation of *Kaempferia galanga* (*Zingiberaceae*) and comparison of larvicidal activity and phytochemical identities of rhizomes of tissue cultured and naturally grown plants. *J. Appl. Biotechnol. Bioeng.*, 2(4), 1–7. <https://doi.org/10.15406/jabb.2017.02.00040>.
- Sahoo, S., Parida, R., Singh, S., Padhy, R. N., & Nayak, S., (2014). Evaluation of yield, quality and antioxidant activity of essential oil of *in vitro* propagated *Kaempferia galanga* Linn. *J. Acute Dis.*, 124–130. [https://doi.org/10.1016/s2221-6189\(14\)60028-7](https://doi.org/10.1016/s2221-6189(14)60028-7).
- Sass, C., Iles, W. J. D., Barrett, C. F., Smith, S. Y., & Specht, C. D., (2016). Revisiting the *Zingiberales*: Using multiplexed exon capture to resolve ancient and recent phylogenetic splits in a charismatic plant lineage. *PeerJ*, 4(e1584). <https://doi.org/10.7717/peerj.1584>.
- Schwabl, H., & Vennos, C., (2015). From medical tradition to traditional medicine: A Tibetan formula in the European framework. *J. Ethnopharmacol.*, 167, 108–114. <https://doi.org/10.1016/j.jep.2014.10.033>.
- Setiarso, P., Rusijono, R., Samik, S., & Kusumawati, N., (2018). The production and characterization of *Kaempferia galanga* L. N-based herb powder: Blanching and drying procedure influence on proximate, metal, and microbial contamination. In: *Proceedings of the Seminar Nasional Kimia – National Seminar on Chemistry (SNK 2018)*. <https://doi.org/10.2991/snk-18.2018.12>.
- Shanbhag, T. V., Chandrakala, S., Sachidananda, A., Kurady, B. L., Smita, S., & Ganesh, S., (2006). Wound healing activity of alcoholic extract of *Kaempferia galanga* in Wistar rats. *Indian J. Physiol. Pharmacol.*, 50(4), 384–390.

- Shirin, F., Kumar, S., & Mishra, Y., (2000). *In vitro* plantlet production system for *Kaempferia galanga*, a rare Indian medicinal herb. *Plant Cell. Tissue Organ Cult.*, 63(3), 193–197. <https://doi.org/10.1023/A:1010635920518>.
- Sirirugsa, P., (1997). Thai *Zingiberaceae*: Species diversity and their uses. In: *International Conference on Biodiversity and Bioresources: Conservation and Utilization*. Phuket, Thailand. <https://doi.org/URL: http://www.iupac.org/symposia/proceedings/phuket97/sirirugsa.html> (accessed on 31 August 2023).
- Sivarajan, V., & Balachandran, I., (1994). *Ayurvedic Drugs and Their Plant Sources*. Oxford and IBH Publishing: New Delhi.
- Srivastava, N., Ranjana, Singh, S., Gupta, A. C., Shanker, K., Bawankule, D. U., & Luqman, S., (2019). Aromatic ginger (*Kaempferia Galanga* L.) extracts with ameliorative and protective potential as a functional food, beyond its flavor and nutritional benefits. *Toxicol. Reports*, 6, 521–528. <https://doi.org/10.1016/j.toxrep.2019.05.014>.
- Sulaiman, M. R., Zakaria, Z. A., Daud, I. A., Ng, F. N., Ng, Y. C., & Hidayat, M. T., (2008). Antinociceptive and anti-inflammatory activities of the aqueous extract of *Kaempferia galanga* leaves in animal models. *J. Nat. Med.*, 62(2), 221–227. <https://doi.org/10.1007/s11418-007-0210-3>.
- Sunitibala, D. H., Devala, D. K., Brojendro, S. S., Samarjit, S. N., & Punyarani, K., (2015). Evaluation of genetic relationships and chemical assay of *Kaempferia galanga* L. cultivars found in Manipur, North-East India. *Int. J. Recent Sci. Res.*, 6(6), 4366–4373.
- Sutthanont, N., Choochote, W., Tuetun, B., Junkum, A., Jitpakdi, A., Chaithong, U., Riyong, D., & Pitasawat, B., (2010). Chemical composition and larvicidal activity of edible plant-derived essential oils against the pyrethroid-susceptible and -resistant strains of aedes aegypti (*Diptera: Culicidae*). *J. Vector Ecol.*, 35(1), 106–115. <https://doi.org/10.1111/j.1948-7134.2010.00066.x>.
- Swapna, T. S., Binitha, M., & Manju, T. S., (2004). *In vitro* multiplication in *Kaempferia galanga* Linn. *Appl. Biochem. Biotechnol.*, 118(1–3), 233–241. <https://doi.org/10.1385/ABAB:118:1-3:233>.
- Techaprasan, J., Klinbunga, S., Ngamriabsakul, C., & Jenjittikul, T., (2010). Genetic variation of *Kaempferia* (*Zingiberaceae*) in Thailand based on chloroplast DNA (Psba-Trnh and Peta-Psbj) sequences. *Genet. Mol. Res.*, 9(4), 1957–1973. <https://doi.org/10.4238/vol9-4gmr873>.
- Tewtrakul, S., Yuenyongsawad, S., Kummee, S., & Atsawajaruwan, L., (2005). Chemical components and biological activities of volatile oil of *Kaempferia galanga* Linn. *J. Sci. Technol.*, 27(2), 503–507.
- Thakur, N. S., Attar, S. K., & Chauhan, R. S., (2017). Horti-medicinal agroforestry systems: A potential land use for commercial cultivation of medicinal and aromatic plants. In: *Agroforestry for Increased Production and Livelihood Security in India* (pp. 163–184). New India Publishing Agency: New Delhi.
- TianZhu, Z., Yong, Z., FuWei, Z., MeiYing, H., & QunFang, W., (2010). Isolation and identification of nematicide component from *Kaempferia galanga* L. *Acta Bot. Boreali-Occidentalia Sin.*, 30(12), 2524–2529.
- Umar, M. I., Asmawi, M. Z. B., Sadikun, A., Altaf, R., & Iqbal, M. A., (2011). Phytochemistry and medicinal properties of *Kaempferia galanga* L. (*Zingiberaceae*) extracts. *African J. Pharm. Pharmacol.*, 5(14), 1638–1647. <https://doi.org/10.5897/AJPP11.388>.
- Umar, M. I., Asmawi, M. Z., Sadikun, A., Atangwho, I. J., Yam, M. F., Altaf, R., & Ahmed, A., (2012). Bioactivity-guided isolation of ethyl-p-methoxycinnamate, an anti-inflammatory

- constituent, from *Kaempferia galanga* L. extracts. *Molecules*, 17(7), 8720–8734. <https://doi.org/10.3390/molecules17078720>.
- Vimala, S., Norhanom, A. W., & Yadav, M., (1999). Anti-tumor promoter activity in Malaysian ginger rhizomes used in traditional medicine. *Br. J. Cancer*, 80(1, 2), 110–116. <https://doi.org/10.1038/sj.bjc.6690329>.
- Vincent, K. A., Bejoy, M., Hariharan, M., & Mathew, M., (1991). Plantlet regeneration from callus cultures of *Kaempferia galanga* Linn.-a medicinal plant. *Indian J. Plant Physiol.*, 34(4), 396–400.
- Vincent, K. A., Mathew, K. M., & Hariharan, M., (1992). Micropropagation of *Kaempferia galanga* L. – a medicinal plant. *Plant Cell. Tissue Organ Cult.*, 28(2), 229–230. <https://doi.org/10.1007/BF00055522>.
- Vittalrao, A. M., Shanbhag, T., Meena, K. K., Bairy, K. L., & Shenoy, S., (2011). Evaluation of anti-inflammatory and analgesic activities of alcoholic extract of *Kaempferia galanga* in rats. *Indian J. Physiol. Pharmacol.*, 55(1), 13–24.
- Wijekoon, K. M. R., & Senarath, W. T. P. S., (2006). *In vitro* propagation of *Kaempferia galanga* (L). *Proc. Int. For. Environ. Symp.*, 26, 27. <https://doi.org/10.31357/fesympo.v0i0.1731>.
- Wood, T., (1991). Biogeography and the evolution of the *Zingiberaceae*. In: *Zingiberaceae Workshop, Prince of Songkla University* (pp. 6, 7). Hat Yai, Thailand.
- Xue, Y., & Chen, H., (2002). Study on the anticarcinogenic effects of three compounds in *Kaempferia galanga* L. *Wei Sheng Yan Jiu (Journal Hyg. Res.)*, 31(4), 247–248.
- Yang, X., Ji, H., Feng, Y., Yu, J., & Liu, A., (2018). Structural characterization and antitumor activity of polysaccharides from *Kaempferia galanga* L. *Oxid. Med. Cell. Longev.* <https://doi.org/10.1155/2018/9579262>.
- YueYe, D., QunFang, W., TianZhu, Z., MeiYing, H., & FuWei, Z., (2011). Effect of *Kaempferia galanga* L. on the development of *Meloidogyne incongnita*. *J. Northwest A F Univ.*, 39(12), 134–138.



## CHAPTER 8

---

# *Lavandula* spp. (Lavender): A Herb More Than Just a Relaxing Scent

MOUMITA MALAKAR

*Assistant Professor, Department of Horticulture,  
Central University of Tamil Nadu, Neelakudy, Thiruvarur,  
Tamil Nadu, India*

---

### ABSTRACT

*Lavandula*, belongs to the family Lamiaceae, is perennial, sub-shrub or shrub in nature and contains 28 species. The distribution of this aromatic herb ranges from North temperate to tropical regions of old world. Generally, three species of lavender viz. *L. officinalis* Mill. (True Lavender), *L. latifolia* Medic (Spike Lavender) and *L. hybrida* Reverchan (Lavandin; *L. officinalis* x *L. latifolia*) are in cultivation throughout the world especially in Europe and Mediterranean region while out of these only first two are popularly cultivated in India. These three species are known for their outstanding potential for the extraction of essential oil (EO). Since time immemorial plant extracts including essential oils have utilized for therapeutic purpose and too evinced to have multitudinous biological activities, anti-bacterial, and anti-fungal activities. The EOs derived from lavender are rich in wide range of phytoconstituents (~100) which secured their position for aromatherapy. The major constituents of its EOs are caryophyllene (8%), linalool (20–35%), tannins (5–10%) and linalyl acetate (30–55%). The meagre quantity of esters, oxides, ketones, cineole, camphor, sesquiterpenoids, beta-cimene, limonene, caproic acid, p-vinylguaiacol, methanecarboxylic acid, dimethylamin, cyclopropyl, N,N-dimethyl methanesulfonamide, cyclopropyl carbonyl-D-2-methyl ether, melitoti, herniarine, heptanoic acid, acetic acid, pentadecanoic acid, propane chemicals are also evident in lavender EOs.

The percentage of phyto-chemicals are species dependent. Sequence-related amplified polymorphism (SRAP) markers are potent enough among other available molecular markers to study the genetic relatedness of lavender species at intra and inter-specific level.

## 8.1 INTRODUCTION

Lavender (*Lavendula* sp.) synonymously known as ‘light shade of purple’ is securing its position from ancient era and well-known for its uses for a vital aromatic ingredient since the foundation of human civilization. It contains 47 species, reside to the family Lamiaceae. Lavender has gained huge popularity in aromatic and medicinal field for their usage of their ingredients in perfumes, essential oils and variety of personal care products. On the other hand, the delicate foliage and distinct fragrance of its flowers make it a mandatory garden item. The genus *Lavandula*, means ‘to wash’ in Greek. The antiseptic and medicinal properties of lavender also used as used as disinfectants, fresheners, and laundry and bath additives. > 20 commercially vital lavender varieties need different atmospheric conditions and cultural practices too. Key limiting factors for commercial cultivation of lavender are low humidity, low winter temperatures, poorly drained soils. According to Ernst (2017), owing to rapidly increasing agrotourism enterprises, it is cultivated as ‘Niche’ crop in Kentucky farms.

This crop is native to old world. In Cape Verde, Canary Islands, Mediterranean region, Northern, and Eastern Africa, South-West Asia and South-East India the existence of lavender is evident (Retrieved from: <https://www.hgtv.com/outdoors/flowers-and-plants/houseplants/mona-lavender>). Soil with moderate fertility (e.g., rocky soil) is well suited for its growing. It prefers basically coastal climate but could also withstand chilling temperature (for example *L. angustifolia* var. ‘Grosso’ and *L. x intermedia* are winter hardy crop and thrive well throughout US countries). Wide range of Gulf countries like British Isles, Ukraine (especially surrounding areas of Black Sea), Japan, Argentina, Brazil, and East Africa are successfully producing lavender at commercial level owing to the adaptability of some lavender species and cultivars (*L. angustifolia* [English lavender]) at high water level condition. Some other places like Lake Champlain (in New York), Southern part of Lake Ontario, Illinois, Northern Nevada, Idaho, and Minnesota also producing lavender successfully although the growth patterns may affect due to location-based microclimate to some extent. In nutshell, elevation, topography, and degree of low temperature are 3 key factors influence lavender farming.

Other factors like level of elevation, mulching pattern and its thickness, drainage facilities, etc., are crucial for plant survival (Aam, 2016). Beyond its use as culinary herbs and for EO extraction, it is also used as a garden component in temperate countries (Retrieved from: <http://www.missouribotanicalgarden.org/PlantFinder/PlantFinderDetails.aspx?kempercode=j560>). Its health benefits, endorsed by so many researchers, without any adverse effects also paved their position in ethnomedicine and cosmetics industry (Retrieved from: “Lavender” [<https://www.drugs.com/npp/lavender.html>]; <https://www.nccih.nih.gov/health/lavender>).

By habit, lavender is a perennial herb to sub-shrub (Upson & Andrews, 2004). Leaf morphology is simple to pinnately toothed or sometimes pinnately compound and dissected also. Actually, leaf shape is species specific. Leaves surface covered by fine hairs or indumentum hold essential oils (Upson & Andrews, 2004). Flowers are borne in whorls, spike inflorescence often branched in some species. Bracts may be colored at the apex. Bloom colors range from blue–violet or lilac, sometimes blackish purple or yellowish. Tubular calyx and corolla are its taxonomical features. Corolla is 5 lobed (upper lip sometimes cleft while lower lip has 2 clefts) (Upson & Andrews, 2004; Bailey, 1949). Flowering spines of *L. officinalis* (known as ‘Genuine lavender’) are employed for production of highly fragrant lavender oil which has great demand in flavoring, perfumery, cosmetics, and soap industries. The reason of huge requirement of its oil is its medicinal (antiseptic and bactericidal) properties. According to Shahl & Kumar (2000), at CIMAP farm, Pulwama, Kashmir, high oil yielding lavender flowers (oil content ranges from 1–1.2%) are produced, in fact Kashmir is world famous for the production of international standard lavender EO may be due to the conducive agro-climatic condition and developed agro-technology. Linalool, 1,8-cineole, B-ocimene, linalyl acetate, terpinene-4-ol and camphor – are key chemical ingredients of lavender EO but their relative amount usually varies according to the species (Cavanagh & Wilkinsn, 2002). *L. angustifolia* derived EO (by steam distillation) majorly contains linalool (3,7-dimethyl-octa-1,6-dien-3-ol), linalyl acetate (3,7-dimethyl-1,6-octadien-3yl acetate), 1,8-cineole, lavandulol, lavandulyl acetate and camphor. Many authors (Cavanagh & Wilkinsn, 2002; Prashar et al., 2004) reported that linalyl acetate (51%) and linalool (35%) are the chief components of lavender oil (as measured by Gas Chromatography and Gas Chromatography-linked FTIR) while these 2 components are hugely used in aromatherapy.

The use of lavender oil for its fragrance is well known whereas for having medicinal properties it is also used by topical application in aromatherapy

(Sarkic & Stappen, 2018; Groom, 1997). Body massage therapy using this oil reduces stress and cause total body and mental relaxation both (Fismer & Pilkington, 2012; Sarkic & Stappen, 2018). Lavender oil capsule are often prescribed by medical practitioners as anxiety medication (Retrieved from: <https://compendium.ch/product/1354538-laitea-kaps-80-mg>; <https://compendium.ch/fr/Product/Index/1321709-lasea-kaps-80-mg>) since its evident that it may decrease the anxiety up to sub-threshold level (Moler et al., 2019). Its oil is also used as a solvent component in oil painting (Ward, 2008).

## 8.2 HISTORICAL USES

In Mediterranean, Middle East and India lavender was first spotted around 2,500 years ago. Lavender word comes from the Latin '*lavare*' meaning 'to wash.' It was earlier known as 'Lavender Nardus' in Greece but later popular as 'Nard' which goes to the name of Syrian city Naarda. Its famous for its alluring fragrance and multitudinous uses like to scent baths, beds, clothes, and even hair on one hand and for medicinal properties on other hand. It is cultivated across the world counting Europe, Australia, New Zealand, North, and South America.

Versatile usages of lavender in diversified sectors (like perfume, cosmetic, and medicine industries along with household domain since antiquity) make it a mandatorily cultivable crop. Barring this, Vokou (1993) reported that the treatment using lavender extracts could effectively inhibit potato sprouting during the storage. Hence, it can substitute other chemical treatments. Bioactive constituents of its extracts are potent enough to control insects and pests (Sharma et al., 1992). Buchbauer et al. (1992) studied in Austria on the sedative impacts of lavender EOs. They found notable impact after inhalation. Presently, most of the lavender value-added products contain aromatic ingredients are chiefly used for essential oil production.

Since antiquity, the involvement of lavender in traditional medicine is known. Dioscorides, a Greek Naturalist also scripted the medicinal benefits of lavender during 1<sup>st</sup> century A.D. For Greeks and Romans, it was the preferred component in herbal baths, for Egyptian lavender perfume and nense sticks were most favorite. As aphrodisiac it was well liked during Middle Ages while lavender water was an emblem of purity, it supposed to elevate one's righteousness. The insecticidal properties of lavender extract prevent linen spoilage caused by moths, hence, in turn people get influenced to use it as disinfectant and deodorant. In ancient times, lavender was a mandatory component for 'White Flower Oil' (commonly known as 'Cure

All' medicinal oil) and 'Smelling Salt' in China. Apart from these uses, its efficacy to tame animals, to embalm corpses, to repel mosquitoes, and also as snuffing material and as an ingredient in lacquers and varnishes had been proved since earlier. In historical times also, in variety of culinary items (like flavored vinegars, salads, jellies, etc.) it was used. To heal nervous palpitations, toothaches, sore joints, hysteria, chronic headache, cold, and coughs, apoplexy, its potency was peremptorily noticeable. Romans believed that nest of asp (a venomous viper) in lavender bushes enhance its value and indicate its judicious use. Culpeper (1652) revealed that to get rid of frequent fainting, swooning, abnormal heartbeats, palpitations, and choke throat, 2 spoonfuls of lavender flower derived water is sufficient. Use of different plant parts of lavender as poultice could aid to protect against some intense infections caused by biting of serpents, mad dogs and other venomous creatures (Sturdivant & Blakley, 1999). Dehydrated leaves and seeds of lavender also have potential to heal severe hysteria.

### **8.3 AREA AND PRODUCTION**

Lavender cultivation basically flourished in Bulgaria, France, UK, Spain, China, Russia, Italy, Morocco, Yugoslavia, Hungary, Romania, Poland, Tukey, Ukraine, Moldova, South Africa and USA (Grebenicharski, 2016; Stanev et al., 2016). Barring these countries lavender is also cultivated successfully in Western and Eastern Cape, Kwa-Zulu-natal, Gauteng, Mpumalanga, and Limpopo provinces to have identical weather condition like of Mediterranean climate. Based on location, management practices and cultivar, yield of flowers and other value-added products actually varies, as for example the yield of true lavender flowers in South Africa usually range from 8–30 kg/ha while 40–220 kg/ha and 500–1,000 kg/ha of essential oil (lavandin) and dried flower stems, respectively found highly profitable for grass-root level producers.

According to the global statistics of lavender oil production, the ratio of lavender to lavandin is 1:5 which denotes the production of quality lavender oil is around 200 metric tons/year globally. Habit of lavender plants usually affect the yield. It has found that more robust plants contain more lavandin oil (may be >1,000 metric tons/year). Lavandin oil is much cheaper as compared to lavender oil. France is the center of true lavender cultivation essential for perfume production. Along with Spain, France, Italy, the Balkan Peninsula, Australia, and Tasmania, Bulgaria is also an emerging country

for lavandin production now-a-days. Cooler and higher altitude is preferred place for lavender and lavandin production whereas warm and lower regions found suitable for spike lavender. Global production of spike lavender oil is 150–200 tons/annum and Spain contribute at least 30% of total production as it is the key producer of spike lavender while throughout the Mediterranean areas this type of lavender grows wildly.

Production of essential oil of lavender in India (up to year 2011) was 2 m. tones. Currently, India imports 42 tons of Lavender oil worth Rs. 18 million per annum (Stanev et al., 2016). In, 1957, Sir Col. R. N. Chopra introduced this plant in Kashmir valley (Handa et al., 1957). However, in India lavender cultivation and its oil production are not satisfactory. It was systemically cultivated at CIMAP (Central Institute of Medicinal and Aromatic Plants). Consequently, the total area, in Kashmir, under lavender cultivation is 100 hec (Shawl, 2000; Farooqi et al., 1996; Handa et al., 1957; Guenther, 1972; Lawrence, 1985). The grade of oil produced at CIMAP meets the global standard and secures a steady supply to the perfumery industry.

Among 30 different flowering species of *Lavandula*, 3 namely *L. angustifolia* Mill. (Lavender), *L. latifolia* L. (Spike lavender) and *L. angustifolia* x *L. latifolia* ‘Lavandin’ (a sterile hybrid) are the mainstream cultivated species (Lesage-Meessen et al., 2015 and Lis-Balchin, 2002). Bulgaria, France, UK, China, Spain, and others are key lavender producing countries. Bulgaria ranks top in the world for producing (occupied > 6,000 ha. of land for wide range of lavender varieties) high quality and quantity lavender oil as compared to France (Stanev et al., 2016). ‘Lavandin’ is mainly cultivated in France securing alone 90% of the total production of lavandin oil. Spain concentrates on cultivation and production of essential oils from exclusively *Lavandula latifolia*. Commercial usefulness (like pharmaceuticals, cosmetics, household products and perfumes) of both lavandin and lavender oil are highly significant (Lesage-Meessen et al., 2015; Cavanagh & Wilkinson, 2005) but the former one is of superior quality and sold at 3–5 times higher price than the latter one. Furthermore, in emerging field of aromatherapy, lavender oil is considered as a major component owing to its great impact for anxiety, insomnia, and hair loss treatment (Cavanagh & Wilkinson, 2002; Kashani et al., 2011; Soltani et al., 2013; Lis-Balchin & Hart, 1999; Sienkiewicz et al., 2011). All aforementioned quality attributes facilitate the popularity of lavender as medicinal, ornamental, and aromatic plant. It is evident from historic literature that Konstantin Malkov popular agronomist and founder of agricultural science in 1903 first introduce lavender in Bulgaria while later Bulgaria focused only on common lavender for commercial cultivation.

After a decade in 1925 Konstantin Georgiev re-initiated the cultivation of existing bushes of lavender. According to Georgiev (1964), 1<sup>st</sup> lavender plantation was taken place at Kazanlak and Karlovo while after few years' lavender plantation spread rapidly in Bulgaria after procuring seeds and planting materials from England and France. Since that period, Bulgaria is cultivating lavender successfully, but shrinkage of open spaces are the chief limiting factors now-a-days for its wide cultivation.

### **8.3.1 21<sup>ST</sup> CENTURY DEVELOPMENTS OF LAVENDER CULTIVATION IN BULGARIA**

More than 7,000 ha. of land had been found since 20<sup>th</sup> century under lavender plantation but further magnificent popularization and enhancement was evinced during early of 70's. The *in-situ* state distillery units basically carry out the distillation procedure of lavender oil followed by further export. During 1990s the dwindling condition of lavender cultivation and its essential oil distillation industry in Bulgaria yielded a major impact on agricultural sector. During this transition period any renovation of the existing lavender industry and fresh establishment of new lavender plantations hadn't made those results in manifold deterioration of quality lavender production and chances of formation of new plantations (Figure 8.1) (Stanev et al., 2016). This dwindling condition invited privatization of many EO distillation units. Early of 21<sup>st</sup> century showed the significant recovery rate of Bulgarian fiscal condition hugely dependent on lavender based essential oil production. Furthermore, substantial Agriculture State Fund investments also caused the significant resurrection of lavender cultivation and oil distillation facilities. Consequently, expansion of lavender industry highlighted the national importance of this crop. Earlier lavender was only cultivated in South Bulgaria (especially Blagoevgrad, Pazardzhik, Stara Zagora, Plovdiv) but currently lavender cultivation has extended its wings at North Bulgarian regions (including Varna, Shumen, Turnovo, Vidin, Veliko, and Dobrich) also. Figure 8.1 highlights the massive growth rate of lavender cultivation which reached in 6892 ha of total areas in 2014. In present days, Bulgaria is at the pinnacle of the production of lavender and its oil. Based on the statistical data of 2014, total production of lavender blooms ranged from 175–259 kg/ha during 2005–2014 (Figure 8.2). Although environmental factors significantly affect lavender yield but in average harvest of 259 kg/ha fresh lavender flower stalk was evident during preceding years.

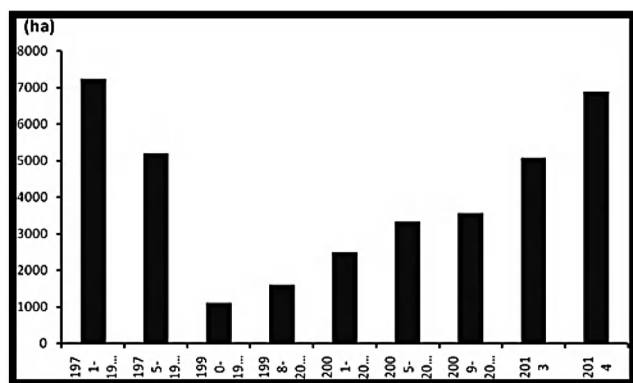


FIGURE 8.1 Total area (ha) of lavender cultivation in Bulgaria.

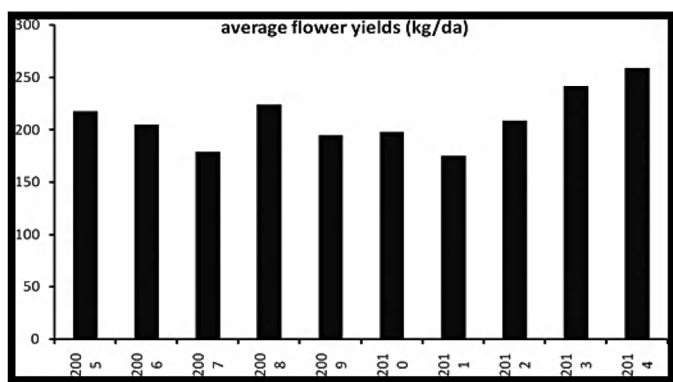


FIGURE 8.2 Average flower yields from lavender plantations in Bulgaria during 2005–2014 period.

## 8.4 MARKETING AND TRADE

Lavender is one of the best-known essential oil-bearing plants, but grown for multifaceted uses (Petkova et al., 2018; Reid, 2000). Now-a-days lavender plantations has enhanced in Turkey also multitudinous usefulness and rural tourism too. Traditionally, Turkey occupies the market for rose, jasmine, and oregano oils, but recent interest in lavender motivates entrepreneurs to evaluate the current status of lavender oil markets worldwide. However, insufficient information(s) and database on world trade and production of lavender oil influence the producers to focus on the quality aspects and dynamics of price in pan world of lavender oil. *L. intermedia* is basically cultivated in Turkey. The trade potential of ‘lavandin’ is more as compared



to the essential oil produced from ‘True Lavender’ (*L. angustifolia*), the most famous and superior type. Bulgaria, France, China, and other few countries are now become the world’s top most suppliers of lavender oil. The extended establishment of lavender plantations in Bulgaria caused the enhanced essential oil supply although the quantity and quality of oils are very much weather dependent. The qualitative and quantitative attributes of oils usually determine the demand but generally it remains more or less same in year after year although sometimes low production rate coupled with higher price. The health awareness of consumer makes them akin to use natural and organic ingredients which ultimately influences additional demand of lavender essential oil. Even after knowing its huge demand round the world, due to meagre farm size and complex value chain procedure, most of the farmers refrain them from the cultivation of lavender. To make it economical for farmers, low production cost should be coupled with high profit ratio which may force them to consider lavender as a vital crop for cultivation (Giray, 2018).

Maximum scientific studies on lavender have been made on medicinal, agricultural, and biological aspects. A case study made by Gül et al. (2016) exhibited that the relative profit (\$1.65), average yield (1,636.70 kg/ha), production cost (\$0.95 for 1 kg lavender) and net profit per hectare (\$1,018.37) of lavender cultivation were quite high as compared to other agricultural produces. Another alike case study on organic lavender cultivation in Bosnia and Herzegovina regions made by Peco et al. (2015) calculated that total profit/hectare as around \$1,237 on average. According to Singh et al. (2007) Chamba District of Himachal Pradesh was the most potent place to flourish lavender oil business. Previous studies by Giray (2018) were focused on farm and market analysis. In nutshell, commercialized production of lavender is vital for societal and environmental benefits except the upliftment of economic status of marginal farmers.

#### **8.4.1 MARKETING STRATEGIES OF LAVENDER OIL**

Wide diversity in lavender species influence the trade of lavender oils and its blends on world markets (Adam, 2006). As for example, according to Stanev et al. (2016) majority of volatile compounds found in lavender essential oil has some sedative impact on human being while variety of lavender oils were used for chemical analyses in Japanese market (Tomi et al., 2018). The useful species for essential oil is *L. intermedia*, *L. angustifolia*, and *L. latifolia* (hybrid of the first two).

‘English Lavender’ botanically known as *L. angustifolia*. It has also secured another name, i.e., ‘Bulgarian Lavender’ for its highest production in Bulgaria. The other species, *L. intermedia*, the hybrid variety (*L. angustifolia* x *L. latifolia*) is popular as ‘lavandin.’ Several morphological differences (like flower and leaf shapes, hues, fragrance, robustness, etc.) at interspecific and intraspecific level are quite prominent while varied geographic locations also contribute towards this (Cristea & Boros-Iacob, 2017). Habitats also contribute towards the naming of several lavender species such as modern French and Bulgarian lavenders were earlier known as ‘English Lavender’ (Tomi et al., 2018). The high-quality oil yielding capacity of *L. angustifolia* is liable to its fame but the price factor determines its demand. Yield of low quantity of essential oil makes it highly expensive. Several factors like genotype, phyto-geographical conditions, mode of propagation and morphological features greatly influence the qualitative and quantitative compositions of essential oil extracted from *L. angustifolia*. But the oil yield potential of *L. latifolia* is much improved than *L. angustifolia* led to its huge market demand. High yield and adaptability of growing at lower altitudes make its essential oil quite pocket-friendly although intense odor of camphor deteriorates its quality (Agrifutures, 2017).

On the other hand, *L. intermedia*, the hybrid cultivar yields huge quantity of oil usually surpasses all other species but possess less demand for inferior quality attributes (Agrifutures, 2017). Tomi et al. (2018) reported that amalgamation of essential oils obtained summoned from various species (known as adulterated essential oils) are unsuitable for desirable aromatherapy effects on human beings. The market price of essential oil derived from *L. angustifolia* is quite less. According to Tomi et al. (2018) adulterated lavender oil, nothing but the mixture of synthetic linalool and linayl acetate, is much cheaper in price. Hence, ‘Lavender Oil’ is the actual essential oil extracts from *L. angustifolia* while ‘Lavandin Oil’ is the mixture of essential oils derived from all species of Lavender and ‘Lavandula Oil’ is the blended version of these two.

#### **8.4.2 WORLD LAVANDULA OIL MARKETS**

Cultivation of lavender is popular in pan world but few countries counting France, Bulgaria, Russia, and some Eastern European countries are exclusively known for lavender oil production commercially. Several chronicles, national, and international market reports could be considered as vital resources to have an updated idea about business and transport chain of lavandula oil (*L. angustifolia*) markets. For last few years, New Zealand

is also another addition in world market (Anon., 2015). As we know that Bulgaria and France both are the leading producers of lavender oil contribute almost 2/3<sup>rd</sup> of total world's essential oil production. They're potent producer and exporter of lavender oil. Spain is now a relatively newcomer in the world market. Overall, Europe is the hub of lavender and lavandin oils while USA and Asian countries have started to emerge in this sector. Figure 8.3 shows approximate shares of main lavender oil producing countries in the world.

According to the Bulgarian statistical report in 2017, 4,500 ha of lands of Bulgaria are under lavender cultivation which consequently yield 230 tons of lavender oil. If we review last 5 years essential oil production statistics of Bulgaria (200 tons in 2016, 180 tons in 2015, 140 tons in 2014, 120 tons in 2013 and 45 tons in 2011) then it manifests a steep increase in production. Owing to continuous expansion of production areas, the predicted production of essential oils by Bulgaria alone will be around 350 tons in 2018 while fluctuating weather conditions led to lower production and yield (Anon., 2018b, c). Apart from abiotic stresses some biotic hazard namely *Stolbur phytoplasma* bacteria significantly lowers down the lavender oil production in France but in Bulgarian province absence of this stress facilitates the production to meet the worlds demand. Institute of Rose and Essential Oil Cultures in Bulgaria during 1960s contributed towards the production of first improved lavender hybrid but later (during 1970s and 1980s) totally 7 cultivars were made while 5 by hybridization and 2 using chemical mutagens (Greibenicharski, 2016). Presence of some chemical compounds act as quality indicators. Among those compounds linalyl acid content and proportion of linalyl acetate and linalool are key compounds. Bulgarian essential oil contains linalyl acetate content as high as 50% and ratio between linalyl acetate and linalool remains 1: 0.7 (Petkova et al., 2018). This high-quality index made Bulgaria frontrunner since 2005. According to Petkova et al. (2018) in total 1,600 farms are under lavender production which was much higher than the other routine crop farms. It's almost 4 times higher than 2017's statistics. Through this data a paradigm shift of farmers from grain producers to lavender producer is quite lucid. It's because of its simple cultivation and management strategies, common climate and soil requirements and high yield potential. Interestingly, small farmers are not only dealing with its cultivation but also concerned about its essential oil production adopting comparatively less expensive steam distillation technology. Despite having pharmaceutical and cosmetic properties its domestic consumption is insignificant, hence, Bulgaria's lavender oil production chiefly focuses on foreign exports (Greibenicharski, 2016).

France still steadily maintains the supply of *Lavandula* omitting biotic challenge caused by *Stolbur phytoplasma*. Even after having a smaller number of lavender farms, the area under its production has increased manifold times than earlier. It proves the modern day demands of lavender and its value-added products. France secured first rank being the highest producer of lavandin essential oil. France alone produces 1,439 tons in 2016 which contribute significantly to world's lavandin oil production. Based on the plants' origin its distribution is classified as 'Grosso' (89%), 'Sumian' (4%), 'Super' (4%) and 'Abrial' (3%) (Giray, 2018).

Xinjiang Autonomous province – collectivist units present China had produced lavender under 1,500 ha of land and resulted in production of 40 tons of lavandin oil yield but China's contribution towards international market was too insignificant, it was >10 tones. Collaterally, India yields 10 tons of lavender although major proportion is consumed for internal usages whereas in Ukraine 1,000 ha of land is under lavender cultivation another major producer contributes to the world lavender oil market by producing between 10 and 15 tons in recent years despite having adverse environmental factors (Agrifutures, 2017; Anon., 2018b, c).

Spain is a leading producer of spike lavender (*L. latifolia*) essential oil which has allowed them to secure their position behind France. About 2,000 ha of land is under cultivation of spike lavender and produces about 80 tons of oil. Morocco is another traditional supplier of medicinal and aromatic plants especially they've gained fame recently as a dominant producer of lavandin. Currently >1,000 ha of land is under lavender cultivation. United States, New Zealand and Australia – all these are new comer in the world of lavandin essential oil production while the former one successfully produces lavandin from 'Grosso' variety and latter two are at growing phase dealing with an agro-tourism project organized by The Australian Lavender Growers Association (TALGA). About 150 ha of land has been occupied for lavender and lavandin production in Italy while Moldova is at struggling stage although its production has declined (France Agri Mer, 2013).

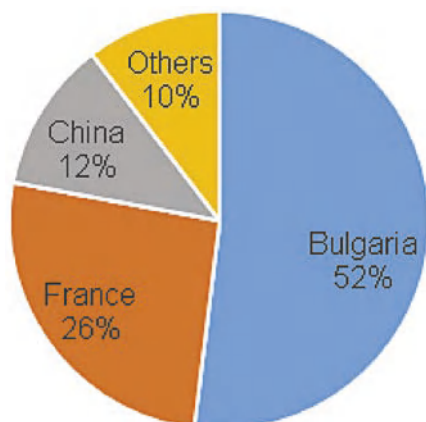
According to Turkstat (2018) report a steep increase in lavender production (production area <50 ha in 2000 and >700 ha in 2018) is really noteworthy but unfortunately their contribution in international market very nominal. They're basically concentrating on *L. intermedia* and *L. angustifolia* production to meet market requirement of lavandin essential oil. A case study made by Bozkiran & Giray (2016) stated the reason of owning lavender cultivation in Turkey is nothing but its low production cost and easy trade, but the key disadvantage is the marketing. The same study revealed that the problem lies

on delayed payments by traders or processors after selling. Lower market price of value-added products demotivates the producers although their low bargaining power may also another reason of it. Marginal farmers with meagre capitals merely depend on the lavender processing/distillation units which aren't enough equipped. So, overall improvement in marketing strategies may change the scenario.

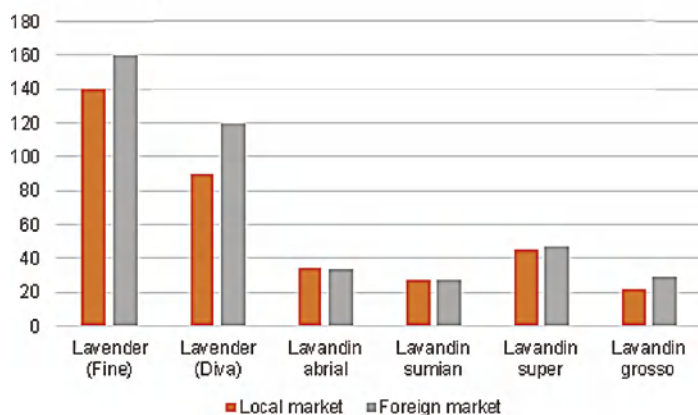
For lavender and lavandin essential oil two basic selling strategies are adopted, i.e.: (i) domestic markets (counting local and niche market and aromatherapy outlets); and (ii) international markets. The former one is focused by small, local traders while the latter one by international companies or giant dealers. Established buyers, flavor, and fragrance industries, distribution units and digital marketing – all are essential components of a successful international marketing. Along with this quality assurance of the produce is also another factor for having a sustainable marketing (Reid, 2000).

The price of lavender produces actually varies depending on its quality attributes. Based on literature survey, it has found that France is the producer of supreme quality of lavender oil. As for example, in Bulgaria during 2016 even after having sumptuous production and the subsequent supply of lavender produces the net turn-over was quite low but in 2018 high production couples with high market price. The reason might be the quality as Bulgaria often experiences fluctuating weather conditions may create some meaningful impact on quality attributes of produces. Qualitative factors of essential oils basically depend on the mode of propagation. For 'Fine Lavender' prices may be as high as Rs. 220/-per kg while for 'Diva Lavender' it's as low as Rs. 40–60/-per kg. On the other hand, the supply rate can also influence the price of produces (price of Bulgarian lavender oil greatly affected due to the supply factor). Generally, the price differences between lavender oil and lavandin oil is noticeable. In national market the price of lavender oil > lavandin oil while the scenario is reverse in international market.

Kentucky is another emerging state for lavender cultivation. The congenial conditions of this state make it appropriate for conducting on-farm agritourism (lavender festival) and also to adopt its cultivation as an ornamental crop. More conclusively, in Kentucky the lavender market can be formed focusing on 3 aspects viz.: (i) agritourism (can anchor seasonal attractions); (ii) value-added products; and (iii) culinary ingredients. Some value-added products like soaps, use as culinary ingredients, potpourri, candles, etc., for daily uses and sometimes floral arrangements are also made using lavender blooms. So, successful market supply-chain (Wholesalers, Restaurateurs, and Florists) may aid to obtain profitable prices (Ernst, 2017) (Figure 8.4).



**FIGURE 8.3** World lavender oil production by countries (2017).



**FIGURE 8.4** French Lavandula oil prices in 2016 (€/kg).

## 8.5 ORIGIN AND DISTRIBUTION

Latin word ‘lavare’ means ‘to wash’ or ‘to bathe.’ This Latin verb is the source of the name ‘Lavender.’ Mediterranean basin especially rocky and calcareous areas are considered to be the origin of lavender as it prefers warm weather conditions and low topography for their luxurious growth. During the Elizabethan era in England and also by the ancient Greeks and Romans lavender was cultivated mainly at North Africa, Europe, and Western India. Mediterranean weather is most suitable spike lavender. At present, lavender essential oil production is distributed in haute province (France), Spain, Portugal, Hungary, United Kingdom, Bulgaria, Australia, China, and USA (McCoy, 1999).

## 8.6 COMPOSITION

Linalool and linalyl acetate are two key components of lavender oil among others (it may be >100 compounds) (Barazandeh, 2002). These different constituents are thujene,  $\alpha$ -pinene, camphene, sabinene, p-cymene, limonene, myrcene, (Z)- and (E) farnesene, (Z)- and (E) ocimene, 1,8-cineole, camphor, terpinene-4-ol, lavandulylacetate-caryophyllene, terpinene, lavandulol, etc. Naeff & Morris (1992) identified key compounds viz. 1,8-cineole (22.9%), camphor (16.25%) and linalool (27.06%) adopting combined analytical techniques with a target of an elaborate analysis of oil extracted from spike lavender. *L. latifolia* grown in Almalagues (Portugal) could yield 0.3% oil (Proneca et al., 1985) enriched in linalool compounds while De Paseual et al. (1989) adopted a combined technique (conventional and modern analytical method) to estimate the chemical compounds found in *L. latifolia* collected from other parts of Portugal. The method of oil distillation and characterization actually affect the quantity of chemical compounds recovered and the nature of chemical composition of the extracted oil (Table 8.1). 1,8-cineole (36%, 34.9%), camphor (8%, 15%) and linalool (30.3%, 18.9%) found as major constituents both in lab-distilled and commercial oils. Carrasco et al. (1989) revealed that the chemical composition of extracted oil varied according to their stage of maturity. Linalyl acetate is the key component of lavender oil. French oils contain 30–60% acetate, English oil contained 8–18% while Kashmir oil contained 24.8% linalyl acetate (Table 8.2) (Agnel & Tiesseire, 1984; Boelens, 1995; Lawareiiice, 1985, 1994, 1996). Other constituents present in the oil were linalool, geraniol, and its esters, lavandulol, nerol, cineole, caryophyllene, liionene, P-ocimene, thujone, and pinocamphone (Schiweisheimer, 1960; Tewari & Sharma, 1987; Venskutonsis et al., 1997; Ramie et al., 1982; Reverchon et al., 1995). Solvent extracted perfumer contains umbelliferone methyl ether (7-methoxy coumarin) and coumarin. The ester content (linalyl acetate) actually determines different grades of lavender oil since this content considered as oil evaluation parameter. French and English lavender oil differ from each other as the former one contains much lower ester content and an appreciable proportion of cineole that imparts a characteristic pungency to the oil (Anonymous, 2001; Porter et al., 1982. Reverchon et al., 1995; Venskutonsis et al., 1997), Two series of carbonyl compounds with either santalane and cadinane skeletons or caryophyllanc and ccdrane skeletons have been reported (Kaiser et al., 1983a, b), Phytochemiscally *L. officinails* was reported to have Turan, coumarins, and related derivatives (Naf et al., 1997; Brown, 1965). Saadatian et al. (2013) investigated the chemical composition of *L. officinalis* using dry and fresh

flowers adopting Maceration extraction method. He used 2 different concentration of ethanol (96 and 70%) during extraction. Characterization of ethanol (96%) based mass extracted lavender oil using Gas Chromatographic method revealed the existence of methanecarboxylic acid, pentadecanoic acid, ethane, dimethylamin, N,N-Dimethyl methanesulfonamide, and p-vinylguaiacol. Heptanoic acid, Acetic acid, 2-Propanone, Melilotin, Herniarine, and cyclopropyl carbonyl-D-2-methyl ether – these constituents have been found to be present in 70% ethanol-based extraction method.

**TABLE 8.1** Composition of Lavender Essential Oil (%)

Sl. No.	Compound	RI*	Leaves	Buds	Flowers
1.	Cumene	979	1.0 ± 0.0	0.2 ± 0.0	0.1 ± 0.0
2.	<i>a</i> -Pinene	982	0.5 ± 0.0	0.4 ± 0.0	0.2 ± 0.0
3.	Camphene	987	1.4 ± 0.0	0.7 ± 0.0	0.2 ± 0.0
4.	Verbenene	993	0.4 ± 0.0	0.2 ± 0.0	Tr**
5.	Octen-3-ol	994	0.9 ± 0.0	0.4 ± 0.0	0.3 ± 0.0
6.	3-Octanone	996	0.2 ± 0.0	0.3 ± 0.0	0.5 ± 0.0
7.	Myrcene	997	0.1 ± 0.0	0.8 ± 0.0	0.6 ± 0.0
8.	<i>dehydro</i> -1,8-Cineole	998	0.1 ± 0.0	–	–
9.	Butyl butanoate	999	–	–	0.1 ± 0.0
10.	<i>dehydro-cis</i> -Linalool oxide	1,007	–	–	Tr
11.	Hexyl acetate	1,012	0.4 ± 0.0	0.1 ± 0.0	0.5 ± 0.0
12.	<i>p</i> -Cymene	1,021	0.7 ± 0.0	0.4 ± 0.0	Tr
13.	<i>orto</i> -Cymene	1,027	1.5 ± 0.0	0.3 ± 0.0	0.2 ± 0.0
14.	Limonene	1,031	3.8 ± 0.2	0.7 ± 0.0	0.3 ± 0.0
15.	1,8-Cineole	1,035	7.3 ± 0.1	1.4 ± 0.0	3.4 ± 0.0
16.	$\gamma$ -Terpinene	1,045	0.1 ± 0.0	3.3 ± 0.0	0.1 ± 0.0
17.	( <i>E</i> )- $\beta$ -Ocimene	1,059	–	tr	1.2 ± 0.0
18.	<i>trans</i> -Linalool oxide	1,070	0.6 ± 0.0	2.3 ± 0.0	1.1 ± 0.0
19.	<i>cis</i> -Linalool oxide	1,086	0.2 ± 0.0	2.1 ± 0.0	0.9 ± 0.0
20.	3,5-Heptadienal	1,089	–	0.1 ± 0.0	Tr
21.	Linalool	1,097	1.9 ± 0.1	23.9 ± 0.2	29.9 ± 0.2
22.	1-Octen-3- <i>y</i> -yl acetate	1,101	0.2 ± 0.0	1.0 ± 0.0	1.7 ± 0.0
23.	<i>trans-p</i> -Mentha-2,8-dien	1,112	0.2 ± 0.0	0.1 ± 0.0	Tr
24.	Octanol acetate	1,115	tr	0.1 ± 0.0	Tr
25.	<i>trans-p</i> -Menth-2-en-1-ol	1,123	0.2 ± 0.0	0.1 ± 0.0	Tr
26.	<i>trans</i> -Limonene oxide	1,128	0.1 ± 0.0	0.1 ± 0.0	0.1 ± 0.0
27.	<i>E</i> -Myroxide	1,136	–	0.1 ± 0.2	0.1 ± 0.0



TABLE 8.1 (Continued)

Sl. No.	Compound	RI*	Leaves	Buds	Flowers
28.	Camphor	1,152	2.0 ± 0.0	0.8 ± 0.0	0.4 ± 0.0
29.	4-Hexen-1-ol	1,165	1.0 ± 0.1	0.6 ± 0.0	0.6 ± 0.1
30.	Borneol	1,178	11.7 ± 0.3	4.3 ± 0.1	1.7 ± 0.1
31.	Terpinen-4-ol	1,184	0.9 ± 0.0	1.7 ± 0.0	5.1 ± 0.0
32.	Cryptone	1,193	10.4 ± 0.5	3.6 ± 0.0	0.6 ± 0.0
33.	<i>α</i> -Terpineol	1,201	0.8 ± 0.0	5.0 ± 0.1	2.4 ± 0.0
34.	trans-Mentha-1(7),8-dien-2-ol	1,212	tr	0.2 ± 0.0	0.1 ± 0.0
35.	Verbenone	1,219	0.7 ± 0.0	0.4 ± 0.0	0.1 ± 0.0
36.	trans-Carveol	1,226	0.6 ± 0.0	0.2 ± 0.0	Tr
37.	Nerol	1,229	0.4 ± 0.0	0.8 ± 0.0	0.3 ± 0.0
38.	Isobornyl	1,238	0.7 ± 0.0	0.4 ± 0.0	0.1 ± 0.0
39.	Linalyl acetate	1,253	5.9 ± 0.1	22.3 ± 0.3	32.1 ± 0.0
40.	Piperitone	1,265	0.4 ± 0.0	0.1 ± 0.0	Tr
41.	Thymoquinone	1,279	0.2 ± 0.0	0.3 ± 0.0	0.1 ± 0.0
42.	Lavandulyl acetate	1,289	0.7 ± 0.0	3.4 ± 0.1	5.9 ± 0.0
43.	Bornyl acetate	1,295	0.1 ± 0.0	0.6 ± 0.0	0.2 ± 0.0
44.	<i>p</i> -Cymen-7-ol	1,303	1.2 ± 0.0	0.6 ± 0.0	0.1 ± 0.0
45.	Thymol	1,308	0.4 ± 0.0	Tr	Tr
46.	2,4-Cycloheptadien-1-one	1,321	0.3 ± 0.0	0.2 ± 0.0	Tr
47.	3-oxo- <i>p</i> -Menth-1-en-7-al	1,349	0.7 ± 0.0	0.8 ± 0.0	0.3 ± 0.0
48.	Neryl acetate	1,362	0.3 ± 0.0	1.1 ± 0.0	0.7 ± 0.0
49.	Ni***	1,380	–	2.4 ± 0.1	–
50.	Sesquithujene	1,421	0.1 ± 0.0	Tr	Tr
51.	<i>α</i> -Santalene	1,428	1.5 ± 0.0	0.7 ± 0.0	0.4 ± 0.0
52.	E-Caryophyllene	1,433	0.3 ± 0.0	1.0 ± 0.0	3.8 ± 0.0
53.	<i>α</i> -trans-Bergamotene	1,444	0.3 ± 0.0	0.1 ± 0.0	0.1 ± 0.0
54.	<i>α</i> -26,33 Farnesene	1,461	0.1 ± 0.0	0.1 ± 0.0	0.5 ± 0.0
55.	<i>α</i> -Humulene	1,474	0.1 ± 0.0	0.1 ± 0.0	0.2 ± 0.0
56.	Germacrene D	1,502	0.3 ± 0.0	0.2 ± 0.0	0.3 ± 0.0
57.	<i>γ</i> -Cadinene	1,530	3.4 ± 0.1	0.4 ± 0.0	0.2 ± 0.0
58.	trans-Calamene	1,537	0.3 ± 0.0	0.1 ± 0.0	Tr
59.	9,11-epoxy-Guaia-3,10(14)-diene	1,576	0.7 ± 0.0	0.1 ± 0.0	Tr
60.	Caryophyllene oxide	1,595	7.2 ± 0.2	4.5 ± 0.0	1.6 ± 0.0
61.	Thujopsan-2- <i>α</i> -ol	1,601	0.2 ± 0.0	Tr	Tr
62.	Guaiol	1,608	0.2 ± 0.0	–	–
63.	1,10-di-epi-Cubenol	1,629	1.7 ± 0.0	0.2 ± 0.0	Tr

**TABLE 8.1** (Continued)

Sl. No.	Compound	RI*	Leaves	Buds	Flowers
64.	epi- $\alpha$ -Cadinol	1,658	17.8 $\pm$ 0.5	2.3 $\pm$ 0.1	–
65.	$\alpha$ -Cadinol	1,665	0.2 $\pm$ 0.0	Tr	Tr
66.	trans-Calanen-10-ol	1,673	0.8 $\pm$ 0.0	0.2 $\pm$ 0.0	–
67.	14-hydroxy-9-epi-(E)-Caryophyllene	1,690	0.3 $\pm$ 0.0	0.3 $\pm$ 0.0	0.1 $\pm$ 0.0
68.	cis-14-nor-Muurool-5-en-4-one	1,708	2.1 $\pm$ 0.1	0.3 $\pm$ 0.0	–
69.	Guaia-3,10(14)-dien-11-ol	1,730	0.5 $\pm$ 0.0	0.1 $\pm$ 0.0	–
70.	Ni	1,757	1.6 $\pm$ 0.1	0.1 $\pm$ 0.0	tr
<b>Total (%)</b>			<b>99.91</b>	<b>99.78</b>	<b>99.49</b>

\*RI – non-isothermal Kovats retention indices (from temperature-programming, using the definition of Van den Dool and Kratz [1963]) for a series of *n*-alkanes (C<sub>6</sub>–C<sub>40</sub>);

\*\*Tr – traces, contents below 0.05%;

\*\*\*Ni – unidentified compound.

**TABLE 8.2** Chemical Composition of Volatile Oil of *L. officinalis*, *L. angustifolia*, and *L. latifolia*

Sl. No.	Components	<i>L. officinalis</i>	
		RI	%
1.	Acetic acid	–	0.1
2.	Octane	–	0.1
3.	Cyclooctanone	–	1.1
4.	$\alpha$ -Pinene	937	0.2
5.	$\beta$ -Myrecene	970	0.2
6.	<i>p</i> -Cymene	1,005	4.4
7.	Decane	–	0.1
8.	1,8-Cineole	1,035	5.9
9.	Linalool	1,080	14.3
10.	<i>t</i> -3-Pinen-2-ol	1,085	1.6
11.	Ipsenol	1,087	1.3
12.	Tagetonol	1,138	0.4
13.	Lavaadulol	1,156	10.0
14.	$\alpha$ -Terpineoil	1,162	3.4
15.	Dihydrocarveol	1,177	3.0
16.	Geraniol	1,260	9.3
17.	1- <i>p</i> -Menthen-8-yl acetate	1,285	1.8
18.	Citronallic acid	1,301	0.3
19.	$\alpha$ -Terpenyl acetate	1,342	1.1

TABLE 8.2 (Continued)

Sl. No.	Components	L. officinalis	
		RI	%
20.	Unknown	–	1.4
21.	C <sub>15</sub> H <sub>24</sub> *	–	0.7
22.	Caryophyllene	1,421	0.6
23.	Oleic acid	–	0.2
24.	C <sub>20</sub> H <sub>42</sub>	–	0.2
<b>L. angustifolia</b>			
25.	Linalool	28.92	
26.	α-Terpineol	0.90	
27.	γ-Terpineol	–	
28.	Borneol	–	
29.	Isoborneol	–	
30.	Terpinen-4-ol	4.32	
31.	Nerol	0.20	
32.	Lavandulol	0.78	
33.	Linallyl acetate	32.98	
34.	Geranyl acetate	0.60	
35.	Neryl acetate	0.32	
36.	Octene-3-yl-acetate	0.65	
37.	Lavandulyl acetate	4.52	
38.	Myrcene	0.46	
39.	α-Pinene	–	
40.	β-Pinene	–	
41.	Camphene	–	
42.	(E)-β-Ocimene	3.09	
43.	(Z)-β-Ocimene	4.44	
44.	β-Phellandrene	0.12	
45.	Eucalyptol (1,8-Cineol)	–	
46.	β-Caryophyllene	4.62	
47.	β-Farnesene	2.73	
48.	Germacrene	0.27	
49.	α-Humulene	–	
50.	Camphor	0.85	
51.	3-Octanone	0.72	
52.	Cryptone	0.35	
<b>L. lattifolia</b>			
53.	Linalool	49.47	

**TABLE 8.2** (Continued)

Sl. No.	Components	L. officinalis	
		RI	%
54.	$\alpha$ -Terpineol	1.08	
55.	$\gamma$ -Terpineol	0.09	
56.	Borneol	1.43	
57.	Isoborneol	0.82	
58.	Terpinen-4-ol	–	
59.	Nerol	–	
60.	Lavandulol	–	
61.	Linayly acetate	–	
62.	Geranyl acetate	–	
63.	Neryl acetate	–	
64.	Octene-3-yl-acetate	–	
65.	Lavandulyl acetate	–	
66.	Myrcene	0.41	
67.	$\alpha$ -Pinene	0.54	
68.	$\beta$ -Pinene	0.33	
69.	Camphene	0.30	
70.	( <i>E</i> )- $\beta$ -Ocimene	–	
71.	( <i>Z</i> )- $\beta$ -Ocimene	–	
72.	$\beta$ -Phellandrene	–	
73.	Eucalyptol (1,8-Cineol)	25.91	
74.	$\beta$ -Caryophyllene	2.10	
75.	$\beta$ -Farnesene	–	
76.	Germacrene	–	
77.	$\alpha$ -Humulene	0.28	
78.	Camphor	13.00	
79.	3-Octanone	0.72	
80.	Cryptone	0.35	

\*Partially identified.

Monoterpene Hydrocabons (3): 4.8%

Oxygenated Monoterpenes (12): 52.4%

Sesquiterpene Hydrocarbons (1): 0.6%

Others (8): 3.9%

Total (24): 61.7%

Actually, lavender essential oil consists of monoterpeneoids and sesquiterpeneoids while among them linalool and linayly acetate are dominant

also contained average quantity of 1,8-cineole, terpinen-4-ol, camphor, lavandulol, and lavandulyl acetate. Latter compounds are generally found in medium to low quality of oils. The concentrations of all these compounds generally vary species to species (Shellie et al., 2002).

## 8.7 USES

The multifaceted use of lavender oil could be proved by its natural antibiotic, antiseptic, antispasmodic, sedative, and detoxifier properties. Wide range of ailments (may be burns, scales, cuts, bruises, skin irritations, etc.) could be healed using its oil. Nervine, diuretic, aromatic, antiseptic, sedative, carminative, cholagogue, antispasmodic, stimulative, stomachic, and tonic, anti-inflammatory, analgesic, anti-infectious, cardiogenic, hypotensive, and anticoagulant properties of lavender essential oil help to fight against several diseases. Along with boosting the immune system, it also causes the regeneration of wound cells. It can be also considered as mood tonic and antidepressant. It can effectively minimize the psychological shock of any major injury (Anonymous, 2001). Barring these, its use as muscle relaxant, soothing agent, skin conditioner. Astringent, headaches, and PMS symptoms reliever is well known. For physical and emotional calmness and also to have soothing effect, the fragrance of lavender oil is actually very much effective (Anonymous, 2001; Schweishmer, 1960). Linalyl acetate, linalool, other aroma components ( $\beta$ -ocimene, cineol, and caryophyllene epoxide) and coumarin derivatives (coumarin, dihydrocoumarin, herniarin, umbelliferone) are principally liable for its soothing fragrance which bring calming, relaxing, and balancing effect physically and emotionally both. This information could endorse its further uses in commercial food and cosmetic industry. Apart from its vast medicinal usages, it could be exploited too for industrial purposes, food, and cosmetic industry.

Apart from its oral usages, it is too used in aromatherapy. Basically, inhalation method is preferred while topical applications (like sirdhara treatment, ayurvedic spa and body massage) are also sometimes adopted. Use of undiluted form of lavender oil, the key merit of its use, is not harmful for the skin due to the chemical nature of bio-constituents which are easy-to-absorb as suggested by Jager et al. (1992). Few research findings exhibited that body massage using lavender essential oil caused great relax owing to instant absorption of linalool and linalyl acetate components. Since time immemorial, its dual usages, i.e., on one hand, as perfumes, soaps, flavorings, crafts, and as anticonvulsant, anti-depressive, anxiolytic, sedative, and calming

agents, on the other hand. Lavender too recommended by few medieval physicians (such as Ebn-e-sina and Razi) to treat epilepsy and migraine attacks (Koulivand et al., 2012). Furthermore, it can be also useful for pain and tremor. According to Koulivand et al. (2012) lavender could be successfully used to heal some neurological disorders. Now-a-days, more advanced research investigations using improved scientific tools are now taking place to extract the utmost benefit of this wonder aromatic crop.

### **8.7.1 CULINARY USE**

‘English lavender’ (*L. angustifolia* ‘Munstead’) is familiar as ‘Culinary Lavender’ popularly used for preparing several cuisines. Its importance is especially for the mesmerizing fragrance and citrus taste (Retrieved from: <https://whatscookingamerica.net/Lavender.htm>). It is consumed in diversified forms like as a raw salad ingredient and sometimes for top dressings and desserts preparation (Kains, 1912), etc. Floral buds and green leaves often used for aromatic tea preparation while honey bees pollinated buds become an imperative ingredient of mono-floral honey. Since Victorian era (around 1600s) preserved lavender in ‘jam’ and ‘jelly’ form was used in England. Apart from this, it is also highly acclaimed as herbal teas. Interestingly, in Southern France usages of lavender was quite restricted based on a myth that during 20<sup>th</sup> century French lambs were intentionally allowed to graze on lavender field to make their meat more fragrant and tender. ‘Herbes de Provence’ – nothing but a blend of herb was introduced in French market during 1970s by spice wholesalers while North Americans used culinary lavenders as spice blend (Laget, 2005).

### **8.7.2 USE OF BUDS**

Dried buds of lavender often used as cooking ingredients, but green, juvenile leaves are used more frequently owing to its subtle flavor as compared to rosemary. Appropriate processing (such as optimum drying of flowers) of lavender blooms are essential before its incorporation in any cuisines to avoid heavy and soapy taste. To bring intense sweet and savory flavors in sheep’s-milk and goat’s-milk cheeses, lavender buds become the first choice. It is useful as blending ingredient with black, green, and herbal teas while occasionally it goes very well for flavored chocolates. In baking industry, flavored sugar syrup (lavender buds are immersed in sugar syrup for 2 weeks

to make it fragrant) seems imperative. Its use has been also stretched in wine industry. Scones and marshmallows become incomplete without lavender syrup and dried lavender buds in United States (Stradley, 2015; Maclain, 2015).

### **8.7.3 USE OF GREENS**

For flavoring meat and vegetables in savory dishes, lavender is more preferred, in fact, it has surpassed rosemary for having its equivalent flavor. They often been used for tea preparation, usually contain milder aroma as compared to bud flavored tea (Retrieved from: <https://livingonagreenthumb.wordpress.com/2015/10/07/lavender-12-uses-beyond-potpourri>).

### **8.7.4 INDUSTRIAL USES**

Lavender has secured its commercial importance since ancient period. Its uses in soap industry and perfumery (such as dried arrangements, filler materials, incense sachets, potpourri, 'eau de cologne,' candles, wands, flower bundles, wreaths, wall hangings, etc.) is indescribable. Its multifaceted uses like as washing agents, mosquito repellents, essential toiletries (soap, shampoo, bath oil, lotion, bath salt), incense sticks, etc., are really fascinating. In fact, its fresh leaves could be successfully used for pest control. As organic pesticide, mixture of 2% Rosemary oil and lavender EO could be also used.

### **8.7.5 COSMETIC USES**

Sedative action and dermatologically friendly nature of lavender oil broaden its application in various sectors including cosmetic industry. Lavender body creams can prevent scar of tissues being maintained skin moisture level.

### **8.7.6 PHARMACEUTICAL AND THERAPEUTIC USES**

Use of lavender as an herbal remedy is well-known. It is used significantly to treat bites, vaginal discharge, anal fissure, scalds, nurns, and sunburns. It is mostly used externally especially on temple region to heal nervous headache than the internal application although having carminative and

vervaine properties. Lavender extracts are also useful to treat various bacterial ailments like typhoid, diphtheria, *Streptococcus*, and *Pneumococcus* while it's also an effective antidote to some snake venoms. Lavender EO is a vital ingredient in aromatherapy. Due to having therapeutic properties, greens are often used in bath water to make it fragrant.

### **8.7.7 FOOD AND FLAVORING**

Exclusively, in bakery industry its importance is indefinable. It is used as food flavoring agents such as ice cream, culinary herb blends, cookies, lavender tea, salt, honey, and jelly. It can emit pleasant fragrance as well as can restrict insects if used as strewing herb.

### **8.7.8 OTHER USES**

In dry flower industry its importance is high. Desiccated pale purple colored flower buds are used mostly in potpourris. Instead of using any commercial chemical insect and pest control agents, sachet sealed dried lavender flowers could be used as a viable alternative specially to make linens fragrant and to deter moths. To make wedding confetti, scented waters and sachets lavender found essential.

### **8.7.9 ADVERSE EFFECTS**

Along with its all-positive health effects, it had found that some health abnormalities like breast development (prepubertal gynecomastia) especially in boys of adolescent period due to the use (both externally and internally) of lavender oil could also take place (Henley et al., 2007). Sedative effect (inhalation application) and allergic rashes (topical application) may cause rarely due to presence of linalyl acetate, linalool, camphor, and terpinen-4-ol as major lavender essential oil constituents (Sarkic and Stappen, 2018; Elshafie & Camele, 2017). Unfortunately, in Australia many adverse results most importantly poisoning incidents among children are evident recently. Findings of Lee et al. (2019) revealed that inappropriate percentage of lavender EO could be poisonous also. Authors mentioned that based on the report of New South Wales during 2014–2018, 271 death cases due to health poisoning after using lavender EO were also found.



## 8.8 BOTANY AND TAXONOMY

During Roman era, 3 species of lavender namely *L. stoechas*, *L. pedunculata* and *L. dentata* were popular while during early of Middle Ages, few European species had started to proliferate. Those European species were classified into 2 genera viz. *Lavandula* (*L. latifolia* and *L. spica*) and *Stoechas* (*L. pedunculata*, *L. dentata* and *L. stoechas*). In ‘Species Plantarum,’ the names of other 5 European species (*L. dentata* and *L. multifida* [from Spain]; *L. spica*, *L. stoechas* and *L. pedunculata* [from Southern Europe]) had been found (Linnaeus, 1753). *L. carnosa* and *L. pinnata* were identified during 1,790 but the former one was repositioned to *Anisochilus* sp. According to Lis-Balchin (2002), lavender species (approx. 18) registered by Frédéric Charles Jean Gingins de la Sarraz in 1848, out of which 12 were already known during 1848. During 1937, a new modern lavender classification was introduced by Dorothy Chaytor where 28 species under 6 sections were included. *Spica*, *Stoechas*, *Pterostoechus*, *Chaetostachys*, *Subnuda*, and *Dentatae* were the respective sections she incorporated. All commercial and cultivable species were added under *Stoechas* (*L. dentata*, *L. stoechas*, *L. viridis*, and *L. pedunculata*) and *Spica* (*L. officinalis*, *L. latifolia* and *L. lanata*) sections. Chaytor (1937) reported that *L. angustifolia* (True Lavender) and *L. latifolia* (Spike Lavender) are the parents of lavender garden varieties. Two major clades are found in its classification, i.e., subgenus *lavendula* and *Fabricia* while all sections are under the former subgenus and under the latter subgenus *Pterostoechas*, *Subnuda*, and *Chaetostachys* are included.

### 8.8.1 TAXONOMIC STATUS

According to the classification of Upson & Andrews (2004), Lavender is classified into three key sub-genus, i.e., I. Subgenus *Lavendula* Upson and Andrews II. Subgenus *Fabricia* (Adams.) Upson & S. Andrews and III. Subgenus *Sabaudia* (Bascal. & Muschl) Upson and Andrews.

#### 8.8.1.1 SUBGENUS LAVENDULA UPSON AND ANDREW

Under this subgenus, *Lavendula* contains three species namely *L. angustifolia* Mill, *L. latifolia* Medik and *L. lanata* Boiss and two hybrids namely *L. angustifolia* sub-sp. *angustifolia* × *L. lanata*, *L* × *Chaytorae* Upson and Andrews and *L. angustifolia* sub-sp. *angustifolia* × *L. latifolia*, *Lavendula*

× *intermedia* Emric ex Loisel. *L. angustifolia* sub-sp. *angustifolia* were identified first from Catalonia and the Pyrenees while *L. angustifolia* sub-sp. *Pyrenaica* from South East France and adjacent areas of Italy. And this *L. latifolia* was native to Central and Eastern Spain, Southern France and Northern Italy and Southern Spain was known as the native of *L. lanata*. And this section under the same sub-genus is *Dentatae* suarex-Cerv. & Seoane-Camba which contains any 1 sp., i.e., *L. dentata* L. This species is native to Eastern Spain, Northern Algeria and South Western Morocco. Two Varieties of *L. dentata* have been identified, i.e., *L. dentata* Var *Dentata* (Batt) & *L. dentata* Var *candicans* (Batt). *Stoechas* Ging is another section under the currently discussed subgenus. It contains 3 Species namely *L. stoechas* L., *L. Pedunculata* and *L. viridis* L., *L. stoches* sub-sp. *Stoechas* is native to Eastern Spain, Southern France, Western Italy, Greece, Bulgaria, Mediterranean Turkey, Levantine Coast and most of the Mediterranean island. One more sub-sp. under *L. stoechas* had been identified, i.e., *L. stoechas* sub-sp. *luisieri* which was native to coastal and inland Portugal and adjacent Spain. *L. pedunculata* Mill (Cav.) contains 5 sub-sp. namely *L. pedunculata* sub-sp. *pedunculata* (native to Spain and Portugal), sub-sp. *Cariensis* (native to Western Turkey and Southern Bulgaria), sub-sp. *atlantica* (native to Montane Morocco), sub-sp. *lusitanica* (native to Southern Portugal and South Western Spain), sub-sp. *Sampiana* (native to Portugal and South west Spain). One more species *L. viridis* L'Her. was originated from South West Spain, Southern Portugal and also from Madeira. Barring these three species, three Intersectional Hybrids (*Dentatae* and *Lavendula*) are found to be present like *L. × heterophylla* Viv. (*L. dentata* × *L. latifolia*), *L. allardii* and *L. ginginsii* Upson and Andrews (*L. dentata* × *L. lanata*).

#### 8.8.1.2 SUBGENUS FABRICA (ADAMS.) UPSON & S. ANDREWS

Under this subgenus 4 sections had identified which are section *Pterostoechas* Ging, Section *Subnuda* Chaytor, section *Chaetostachys* Benth. and section *Hasikenses* Upson and Andrews. Under section *Pterostoechas* 16 species reside like *L. multifida* (from wide Range Like Morocco, Southern Portugal, Spain, Northern Algeria, Tunisia, Tripolitania, Calabria, Sicily, and in Nile valley), *L. canariensis* (native to Canaries), *L. minutolii* Bolle. (From canary Isles), *L. brammwellii* Upson and Andrews (from Gran canaria), *L. pinnata* L. (from the canaries and maderia), *L. buchii* Webb. and Berthef (from Tenirife), *L. rotundifolia* Benth. (from Cape Verde islands), *L. maroccana* Murb. (from Atlas Mountains of Morocco), *L. tenuisecta* coss.ex Ball (from

Atlas Mountains in Morocco), *L. rejdalii* Upson and Jury (from Morocco), *L. mairei* Humbert (from Morocco), *L. coronopifolia* Poir. (from North Africa, Northeast of tropical Africa, Arabia, and Eastern Iran), *L. saharica* Upson & Jury (native to Southern Algeria and nearby regions), *L. antinaea* Maire (native to Central Sahara region), *L. pubescens* Decne (from Egypt and Eritrea, Sinai, Israel, and Palestine, Jordan, western Arabian Peninsula to Yemen) and *L. Citriodora* A.G. Mill (from Southwestern Arabian Peninsula).

*L. canariensis* possesses 7 sub-sp. namely subsp. *palmensis* (from La Palma), subsp. *hierrensis* (from El Hierro), subsp. *canariensis* (from Tenerife), subsp. *Canariae* (from Gran Canaria), subsp. *fuerteventurae* (from Fuerteventura), subsp. *gomerensis* (from La Gomera), subsp. *lancerottensis* (from Lanzarote), while *L. minutolii* contains two sub-sp., i.e., subsp. *minutolii* and subsp. *tenuipinna*. *L. antinaea* Maire also possesses 3 sub-sp. namely subsp. *antinae*, subsp. *marrana*, subsp. *tibestica*.

Under there Pterostoechas section, hybrid has also been identified *L. × christiana* Gattef. and Maire (*L. pinnata* × *L. canariensis*).

Under section Subnuda, 10 species reside such as *L. subnuda* Benth. (from mountains of Oman and UAE), *L. macra* Baker (from Southern Arabian Peninsula and Northern Somalia), *L. dhofarensis* A.G. Mill. (native to Dhofar in southern Oman), *L. samhanensis* Upson & S. Andrews (from Dhofar, Oman), *L. setifera* T. Anderson (from coastal regions of Yemen and Somalia), *L. qishnensis* Upson & S. Andrews (from Southern Yemen), *L. nimmoi* Benth. (from Socotra), *L. galgalloensis* A.G. Mill. (from Northern Somalia), *L. aristibracteata* A.G. Mill. (Northern Somalia), and *L. somaliensis* Chaytor (from Northern Somalia). Among these 10 species only 1 species, i.e., *L. dhofarensis* contains 2 subsp. namely subsp. *dhofarensis* and subsp. *Ayunensis*.

Under section *Chaetostachys* Benth. Only 2 species have been identified which are *L. bipinnata* (Roth) Kuntze (from Deccan peninsula and Central North India) and *L. gibsonii* J. Graham (native to Western Ghats, India).

Under section *Hasikenses* Upson & S. Andrews also 2 species have been found, i.e., *L. hasikensis* A.G. Mill. (Native to Oman) and *L. sublepidota* Rech. f. (from Southern Iran).

### 8.8.1.3 SUBGENUS SABAUDIA (BUSCAL. & MUSCHL.) UPSON & S. ANDREWS

Under this subgenus only one section has been found, i.e., Section *Sabaudia* which contains only 2 species namely *L. atriplicifolia* Benth. (Native to

Western Arabian Peninsula, Egypt) and *L. erythraeae* (Chiov.) Cufod. (Native to Eritrea).

### **8.8.2 HARDY LAVENDERS**

English Lavender (*L. angustifolia*) synonymously known as *L. vera*, *L. latifolia*, *L. officinalis*, *L. spica*, *L. delphinensis* is commonly available lavender species. They usually attain the height of 1–3 ft. Morphologically, these are the narrow-leaved type (ovate in shape) having irregular, multi-branched, erect, slender stem enveloped with yellowish-grey bark (flakes type). Branches are often slender, bluntly quadrangular, finely pubescent with stellate hairs. Taxonomically, leaves are lance-shaped with entire margin, sessile, blunt ended with opposite phyllotaxy. Juvenile leaves are white and densely stellate on both dorsal and ventral surfaces with strongly revolute margins, but dark green colored full-grown leaves (usually 2.5 cm long) possess different taxonomical features. The dorsal surface of leaf is enveloped by scattered hairs while ventral surface with smooth, fine hairs with slightly revolute margins. They have spike inflorescences which produce 6–10 whorls of 1.5 inches long flowers. The flowers are short stalked found in cluster (3–5) in the axils of rhomboidal, brown, thin, and dry bracts. Leafy, small bracts are arranged in opposite aestivation below each whorl. Tucker & Hensen (1985) suggested that based on the features of bracts lavenders could be classified. As for example, leaves of *L. angustifolia* are ovate rhombic (length: width 0.83: 2.20), bracteoles absent, calyx purple-grey in color, tubular, and ribbed (13 prominent veins), 5-toothed, pubescent, and sleek surface for having oil glands chief source of oil for extraction, corolla bi-lipped with bluish-violet hue. Flowering takes place during mid to late June to early July.

Popular ‘English Lavender’ cultivars are ‘White Dwarf Nana Alba’ (white), ‘Rosea,’ ‘Jean Davis,’ and ‘Lodden Pink’ (pink), ‘Twickle Purple,’ ‘Dwarf Blue,’ ‘Hidcote,’ ‘Royal Purple,’ ‘Loddon Blue,’ ‘Middachten Nana Atropurpurea,’ ‘Mitcham Cray,’ ‘Munstead,’ and ‘Summerland Supreme’ (purple), ‘Backhouse Purple,’ ‘Bowles Early,’ ‘Compacta,’ ‘Folgate,’ ‘Graves,’ ‘Gray Lady,’ ‘Gwendolyn Anley,’ ‘Irene Doyle,’ and ‘Maillette’ (purple-blue). ‘Irene Doyle’ cultivar flowers twice in a year (Tucker & DeBaggio, 1984) and most commercially acclaimed for excellent fragrance and high concentrations of essential oil. It was the first identified recurrent blooming lavender. ‘Susan Belsinger’ (common name – ‘Dark supreme lavender’) is example of another recurrent bloomer variety. A popular variety of lavender namely ‘Lady’ (Late Ted Torrey developed it) possesses unique

attributes such as quick germination (within 14–28 days; 78% germination rate) and blooms in the first year.

Lavandin, botanically known as *L. x intermedia*, synonymously *L. hybrida* (*L. angustifolia* [broad leaf type]  $\times$  *L. latifolia* [short leaf type]). It is a sterile hybrid usually propagated vegetatively. Bracts are ovate-rhombic in shape (width: length 1.33:3) and bracteoles are 1–4 mm long, hints some similarity with English lavender. Plant height (3 ft.) and leaf size duo are larger in lavandin than English lavender while lavandin blooms 1 month later than English lavender. Lavandin contains significantly higher concentrations of essential oil which influence commercial growers for selection. Commercial lavandin cultivars are ‘Grosso,’ ‘Abrialii,’ ‘Super,’ ‘Standard,’ ‘Maime Epis,’ ‘Dutch,’ ‘Grappenhall,’ ‘Hidcote Giant,’ ‘Old English,’ ‘Provence,’ ‘Seal,’ and ‘Silver Gray’ (McCoy, 1999).

### 8.8.3 TENDER LAVENDERS

‘Spike Lavender’ known as *L. latifolia* comes under this category due to its non-hardy nature. It is native of Mediterranean region. It is one of the species used to develop lavandin hybrid and also grown as source of essential oils. It usually attains the height of 3 feet. ‘Woolly lavender,’ a variety of *L. lanata* is used exclusively for potpourri as it has balsam lavender fragrance. It has lilac-colored spikes usually flowers during midsummer. *L. heterophylla*, another tender lavender grows up to height of 4 feet in height and appropriate for container growing. Characteristically, it has irregular shaped, toothed margin, grey-green foliage. ‘French lavender’ or ‘Fringed lavender’ (*Lavandula dentata*) grows commonly in warmer part of Spain. It is treated as an ornamental annual. It has its linear-oblong shaped (1.5 inches long), rounded toothed margin leaves with pubescent texture. It generally attains the height of around 3 feet. It has spike inflorescences (1.34-inches long and 0.5 inch in diameter). Bracts are dark purple, oblong to oval-shaped (1/2 inch in length and 1/4 inch wide) hold purple-colored flowers. It possesses rosemary-scented flowers which promote its use for potpourri production. *L. stoechas*, ‘Spanish Lavender,’ is another one grows up to 4 feet tall. It has linear to oblong, lance shaped leaves (3/4 inch in diameter), dark purple elegant flowers used in dry flower industry. They are quite tolerant in acidic soils than other lavender varieties but tender in nature *L. pinnata*, *L. canariensis*, and *L. multifida* (fern-leaf lavender) have some distinguishing characteristics like lacy, finely divided fern-like leaves and solitary spikes in threes (trident form). They are

well-adapted for container growing especially used in U.S. *L. canariensis*, an annual, characterized for its feathery foliage, spike inflorescence, deep-blue hue and turpentine scent. They are the inhabitant of Canary Islands. *L. x allardii*, or ‘Giant Lavender’ is a tender hybrid (*L. dentata* x *L. latifolia*) usually 5 feet tall, spreads around 4 feet, have characteristic scalloped leaves and violet-purple colored flower heads. Another hybrid is *L. sawyers* (*L. angustifolia* x *L. lanata*) which is a half-hardy type with grey hued foliage, blooms hue ranges from lavender-blue to deep purple commonly used for crafting and potpourri (McCoy, 1999).

## 8.9 CULTIVATION

*L. officinalis*, synonymously known as *L. angustifolia* (English Lavender), is the most common cultivable species of lavender albeit diversified lavender cultivars are found in significant number. *L. dentata*, *L. stoechas* and *L. multifida* (Egyptian Lavender) – these are other commonly grown lavender species. According to Seidler-Łytkowska et al. (2009), to produce high quality raw material and to facilitate the crop rotation, adoption of organic farming is quite vital. In fact, the demand of organically produced lavender flowers is increasing day by day in cosmetic industry. To meet the burgeoning demand of lavender raw materials for pharmaceutical and cosmetic industries, the quality production in terms of high concentration of active ingredients, high yield, pathogens, pesticides, and heavy metals free materials are quite vital. Seidler-Łytkowska et al. (2014) evaluated the efficacy of ‘Organic’ and ‘Conventional’ mode cultivation of lavender with the aim to find the impact of both mode of cultivation on fresh and dried flower yields, quality, yield, and purity of seeds, weight of 1,000 kernels, essential oil content percentage and its composition and microbial contamination. Definitely, they welcomed the produce of organic origin. Another field experiment on the influence of natural (organic) method of cultivation on the quality yield of lavender flowers had been conducted in Poland during 2008–2010. It is evident that organic method is significantly better than the traditional method. Seidler-Łytkowska et al. (2014) also reported that one of the vital attributes of lavender blooms is the essential oil yield which is not at all affected by localization rather the mode of cultivation affect greatly. Investigators confirmed that organically produced flowers yield essential oil and number of seeds at more satisfactory level.

### **8.9.1 CLIMATIC REQUIREMENTS**

‘English Lavender’ is basically a hardy crop. It basically grows in the range of 700–1,000 m above sea level but *L. angustifolia* grows sometimes >1,700 m above sea level while *L. latifolia* prefers lower regions. At the height of 700–1,000 m above the sea level, lavandin can grow satisfactorily. It can tolerate moderate frost to drought while ‘Spike lavender’ can’t withstand frost. Their sensitivity towards high humidity is quite common. In general, high temperature conditions pose negative impact on essential oil quality as cooler conditions are preferable for getting quality oil content (Anon, 2009). Actually, varietal differences are the root cause of different climatic requirements.

### **8.9.2 RAINFALL**

It needs an annual average rainfall range from 300 to 1,400 mm. Excessive irrigations are discouraged. Dry spell is required between irrigational routines.

### **8.9.3 SOIL REQUIREMENTS**

Sandy to sandy-loam soil or gravelly soil with good drainage capacity and pH ranges from 5.8–8.3 found appropriate for lavender cultivation. It requires full sun condition. Low-fertile soils are unsuitable (Anon, 2009). High moisture level in soils results in poor plant growth and causes diseases. Specifically, ‘English lavenders’ prefer alkaline soils while in contrast lavandin requires acidic soils.

### **8.9.4 SOIL PREPARATION**

Natural soil condition is most preferred to develop healthy lavender plants since soil conditions affect the oil qualitative and quantitatively. Soil analysis before site selection should be made, so that, proper soil amendments could be added. Balanced mineral status and correct pH are the key to successful cultivation. Mineral deficiencies or its excess quantity, organic status and carbon ratios affect the growth of lavender plants. Organic matter content (OMC), soil texture, structure, and type, nutrient, and mineral status are

integrally related with each other for having optimum plant growth. Appropriate monitoring of soil health status is quite vital. Good topsoil is another essential requirement for lavender cultivation since it contains high humus content, balanced minerals and plant nutrients. Conclusively, optimum soil status can only cause optimum lavender plant growth.

### **8.9.5 PLANTING**

#### **8.9.5.1 SLOPE**

On a sloppy land, lavender cultivation could be carried out. It has found that North or North West facing slope are better for harvesting quality produce due to receiving maximum sunlight.

### **8.9.6 PLANTING DENSITY/SPACING**

Generally, row-to-row spacing of 1.2–2.0 m and plant-to-plant spacing of 30–60 cm is recommended for lavender cultivation. It results in planting density of 8,000 to 28,000 plants per hectare (Anon, 2009). Several factors like soil moisture content, type of variety, cultivation, and harvesting strategies also affect spacing between plants. High density planting involves higher input cost but causes high yield too consequently provide high profit. Longevity of lavender plants could be as long as 10 or 15 years, if managed appropriately.

### **8.9.7 PLANTING DATE**

Autumn and spring, these 2 seasons are appropriate for lavender plantation. Former planting season is best where climate is mild since lavender prefers winter season. There planting should be started immediately after completion of frost condition.

### **8.9.8 FERTILIZATION**

Lavender cultivation could be adopted in nutrition deficit soils. Excess N<sub>2</sub> content in soil can impair oil quality as well as make plants very lanky and



enhance weed competition. Polydeonny et al. (1979) recommended 0.8 kg of nitrogen, 0.2 kg of phosphorus and 0.8 kg of potassium for the production of 100 kg of inflorescence. The N<sub>2</sub> dose should be applied in 3 to 4 split doses throughout the growing season. Phosphorus and potassium requirements are low but may vary according to soil type and nutritional status. To maintain soil pH lime could be added.

### **8.9.9 IRRIGATION**

Irrigation during the first 2 years is necessary; otherwise, for lavender, moderate irrigations are fine unless they suffer from excessively low rainfall. Irrigation routine should be critically maintained during blooming seasons. Overhead irrigation is discouraged as it may increase the chances of disease infestations, that's why drip irrigation is preferred most. It may also control weed growth effectively. Irrigation may increase production in mature plantings.

### **8.9.10 WEED CONTROL**

Weeding is an essential operation for lavender cultivation. Around 2–3 weeding sessions annually are required to make the land weed free. Hand-hoeing and mechanical weeding with a tractor-drawn cultivator is highly recommended to control of weeds without any root damage. Mulching could be also another effective measure. On one hand, it restricts weed growth and retain soil moisture content for longer period, on the other hand. Drip irrigation is encouraged in this regard. Distillation waste in compost form is quite useful as organic mulching agent. Cover-cropping practices are also advised while mulching with compost or grass will inhibit weed growth. But thick mulching may cause stem rot due to excess retention of moisture, so, sufficient should be taken. As of now, any information regarding application of herbicides has not been found.

### **8.9.11 OTHER CULTIVATION PRACTICES**

Pruning, is an essential operation which involves removal of apical portion of plant shoots to promote emergence of multiple flowering shoots. It also develops a sturdy plant framework. For first 2 years pruning is quite vital

but 2 years onwards it should be made separately in autumn after harvesting because pruned plants usually allowed to retain 2–3 leaf bearing nodes for vigorous growth resumption. But degree of pruning (heavy or low) usually depends on type of cultivars. For quick and slow growing cultivars heavy and light pruning should be adopted, respectively. Specialized trimmers are used for lavender pruning. Development of windbreaks as a protective strategy could be adopted to protect lavenders from winter injury as they are susceptible to freezing injury. During harvesting, flowers and leaves are plucked separately for oil extraction purposes.

### **8.9.12 LAVENDER IMPROVEMENT AND VARIETY CULTIVATION**

In France, Russia, Ukraine, and Moldova diversified augmentation measures for having increased lavender plantations and essential oil production has been adopted. Not only that, hi-tech breeding technologies have also been developed to improve wide array of lavender characteristics counting flower yield, essential oil content's quality and quantity, content of linalyl acetate, cold tolerance, etc. Earlier lavender improvement programs involved chiefly testing, selection, and mode of propagation of superior seed-derived plants but later advanced hybridization techniques, heterosis breeding, polyploidy breeding and mutagenesis (using chemical mutagens and ionization radiation) were also adopted as effective improvement measures (Singh et al., 1989; Louzina, 1968; Romanenko, 1973).

Since 1950s, several lavender improvement strategies had been adopted in Bulgaria (Dimitrova, 1959). Currently, IRAP (Institute of Roses and Aromatic Plants) in Kazanlak, Bulgaria has introduced some more advanced technologies quite effective for further lavender breeding program. Clonal selection, intraspecific hybridization, gamma-irradiation, and chemical mutagenesis had resulted in the development of >10 highly productive lavender varieties (Dimitrova, 1959; Stanev, 2007, 2010; Topalov, 1962, 1969; Staikov & Boyadzhieva, 1989; Raev & Boyadzhieva, 1988). 'Hemus,' 'Druzhba,' 'Karlovo,' 'Sevtopolis,' 'Yubileina,' 'Raya' and 'Hebar' are key lavender cultivars used commercially in Bulgaria currently. Among these varieties, the total cultivation areas under 'Hemus' and 'Sevtopolist' varieties have found more due to their promising essential oil quality attributes.

As compared to the sexually (using seeds) and asexually (by cuttings) propagated lavender populations, selected accessions of lavender are more preferred for commercial propagation since rate of flowering and yield

percentage of essential oils both are manifold times higher. According to Stanev et al. (2016) the essential oil yield percentage is two to threefold times higher in case of seed propagated populations than vegetative propagated one. Around 30% increase in flower yield also found in seed propagated plants. The relative content of all chemical constituents also lies within optimum range. Due to cultivation of many promising selected varieties, the production rate of blended essential oils is also high in Bulgaria. From the above discussion, merits of growing locally available superior lavender varieties commercially are quite lucid.

Supreme quality and high adaptability to adverse climatic condition of Bulgarian lavender varieties facilitate their spreading in neighboring countries. As for example, in Romania the promising Bulgarian variety 'Karlovo' is predominantly cultivated since 1998 (Pohrib & Nistor, 2012). Apart from that in Turkey several other Bulgarian lavender varieties are also cultivated. According to Baser et al. (2005) the varieties 'Druzhiba' and 'Hemus' cultivated in Turkey had shown high enantiomeric purity of linalool and linalyl acetate. A study made by Kara & Baydar (2013) revealed that in Isparta region of Turkey, Bulgarian 'Raya' and 'Vera' varieties had performed very well especially regarding their upliftment of qualitative and quantitative attributes. 'Hemus' and 'Raya' both varieties are highly tolerant to uncongenial climatic conditions (Stanev, 2010). CIMAP Regional Center, Kashmir, India, introduced in 1978 the cultivation of Bulgarian var. 'Karlovo' for cultivation and further breeding improvement (Singh et al., 1989).

### **8.9.13 STRATEGIES AND CONSTRAINTS OF LAVENDER CULTIVATION UNDER BULGARIAN CONDITION**

From the beginning, Bulgaria ranked top for Lavender cultivation, especially during the 21<sup>st</sup> century. The significant increase in its cultivation is really noteworthy. Many new, advanced cultivation management and post-harvest practices have been introduced but effective implementation of those to keep lavender production in sustainable manner. Hence, sustainable production can only maintain the status of Bulgaria as world's top lavender producer and also supplier of supreme quality essential oil. Hence, some specialized strategies and their consequences followed during 21<sup>st</sup> century in Bulgaria have enumerated below.

Owing to complete mechanization system of lavender cultivation and processing the steady production of lavender is evident. The huge enhancement

of total area of cultivation and extended lavender plantations coupled with various machinery agricultural practices (for example harvesting, tilling, etc.) and enhanced demand. Further improvement in plant architecture (like erect plant posture and solid flower pedicel) for easy mechanized tillage and harvesting is need of the hour. These features will cause least damages to the plants during mechanized harvesting.

The burgeoning popularity due to high quality of produce and wide range of adaptability to local weather conditions are the main rationale of expansion of areas under lavender cultivation. In Bulgaria, lavender has also been cultivated at outskirts beyond the conventional growing areas but still it also has some limitations regarding its adaptability. Due to varied soil and climatic conditions (that means nonoptimal conditions) sometimes the quality of extracted lavender oil may get deteriorated. This period considered as 'Bad' years. So, species/variety specific conditions are vital indeed. Further improvement of existing gene pool, selection of superior breeding lines and best performed varieties and successive stability testing in terms of essential traits (for example EO and flower yielding capacity and its quality, growth parameters, etc.) – could be considered as further directions for further improvement of lavender cultivation (Stanev, 2010).

Enhanced flower and essential oil yield are two key tasks for lavender producers. To keep pace with increasing demand, development of high oil yielding varieties through genetic modifications is essential but that needs continuous pursue of cutting-edge research. Complex genetic background of lavender has made this work quite tough. Further research on genes and alleles associated with biosynthesis oil compounds and marker assisted selection (MAS) of superior lavender varieties are only ways to fulfil commercial demands. Not only new variety development, essential infrastructure for optimum preservation of essential oils is also important.

Barring the aforementioned aspects, suitable oil extraction procedures should be also adopted. Generally, steam distillation methods are used in Bulgaria for oil extraction but due to increased consumer interest and demand during last decade, 'Solvent' or 'Supercritical CO<sub>2</sub> extractions' methods are far more appropriate. To adopt such modern extraction technologies, improved, new high oil yielding varieties are also needed. Hence, it can be speculated that to manufacture new, innovative value-added products, new varieties and advanced oil extraction techniques should be introduced which may augment the market demand throughout the world.

Use of quality and certified planting materials are essential measures towards lavender improvement. Use of homogenous, seed, and vegetative

propagated lavender varieties for reestablishment of lavender plantations could be made. It can significantly increase flower and essential oil yields duo. A paradigm shifts in Bulgarian agriculture system have effectively changed the production and supply systems. Rather than free market offering system of planting materials made earlier by marginal farmers now changed into centralized production and distribution system by IRAP. But this new system is putting question mark on maintenance of existing lavender gene pools and also preservation of last century production models used to produce pre-basic, basic, and standard propagation materials. According to Stanev et al. (2016) in Bulgaria there is no well-established system on quality checking of lavender planting materials which may cause the distribution of either mixed varieties or inferior quality seed derived planting materials. Hence, certified asexually propagated planting materials and quality check services at reasonable price rate can merely handle the increased demand.

#### **8.9.14 PROPAGATION**

- 1. Seeds:** Sexual (seed) and asexual (vegetative) propagation both are suitable for lavender but considering the merits and demerits, sexual propagation should be discouraged in lavender due to the slow growth rate and sporadic germination rate. Generally, lavender seeds are planted during late spring or early of summer (30–36 inches apart row-to-row). Usually, after germination 6 months are needed to attain transplantation size. Hence, vegetative propagation using stem cuttings, layering, and division of roots for lavender found most appropriate. Variation at intra-specific level, inconstant growth habit, color, essential oil composition and staggered maturity often noticed in seed propagated varieties due to overlapping of traits. These above stated problems are usually not evident in case of asexual propagation, furthermore, it is highly suggested to retain desirable features.
- 2. Cuttings:** Use of stem tip cuttings for lavender propagation is quite common. Owing to their non-winter hardiness and poor rooting ability cautious selection of cultivars are essential. According to McCoy (1990), disease free stem tip cuttings of 4 inches length could be used as propagating materials, but nipping of buds and stripping off leaves from bottom of cuttings are essential operations to mitigate the transpiration water loss. A soil medium containing

perlite and peat moss, each 1 part found suitable for cuttings growth. The size of plastic pro-trays may be 11×21×2.5-inches can hold 100–300 cuttings. Bottom heat (75–80°F) coupled with light nutrition can enhance the rooting from lavender tip while long day condition (12–14 hrs./day) and proper ventilation can improve rate of germination. These conditions seemed conducive to produce marketable plants within 2 months.

3. **Layering:** Simple layering technique can be a viable mode of propagation for lavender although sprouting time and number of regenerants plant<sup>-1</sup> are quite less in this method. It's the appropriate technique for woody herbs. So, the plants having long, healthy flexible stems are only suitable to propagate by layering. In case of ground layering, the trailing branch is bend down at the soil surface level after removing foliage(s) for easy rooting while for air layering peeling off of 1–2 inches of bark of the selected branch followed by scrapping of exposed cambium portion and covering up with moist soil or a sphagnum moss and perlite combination. The rooting portions should be kept moist to get optimum rooting (Oliver, 1996). After rooting, the regenerants can be detached from mother plant.
4. **Tissue Culture:** *In vitro* or micropropagation is one of the feasible ways for mass production of the target plant. Adopting this technique, lavender varieties can be developed within short span from hybrid stock plants. It is the most effective mode to produce genetically identical plantlets, but its use is limited for high expenditure especially marginal farmers generally avoid this technique for its high cost, specialized laboratory infrastructure and skilled manpower.
5. **Field Culture:** South facing raised beds with fertile, well-drained soil having pH between 6.4 and 8.3 is most suitable field condition for lavender culture (McCoy, 1999). Hybrid soil composed of compost or peat moss will cause good growth while cover crop as a source of organic nutrition or manure could be also grown in lavender field. Optimum P-P distance is 1 feet and R-R is 2 feet. Optionally, another spacing method where spacing of 18 inches are provided P-P during 1<sup>st</sup> year of growth followed by removal of every other plant result in 36 inches gap between P-P in next consecutive year could be also adopted to get maximum flower and essential oil yield. Uprooted plants can be replanted in new rows. Ideal pruning time for lavender is mid-April. Removal of 1/3 to 1/2 of the stem length

of fully established plant could be adopted for boosting growth from plant base. Mulching during frost is highly recommended but heavy organic mulching materials like sawdust, wood chips, etc., should be avoided to restrict fungal and insect infestations. Proper spacing (approximately 2–3 feet), pruning or trimming operations are essential to protect plants from some fungal infections. For commercial lavender species plantations viz. English lavender (*L. angustifolia*), Lavandin (*L. x intermedia*) and spike lavender (*L. spica* or *L. latifolia*) sufficient spacing between rows for tractor access should be given. Dead and dried plants should be uprooted from the main field.

### **8.9.15 HARVESTING**

Generally, hand picking method of harvesting is followed in case of lavender in India but in other foreign countries (especially in Bulgaria) specially designed machineries are employed for getting utmost efficacy. Harvesting time usually varies according to the purpose of utilizations of harvested materials. When lavender flowers are harvested for essential oil extraction then blooms are harvested at half-opened condition while dried and full opened blooms are used to sell as flowers bundles or dried buds at local outlet.

English lavender (*L. angustifolia*) cultivars basically used as dry flowers due to extended persist of flowers on stems whereas ‘Lavandin’ cultivars suitable for essential oil and potpourri purposes. Lavender twigs (flower with pair of leaves) should be cut with sharp secateurs when 1<sup>st</sup> 2 florets have unfolded. Interestingly, not only flowers, but its pedicles can also contribute for essential oils. Effective harvesting of lavender flowers from the same plantations could be made up to 30 years. To get optimal ester levels, flowers should be harvested at full bloom stage from 2<sup>nd</sup> year onwards. Fully sunny conditions should be avoided during harvesting to get maximum oil content (McCoy, 1999).

Biomass production, yield percentage and phytochemical composition of essential oils greatly vary based on shading percentage and harvesting time (Mambri et al., 2018). The author reported that hydroponic (soil less) culture of *Lavandula dentate* can effectively increase all 3 aforementioned parameters. Sand is a good medium for this type of culture can cause the harvesting at 150, 213, and 320 days after planting date (DAP) in winter, spring, and summer, respectively but to get the produce earliest 50% of shading is necessary. About 70 g of fresh mass of leaves and inflorescences were found sufficient for essential oil extraction grown hydroponically.

The maximum FM of inflorescences were found at 213 DAP while highest number of leaves obtained at 320 DAP grown under shade less condition. Around 31 compounds including 1,8-cineol, camphor, and linalool were identified in hydroponically grown lavender variety.

### **8.9.16 MATURING TIME AND METHODS**

Generally, lavender flowers are harvested at full bloom stage as their maturity level determine several qualitative and quantitative parameters. Best harvesting time is ending part of December and early part of January (depends on season of individual countries). Mass harvesting operations should be essentially planned during the soothing weather condition. Very high temperature and windy condition can deteriorate the oils volume. High temperature causes the free water in contact with the oil and reduce oil quality. On the other hand, too cold weather affects the ester development, hence, harvesting should be halted unless and until weather becomes warmer. For fresh and dried flower markets, blooms must contain long pedicels and must be more mature than the blooms/buds usually picked for essential oil extraction purposes. Before subjecting lavender buds into steam distillation process, removal of stems is crucial. Sometimes, organic solvents or CO<sub>2</sub> could be also employed for its effective extraction (Ernst, 2017).

## **8.10 POST-HARVEST HANDLING**

### **8.10.1 SORTING AND DISTILLATION**

Steam distillation is the most effective method for lavender essential oil extraction. It determines the quality of the oils. Optimum pressure and temperature are essential to maintain the quality since higher degree of these two conditions alter the molecular structure of fragrance molecules cause modification of chemical constituents. Quantity of yield may also differ essentially on the maturity level of the produce and weather conditions.

### **8.10.2 SOLVENT EXTRACTION**

Lavender and lavandin based ‘Concrete’ and ‘Absolute’ – are two widely used components of perfumery industry. To make these two usually solvent extraction methods are adopted. In this method toluene, hexane, and petroleum ether are popularly used as potential solvent materials. To produce concretes, first, fresh plant materials are treated in solvents followed by



evaporation of solvents leaving ‘concrete’ residue. It has importance especially in soap industry. Ethanol is sometimes mixed with concrete for further refinement purpose. Interestingly, this concrete-ethanol mixture is used to produce ‘absolute,’ a wax-free residue produced after evaporation of ethanol from cooled and filtered mixture. Conventionally, the loss percentage from concrete to absolute is 50%.

### **8.10.3 DRIED FLOWERS**

The conventional ‘Hang Drying’ (inverted) method is adopted to produce dehydrated lavender flowers employed extensively in pot-pourris. Sometimes, dried flowers are removed from spikes and packed in sachets well-insulated by paper. Generally, to yield 1 kg of dry flowers 8–10 kgs of fresh mass is needed.

### **8.10.4 GRADING**

Esters, linalyl acetate and linalyl butyrate – these three chemical compounds are liable to pleasant fragrances of lavender. Grading plays significant role to produce quality value-added products. Ester content (measured by chemical analysis) is a prime factor to produce quality essential oil, hence, grading of lavender blooms are made following this attribute (Anon, 2009).

### **8.10.5 PACKAGING AND STORAGE**

Careful handling procedure of essential oil is vital for its volatility. It must be stored in glass made air-tight dark colored container without allowing them to come in contact with heat or heavy metals. Fluorinated plastic, treated aluminum, and dark glass or ceramic containers, can be also used as viable storage containers. Higher degree of viscosity and darkness can cause deterioration. Optimum packaging and preservation technique could make it use-worthy up to 6 months to 2 years. Supreme quality, professional, scientific, and clean labelling are essential for value added marketing.

## **8.11 PATHOGENS ASSOCIATED WITH LAVENDER**

- *Armillaria mellea* – root rot.
- *Cuscuta epithymum* – Dodder vine – (parasitic flowering plant).
- *Fusarium* sp. – root rot.

- *Fusarium solani* – wilt.
- *Meloidogyne incognita* – Southern Root-knot Nematode.
- *Phoma lavendulae* – stem blight.
- *Phytophthora nicotianae* – root rot.
- *Phytophthora* sp. – wilt.
- *Pythium* sp. – root rot.
- *Septoria lavandulae* – leaf spot.
- *Verticillium* sp. – wilt.

## 8.12 VALUE ADDITION

### 8.12.1 LAVENDER ESSENTIAL OIL

Qualitative attributes of lavender essential oil usually vary according to the certain species. ‘Lavender flower oil’ and ‘lavender spike oil’ are two distinct categories of lavender essential oil. The former one is a transparent oil, insoluble in water with a density of 0.885 g/ml while the latter one is the distillate form of essential oil with a density of 0.905 g/ml excreted from *Lavandula latifolia* but an impure compound. It is the complex mixture of phytochemicals, including linalool and linalyl acetate.

*L. angustifolia* and *L. X intermedia* used effectively for essential oil extraction. *L. X intermedia* produced in Australia province could yield 4,000 lb of fresh flowers per acre. From this amount off fresh blooms 53 lb per acre of essential oils could be extracted (Foster, 1984). Foster (1984) also found that 300–1,800 lb per acre of fresh flowers of *L. angustifolia* could yield 12–15 lb per acre of essential oil while *L. X intermedia* grown out of the Australian province could yield 53–67 lb per acre of essential oil at the expense of 3,500–4,500 lb per acre of blooms. *L. angustifolia* and *L. X intermedia* grown in New Zealand, could yield 30 gal per acre and 50 gal per acre of essential oil, respectively (Douglas, 1991). The quality of both of these species of flowers is suitable enough to make dry flowers. Sturdivant & Blakley (1999) confirmed that 150–200 lb per acre and 250–300 lb per acre of dry flowers could be produced from *L. angustifolia* and *L. X intermedia*. On the other hand, the dehydrated Lavender blooms could be also used for essential oil extraction as reported by MC Gimpsey (1994). He stated that from 12,000 dried bunches of flowers (per acre) of *L. angustifolia*, 2.6 gal per acre of essential oil could be produced while 16,000 dried bunches of blooms (per acre) of *L. X intermedia* could extract 14.7 gal per acre of essential oil.

Basically, these two species are cultivated at Bridgestowe estates, Australia, and Red bank research center, New Zealand.

### 8.12.2 PROCEDURE OF LAVENDER OIL PRODUCTION

Steam distillation causes the elimination of polar compounds results in production of pure essential oil (Masango, 2005). 'June' harvested blooms are firstly packed in steel containers having some air pockets for necessary air circulation and then steaming is made at the bottom of loaded container (using a boiler) at very low pressure. Owing to the heating process, oil contained floral parts start to release oils, then, to condense the vaporized form of hot lavender oil, a cold-water channel is fixed with steady water supply at the center of steel container. Polarity and density of water and oil make two distinct layers inside the holding tank caused due to condensation of essential oil. At the end of the procedure, barring lavender essential oil, water is drained off (Chanamai et al., 2002).

Essential oil made from 'English Lavender' (*L. angustifolia*) is susceptible towards some antibiotic resistant bacteria(s) (like VRE [Vancomycin-resistant *Enterococcus*] and MRSA [methicillin-resistant *Staphylococcus aureus*]) (Nelson, 1997; Lis-Balchin, 1998; Hammer et al., 1999). Some research investigations support the anecdotal use of wide range of *Lavandula* oils (e.g., *L. angustifolia*, *L. allardii*, *L. x intermedia* var. 'Grosso,' *L. x intermedia* var. 'Seal,' *L. x intermedia* var. 'Miss Donnington,' *L. x heterophylla* and *L. stoechas* var. 'Avonview') which significantly contain antibacterial properties but the antibacterial properties of *L. heterophylla* is still behind the veil. Its inhibitory action against range of bacteria(s) counting *Streptococcus pyogenes*, *Exterobacter aerogenes*, *S. aureus*, *Proteus vulgaitis*, *Pseudomonas aeruginosa*, MRSA, *Citrobacter freundii*, *Escherichia coli*, VRE, *Shigella son net* and *Proyionibacteriuiin acnes*' are really noticeable.

The efficacy of lavender essential oils against bacteria(s) are also species specific [for example oils excreted from *L. angustifolia* and *L. x intermedia* showed effective impact against few bacteria(s)]. Chemical compositional differences of essential oils determine their efficacy against certain bacteria. According to Moon et al. (2004) there is no correlation between the quantity of chemical compounds and its efficacy (such as *P. aeruginosa* was non-susceptible to any *Lavandula* oil). These results endorse their anecdotal uses merely. Barring antibacterial properties, they also possess some clinical utilities. The MIC of lavender oil obtained from *L. angustifolia* and *L. latifolia* is equivalent to tea tree oil. Inouye et al. (2001) reported that the degree of efficacy of essential oils extracted from above stated species were 0.32% against *S. pyogenes* and *S. aureus*, 0.16% against *Haetiioyliilus influenzae*, and >0.32% against *E. coli* which further endorse the above statement. From

the above view, it can be recommended that lavender oils are more appropriate for topical applications (as a prophylactic of minor ailments) rather than using against any serious infections.

Antifungal properties of lavender essential oils had been also identified by Daferera et al. (2000). According to them, their oil prevents germ-tube formation. As for example, to get significant effect against *Trichophyton mentagrophytes* and *Aspergillus nidulans*, EO extracted from *L. angustifolia*, and *L. x intermedia* is most suitable one while EO of *L. stoechus* was only impactful for some agricultural fungal strains (like *Leptosphaeria maculans* and *Sclerotinia sclerotiorum*). Moon et al. (2004) suggested that *Lavandula* oils could be effectively used against both agriculturally and medically important fungal strains. Inactivity of *Lavendula* hydrosols had been also confirmed by some authors (actually distillate water produced as a by-product of steam distillation process contains various chemical components) for any microbial treatments. Thus, for certain therapeutic treatments use of species-specific Eos is beneficial. Further *in vitro* studies on this aspect are need of the hour. Vapor treatment (used in aromatherapy) with optimum vapor concentration and duration could significantly heals ranges of antifungal ailments especially potentially inhibit sporulation at a little amount (Moon et al., 2004; Inouye et al., 1998, 2000, 2001). During early stage of infection, prolonged gaseous contact by vapor treatment with high concentration of essential oils are not necessary (Inouye et al., 2001).

Since time immemorial essential oils are used for getting therapeutic benefit. Lavender essential oil is highly acclaimed in aromatherapy to get relief from stress and depression symptoms, to improving 'mood' and reduce anxiety (Cavanagh & Wilkinson, 2002). Aromatherapy causes both psychological and physiological effect using the odor of volatile compounds of lavender essential oils. It affects the limbic system, particularly the amygdala and hippocampus. Several authors have affirmed that volatiles of lavender essential oils are potent enough to improve moods and sleeping pattern of patients (Cavanagh & Wilkinson, 2002; Bumett et al., 2004; Camped et al., 2004). Usually, inhalation and topical application are two popular methods of use of lavender essential oils in aromatherapy, but the potential benefits of each mode need to be reevaluated in a comparative manner. A study made by Snow et al. (2004) confirmed the affirmative impact cutaneous application as compared to inhalation mode (purely olfactory form of aromatherapy) of lavender essential oils during aromatherapy in chronic dementia patients. 'Linalool,' key ingredient of lavender essential oil can effectively lower down the systolic blood pressure and skin temperature as compared to

placebo group of patients but only through the percutaneous administration (Heuberger et al., 2004). Another study made by Soden et al. (2004) explained that the use of inert oil containing lavender essential oil could not cause any long-term significant benefits to heal pain, but anxiety related problems could be effectively improved by mixed oil massage. But irrespective of massage oil ingredients (i.e., inert carrier oil and mixed lavender oil), generally the depression scores of 'massage group' of patients were less than the 'control group.' Lavender aromatherapy coupled with radiotherapy can also effectively impair the anxiety (Graham et al., 2003). According to some authors, lavender odor has some integral relation with positive emotional states and therapeutic benefit (Alaoui-Ismaili et al., 1997; Tysoe, 2000; Masago et al., 2000; Millot & Brand, 2001). Inhalation treatment using 10% lavender oil for 3 mins could significantly cause relaxation, lower anxiety scores, improved moods and increased alpha power in EEG (an indication of increased drowsiness) (Diego et al., 1998). The aforementioned result can easily exemplify the role of lavender essential oils odor on our olfactory system. Aromatherapy using tea tree, rosemary, and *L. angustifolia* oils can minimize psychological stresses of chronic neurological patients without causing any harmful physical or behavioral changes as reported by Walsh & Wilson (1999) by their pilot study. Short-term treatments through acupoint stimulation using lavender essential oil can also bring down pack pain (Yip & Tse, 2004). Aromatic lavender oil is also used in acupressure treatment for getting relief from pain. One-hour inhalation treatment by essential oil extracted from *L. x intermedia* 'Grosso' can bring analgesic effect without developing any sedative symptoms (Barocelli et al., 2004). This oil can significantly reduce the acetic acid-writhing response in a naloxone-sensitive manner. Barring analgesic effects, inhalation mode of aromatherapy can also elicit several other affirmative appraisals and positive retrospective evaluation (Cavanagh & Wilkinson, 2005; Gedney et al., 2004). It has been also reported that the oral administration of lavender oil, or its key components like linalool or linalyl acetate, could prevent acute ethanol-induced gastric ulcers in group of animals (Barocelli et al., 2004). Further extensive investigations should be carried out to determine the synergistic effects of biologically active constituents of 'mixed' lavender essential oils since meagre information(s) are in hand. Several existing inconsistencies in lavender oil research could be solved, through identification of biologically active components and determination of their mode of action which can aid in recognition of a novel therapeutic compound (Lis-Balchin et al., 1998). A constituent of lavender oil namely perillyl alcohol (POH) had been identified

by Samaila et al. (2004); and Liston et al. (2003) as a potential anticancer agent. But in contrast, several authors (Prashar et al., 2004; Matthieu et al., 2004) refuted the statement that ‘lavender – a safe oil’ by highlighting the toxic effects of linalyl acetate (a major constituent) on human skin cells *in-vitro*. Although, lavender oil as a safe topical agent has been recommended by several scientists but as of now its oral administration is not advisable.

## **8.13 BIO-PROSPECTION**

### **8.13.1 ANIMAL STUDIES**

Anxiolytic, sedative, analgesic, anticonvulsive, anticonflict, and neuro-protective properties of lavender is well-known. Inhibition capacity of lavender essential oils against anxiety and depression has been proved based on the results of animal test models (7 days treatment). The antianxiety property of lavender oils had been also evinced by Geller conflict and the Vogel conflict tests in mice. ‘Linalool,’ a key component of lavender oil is liable to anticonflict effects. Koulivand et al. (2012) reported that the anxiolytic effect of lavender oil in rats was almost equivalent to ‘Chlordiazepoxide’ (used as reference anxiolytic). Several authors further confirmed by light/dark test that odor of ‘linalool’ (by inhalation) could effectively cause affirmative impact on anxiety, aggressiveness, and social interaction in mice (Koulivand et al., 2012; Umezu, 2000). On the other hand, ‘linalool’ and ‘linalyl acetate’ – two major constituents can cause local anesthetic effect proved in rabbit conjunctival reflex test (*in situ* and *in vivo* experiments). The test oil (lavender essential oil + linalyl acetate/linalool) dose-dependently provoked the reflex. The dose rate of 200–600 mg/kg of methanolic extracts of lavender can also cause sedative effects in mice proved by their immobility after lavender oil inhalation. Repeated lavender administration results in quick onset of sleep for prolonged duration in mice. Reduced neuro-motor activity and increased plasma level had been observed in mice exposed for 4 hrs. in lavender-fragrance dark cage (Sakurada et al., 2009). Capsaicin induced nociceptive response could be lessened through intra-plantar injection of linalool. Cholinergic neurotransmitter system enacts vital role in lavender analgesia (Koulivand et al., 2012; Buchbauer et al., 1991; Sakurada et al., 2009). Hence, irrespective of mode of treatments (oral administration or inhalation) lavender essential oils can effectively reduce pain without causing any detrimental effects. Defunct cholinergic system induced ‘spatial memory deficit’ problems could be solved by lavender essential oil treatment. To heal Alzheimer’s disease,

efficacy of dose-dependent lavender oil treatment was proved in rat model while hydroalcoholic extract of lavender could cause anticonvulsant effect in male mice. Pentylentetrazol, nicotine, or electro shock induced convulsion could be minimized by inhalation of lavender in mice. Linalool component is responsible for this anticonvulsant effect may cause a straight interaction with the glutamatergic NMDA sub-receptor as well as GABAA receptors. Its neuroprotective effect had been also investigated on animal models. Water based extract of lavender can minimize glutamate-induced neurotoxicity in rats. Lowered neurological deficit scores, decreased levels of mitochondria-generated ROS and attenuated neuronal injury in focal cerebral ischemia could be caused by lavender essential oil treatment which was proved in mice model (Koulivand et al., 2012; deSousa et al., 2010; Silva Brum et al., 2001).

### **8.13.2 MECHANISMS OF ACTION OF LAVENDER IN THE NERVOUS SYSTEM**

To prove the efficacy of lavender oil on neuronal tissues by inhibiting lipopolysaccharide induced inflammatory reaction in human monocyte (THP-1), a report by Salah & Jager (2005) has been found. Linalool is the key healing agent of lavender essential oil could be used for the treatment of Alzheimer's disease and also as anticholinergic and neuro-protective component. Antioxidant effects of lavender oil provide neuro-protective effect against cerebral ischemia/reperfusion injury. Rotarod activity and level of dopamine receptors (subtype D3) in olfactory bulbs could be enhanced by intra-peritoneal application of lavender oil in mice model due to its association with dopaminergic neurotransmission. Lavender oil modulate GABAergic neurotransmission can improve several nervous system disorders (Aoshimaand & Hamamoto, 1999; Koulivand et al., 2012).

Fos is a nuclear transcriptional factor and neural activation marker controls expression of genes. Lavender oil can inhibit c-fos expression in paraventricular and dorsomedial nucleus of hypothalamus, can control histamine release and anti-DNP IgE-induced tumour necrosis factor-alpha secretion from peritoneal mast cells in mice (Koulivand et al., 2012). Lavender oil can reduce the activity of sympathetic nerves whereas can excite the parasympathetic gastric nerve. 'Linalool' component affects greatly the autonomic nervous system by histaminergic response. Its odor also decreases lipolysis by activating H<sub>3</sub> receptors (histamine neurons and hypothalamic

suprachiasmatic nucleus), heat generation, and increased body weight with high appetite in rats. Other related signaling pathways are activated by lavender induced tyrosine phosphorylation of BIT (immunoglobulin like molecule) (Koulivand et al., 2012; Shen et al., 2007).

### **8.13.3 HUMAN STUDIES**

Clinical efficacy of lavender essential oils obtained whether by its single use or as an adjunct in its other carrier components, raise a serious debate issue although its noteworthy effect on several neurological and psychological disorders have been studied well. Predominant ways of using lavender oil are generally through oral administration and aromatherapy but the latter one gets preference for maximizing the psychological benefits of patients due to inhalation mode of treatment. In inhalation mode, lavender oil acts via limbic system (especially affect amygdala and hippocampus) while in topical application essential constituents (linalool and linalyl acetate) are absorbed by skin and affect our central nervous system (Koulivand et al., 2012).

### **8.13.4 ANXIETY, DEPRESSION, AND LAVENDER**

Importance of lavender essential oils to heal various anxiety disorders are well-informed. Woelk & Schlafke (2010) studied the effect of 'Silexan–essential oil,' prepared from lavender flowers by steam distillation method oil through some clinical trials. The said essential oil at the rate of 80 mg day<sup>-1</sup> was administered orally once in a day for 6 weeks. Treatment was implemented on three categories of patients such as patients having (i) sub-syndromal (mixed) anxiety disorder; (ii) generalized anxiety disorder; and (iii) restlessness and agitation. Consequently, significant improvements of treated group of patients were found over the placebo (control) group of patients. Additionally, it reduced restlessness, disturbed sleep and somatic complaints significantly. Overall, quality of life was improved subsequently. The oral administration of lavender oil preparation (Silexan, 80 mg/day) performed better than lorazepam (used as reference medicine at the dose of 0.5 mg daily<sup>-1</sup>) specially for treating generalized anxiety disorder. Alleviation of anxiety and mood improvement of group of 31 patients were observed as reported by Dunn et al. (1995) through using diluted lavender oil (1% concentration). Another study made by Itai et al. (2000) where significant improvements in 14 female patients who were earlier gone through the



chronic emodialysis process were found after lavender oil treatment. A survey report showed that lavender oil mixed with tea tree and rosemary oils can increase mood scores and psychological distress. Conrad & Adams (2012) reported that lavender aromatherapy (diluted oil @ 2% concentration) in case of any postpartum woman could effectively cause improvements on anxiety and depression level (measured by Edinburgh Postnatal Depression Scale and Generalized Anxiety Disorder Scale) after 1 month of continuous lavender administration. Lavender odor minimizes anxiety of dental patients (Kritsidima et al., 2010). To improve pre-operative anxiety, lavender administration is enough worthy in terms of its efficacy, simple procedure and cost-effectiveness. Clinical research proved that induced anxiety (may be made by some anxiety-provoking film clips) could be reduced by oral administration of lavender capsules, containing 100 or 200 $\mu$ L of organic *Lavandula angustifolia* oil (Bradley et al., 2009). Braden et al. (2009) revealed that positive mood, controlled heart rate, improved galvanic skin response – could be evaluated by continuous administration but non-persistent in nature especially for long duration. A clinical investigation points to anti-depressive effect of lavender. Akhondzadeh et al. (2003) got affirmative response by adopting adjuvant therapy using imipramine (100 mg day<sup>-1</sup>) and lavender tincture (1:5 in 50% alcohol; dose rate 60 drops day<sup>-1</sup>) for 48 adult patients of mild-to-moderate depression. Authors confirmed that the combined effect of lavender and imipramine treatment had effectively reduced the anticholinergic side effects (dry mouth and urinary retention) caused by imipramine (Akhondzadeh et al., 2003; Koulivand et al., 2012).

### **8.13.5 DERMATOLOGICAL USES OF LAVENDER**

The wound healing potential of lavender oil is well-known since World War I, but very finite scientific evidence is available on its success history. It can effectively heal various skin problems viz. psoriasis, dermatitis, and eczema not only that can significantly reduce the scarring. Its topical application can cause obstructions in many allergic pathways (Kim & Cho, 1999).

It is evident in many scientific literatures that application of essential oils can cause allergic or skin irritation reactions. In tune of this, Tisserand & Balacs (1999) cited that the essential oils extracted from *L. latifolia* and *L. angustifolia* couldn't cause any skin irritations, in fact, essential oil of the latter one never causes any phototoxicity, but authors were unable to cite any proves in support of their statement. According to Thomson & Wilkinson (1998), the incident of contact dermatitis was quite less after

lavender administration as compared to tea tree administration, but the report published by Clinical in 2000 exhibited the opposite view. During 1997 the incident of contact dermatitis had increased owing to the enhanced rate of use of essential oils. Sugiura et al. (2000) had reported that the chances of contact dermatitis were as low as 13.9% after lavender oil treatments, but frequent exposure at dried lavender products continuously might enhance the frequency of this disease, as reported during their later parts of study. Coulson & Khan (1999); and Benito et al. (1996) mentioned that the use of lavender pillow, may trigger the allergic reactions. To treat eczema efficacy of lavender essential oils are quite limited but could be used as an alternative of conventional steroids. Anderson et al. (2000) recommended to add 6 drops of lavender essential oil in bath water (at least for 2 months continuously) to lessen the eczema irritations. Walsh et al. (1996) reported the significant improvement in terms of physical symptoms, confidence and self-esteem of severe psoriasis patients. Lavender oil coupled with rosemary, cedar wood and thyme oil could cause new hair growth in alopecia patients. Hay et al. (1998) in their investigation applied the mixture of *Rosmarinus officinalis* (114 mg), *Cedrus atlantica* (94 mg), *Thyme vulgaris* (108 mg) and *L. angustifolia* (108 mg) oil in the scalp of severe alopecia areata patients every night. The evaluation report at an interval of 3 and 7 months revealed the significant reduction of alopecia area with new hair growths.

### **8.13.6 NEUROIMAGING AND LAVENDER**

Different neuronal enhancement (especially in posterior cingulate gyrus, orbitofrontal, thalamus, brainstem, and cerebellum) could be obtained through lavender odor stimulus which indicate the supplemental impact of aromatherapy using lavender oils (Duan et al., 2007). To get improved function in vital olfactory brain structures (entorhinal cortex, hippocampus, thalamus, parahippocampal cortex, primary olfactory cortex, orbitofrontal cortex, insular cortex and hypothalamus), use of diluted form (using dipropylene glycol) of 10% lavender oil could be beneficial (Wang et al., 2005) as evident by functional magnetic resonance imaging (fMRI) (DiNardo et al., 2000). Cortical perfusion increment was also reported after lavender administration. The application of lavender odor through orthonasal (odor perceived through the nose) and retronasal (odor perceived through the mouth) routes could cause activation at central sulcus. Koulivand et al. (2012) reported that orthonasal application resulted a peak in ventral insula while retronasal in right caudate nucleus.

### **8.13.7 ELECTROENCEPHALOGRAPHY (EEG) AND LAVENDER**

According to Gorjiand & Ghadiri (2002), aromatherapy using lavender oil could be useful to treat epilepsy (a neurological disorder). Along with its anxiolytic effect, lavender administration could also improve the EEG pattern. This could be validated by the research report of Holmes et al. (2002) where they found that inhalation of 10% diluted concentration of lavender essential oils for 3 mins could reduce the anxiety level and uplift the mood by increasing alpha power of EEG. Enhanced theta (4–8 Hz) and alpha (8–13 Hz) wave activity could also bring general relaxation effects in treated group of patients. Steam inhalation of lavender oils during aromatherapy could also ameliorate the agitated behavior of severe dementia patients, in fact they become quite modest as reported by (Koulivand et al., 2012; Holmes et al., 2002). According to Sanders et al. (2002) and Moscovitch et al. (2011) lavender application could cause immense relative right frontal EEG activation at baseline.

### **8.13.8 SLEEP AND LAVENDER**

To heal insomnia problem, natural treatment using lavender products could be considered as the most effective remedy. Experimental consequences revealed that lavender odor could improve the sleep quality and lower down the intensity of ischemic heart disease also along with its potential for treating insomnia. Experiment conducted by Lewith et al. (2005) reported the significant lower scores of insomnias verified by Pittsburgh Sleep Quality Index (PSQI) after treating patients (notable female and young aged patients) with lavender odor (6–8 drops). Kasper et al. (2010) exhibited that the oral administration of lavender oil at the dose rate of 80 mg/day could efficaciously improve general mental and physical health, sleep quality and its duration of patients with mixed anxiety disorder without any sedative or drug intervention. Furthermore, the concoction of lavender, basil, juniper, and sweet marjoram's essential oil can improve insomnia in older patients. Aromatherapy using lavender oil could significantly restore the normal sleep duration in case of Benzodiazepine dependent geriatric patients after withdrawing this chemical drug administration (Koulivand et al., 2012). This treatment can cause impermanent relief from continuous insomnia medication and lessen the side-effects of these drugs. It also improves the quality of daytime wakefulness. Williams (2006) found the advantages of lavender oil massage on sleep patterns of children suffered from autism.

### **8.13.9 PAIN AND LAVENDER**

Lavender, as a natural remedy for intractable pain, has gained huge fame. For lowering heart rate, blood pressure, pain, wakefulness, and respiratory rate, foot massage using lavender EO could be beneficial. Lavender oil is not only useful to treat the recurrent aphthous ulceration but also to reduce ulcer size and to increase the rate of mucosal repair. As compared to placebo groups, the patients received oxygen through lavender coated facemask (for 5 mins) had experienced reduced stress level and pain intensity of needle insertion. Blended aromatic oil (lavender, clary sage, and marjoram@ 2:1:1 ratio) massage could reduce the duration of dysmenorrhea. Aromatherapy with lavender essence could cause lowered pain at caesarean section (Sheikhan et al., 2012; Dell & Cornwell, 1994). Opioid administration is mandatory for post-operative breast biopsy surgery. To avoid the use of unsafe drugs, inhalation of 1–2 drops of lavender oil (2%) using oxygen face mask could be highly impactful. Its analgesic effect could be proved by its application on patients who have undergone laparoscopic adjustable gastric banding. But its inefficacy to reduce the perception of pain generated during botulinum toxin facial injection should be also noted. Around 3% lavender oil could alleviate the neck and back pain and cervical and lumbar spine movements through the mode of acupressure treatment. Inhalation treatment of lavender essential oil (by rubbing 2–3 drops onto the upper lip) could heal acute migraine headaches and its associated symptoms. Blended version of body massage oil (in aromatherapy) using lavender oil with geranium, rose, jasmine, almond, and primrose oils could heal menopausal symptoms (like menstrual pain, hot flushes and depression) (Koulivand et al., 2012).

### **8.13.10 COGNITION AND LAVENDER**

Since time immemorial, the use of diversified aromas was evident as mood modulator. The beneficial impact of medicinal plants and their essential oils on olfactory organs as cognition enhancers are well known. Jimbo et al. (2009) made the cognitive drug research under the computerized cognitive assessment and revealed the efficacy of lavender odor on lowering the activity of working memory and also the reaction times for memory and attention duo. Additionally, it can also uplift the level of contentedness and mood. Lavender oil burners (after continuous use for 3 months) can effectively elevate the emotional state. Successful application of rosemary and lemon essential oils during morning hours followed by lavender and orange essential oils during

evening hours in aromatherapy treatment can upgrade the cognitive function (related to personal orientation) of dementia patients (Jimbo et al., 2009). In one of the investigations made by Degel & Koster (1999) found that lavender odor could effectively ameliorate the rate of errors during mathematical tests, but the odor of jasmine essential oil was less effective in this regard. Furthermore, lavender odor could impair the arithmetic reasoning capacity, but not memory, while the blended effect of lavender and clove never cause any concomitant effect on mood. Oral administration of lavender (80 mg/day) (for 2.5 months) can improve general mental health in case of patients suffering from neurasthenia (Uehleke et al., 2012).

### **8.13.11 SAFETY**

The efficacy of lavender for short-term diseases (especially some neurological disorders) is well established, but its effectiveness and safety for some chronic diseases and long-term uses are yet to be proven. Although the safe nature of lavender is proved but some reports have highlighted the adverse effects. Koulivand et al. (2012) reported the negative impact of lavender oils being blended with tea tree oil on Gynecomastia (Swollen male breast tissue caused by a hormone imbalance). On the other hand, also possesses estrogenic and anti-androgenic activities. Hence, before its application the allergy proneness of the individual should be evaluated appropriately. Kasper et al. (2010) and Woelk & Schlafke (2010) found that gastrointestinal disorder (like nausea, dyspepsia, etc.) and other neuro disorders could be induced by oral administration of lavender products while its ingestion may also cause problem for a pregnant woman (i.e., emmanagogue effect) and breastfeeding women (Koulivand et al., 2012).

### **8.13.12 LAVENDER AS ANTIMICROBIAL AGENT**

Lavender oil especially essential oils of *L. angustifolia* (English Lavender) could be used to treat wide range of bacterial and fungal infections (Lis-Balchin et al., 1998; Hammer et al., 1999) even antibiotic resistant bacteria(s) too. Nelson (1997) found the efficacy of *L. angustifolia*'s essential oil at the dose rate of <1% under *in vitro* condition against both vanomycin-resistant *Enterococcus faecalis* (VRE) and methicillin-resistant *Staphylococcus aureus* (MRSA). Lavender oil and oil vapor have some antifungal activity. As for example, *L. angustifolia* at 1% and 10% concentrations could restrict germination of conidium, hyphal growth and germ tube growth

of *Botrytis cinerea* (Antonov et al., 1997) while it doesn't possess any efficacy to prohibit the conidial production of *Penicillium digitatum* even at 1,000 g/mL concentrations (Daferera et al., 2000). Interestingly, Inouye et al. (1998) reported the potential of gaseous contact of lavender oil (*L. angustifolia*) than solution contact which could effectively restrict the growth of some filamentous fungi. They described that the gaseous form of lavender oil rightly binds with the spore-forming aerial mycelia. Among two major constituents, 'linalyl acetate' can prohibit spore formation due to respiratory suppression of aerial mycelia while linalool only restricts spore germination and fungal growth. The latter one has less inhibitory capacity for sporulation. Inouye et al. (2000) revealed that lavender vapor (63 mg/mL air) could inhibit the mycelial growth of *Aspergillus fumigatus* and its efficacy is higher than tea tree, lemon grass, cinnamon bark and thyme oils. At the dose rate of 10–20 g/mL of air, *L. angustifolia* could inhibit the germination and hyphal elongation of *Trichophyton mentagrophytes* and *Trichophyton rubrum* might be due to the straight deposition and absorption of it on fungal mycelia (Inouye et al., 2001a). The merits of lavender vapor treatment at appropriate concentrations and duration are higher than the solution treatment owing to their direct mode of action. At this condition, extensive research on biologically active substances of lavender oil and their synergistic impact on antimicrobial activity, is need of the hour. According to, Lis-Balchin et al. (1998) there is no correlation between the chemical constituents (like linalool/linalyl acetate) of lavender oil and antibacterial/antifungal activity. But origin of lavender plants affects its chemical composition like lavender of Bulgarian origin contains 51.9% linalool and 9.5% linalyl acetate and effective against ESKAPE pathogens while French origin lavender contains 29.1% linalool and 43.2% linalyl acetate and potential for the treatment of 13 bacteria(s) only. The extracts (by) of both Bulgarian and French lavender varieties are effective against *Aspergillus niger* and *Fusarium culmorum*. The mode of extraction also determines the degree of antibacterial and antifungal efficacy. Pattnaik et al. (1997) found that steam distillation and supercritical CO<sub>2</sub> – these processes are most effective. Disc/well diffusion method and agar/broth dilution method are the most common, effective, and accurate methods to evaluate the antimicrobial activity *in vitro* but since essential oils are volatile, insoluble in water, viscous, and complex in nature that's why afore mentioned tests are insufficient to measure the antimicrobial testing of oil. Basically, different factors vary for different methodologies such as inoculum size, medium used, use of sealants, surfactants, and solvents (like

Tween, dimethyl sulfoxide and ethanol) (Cavanagh & Wilkinson, 2002). The antimicrobial activity of lavender oils is not only depending on species and origin but also on their growing conditions and distillation procedures. According to Inouye et al. (2001) the MIC values of lavender oil (*L. angustifolia* and *L. latifolia*) was reported as 0.16% against *Haemophilus influenza*, 0.32% against *Streptococcus pyogenes* and *Staphylococcus aureus* and >0.32% against *Escherichia coli* evaluated *in vitro* which suggested its efficacy as a prophylactic not for any chronic infections. The immune stimulating, anti-inflammatory, and other pharmacological effects of lavender oil under *in vivo* condition are very limited and inconclusive (Ferley et al., 1989).

#### **8.13.13 PESTICIDAL ACTIVITIES OF LAVENDER OIL**

The acaricidal activity of both linalool and *L. angustifolia* oil is well demonstrated. Perrucci et al. (1996) in his study investigated the effect of *L. angustifolia* oil and linalool on *Psoroptes cuniculi*. They concluded that the acaricidal activity could be taken place through inhalation of volatile essential oils rather than its direct contact. Lavender oil, its grounded foliage and blooms could be also successfully utilized as commercial and domestic pesticide, in fact lavender can control mites, grain weevils, aphids, clothes moth, etc. (Perrucci, 1995; Ignatowicz, 1997).

#### **8.13.14 CURRENT AND FUTURE DEVELOPMENTS OF LAVENDER ESSENTIAL OILS**

Recent developments on lavender essential oils can combat the multidrug resistant strains of bacteria on one hand while their effectiveness in terms of human treatment is also noteworthy, on other hand. Essential oils are useful as natural preservatives in cosmetics, toiletries, drugs, and food products. Even after having the detailed information (like detailed monographs published in Native Pharmacopeia, European Pharmacopoeia, ISO, WHO, Council of Europe) about its source, chemical compositions and their effective therapeutic doses, rarely they are utilized by medical practitioners for healing any infectious diseases. More in-depth *in vitro* and *in vivo* studies are needed to establish their therapeutic properties and side effects (Sienkiewicz et al., 2012). Conclusively, the value-added products of lavender could be an essential weapon to combat against pathogenic microorganisms and insects.

## 8.14 PATENTS

Sl. No.	Patent/ Publication No.	Title/Name of Lavandula Plant	Description of Patent	Applicant and Inventor	Publication Date
1.	CN104739722A	Preparation of lavender essential oil using microemulsion method.	Microemulsion method of lavender essential oil (EO) extraction is unique and effective enough. In this method as raw materials 15–40% of lavender EO, 10–35% non-ionic emulsifier, 10–35% of an ionic emulsifier, 0–30% water and 15–40% of co-emulsifier was used (in percentage by weight). Along with lavender EO (an active component) reuse of emulsifier and co-emulsifier become useful for stable delusion and dispersion of oil into water required to form nano-scale emulsion. The uniqueness of this invention is that based on requirements, additional dilution with water can be made to form an O/W nano-scale emulsion with good stability and free from layering. Additional merits of this invention are its low cost, simple, and convenient technique, economic benefit and huge demand in cosmetic industry.	Wang Yifei, Zheng Feng, He Yan, Zhang Yunbin, Yu Ling	July 1, 2015
2.	CN1904012A	Method of lavender nano-EO formulation.	In this method, firstly acetone or n-hexane is sprayed on the surface of lavender petals uniformly based on the ratio of solvent and raw materials (1:1–3) using ultrasonic technique. After that for the removal of solvent and to extract lavender oil, pressure distillation and steam distillation techniques are utilized. Here, ion condensation action of chitosan and sodium tripolyphosphate is used as nano-carrier. The nano-carrier is used as embedded material for the formulation of lavender nano-EO.	Zhang Jian, Zhang Suning, Xiao Zuobing, Cai Baoguo, Fu Guanming	January 31, 2007
3.	CN1295310C	Extraction and refine methods of lavender oil.	Investigation relates to supercritical CO <sub>2</sub> .	Liao Bing, Che Guoyong, Pang Hao, Zhang Jingcheng, Liu Junling	January 17, 2007



(Continued...)

Sl. No.	Patent/ Publication No.	Title/Name of Lavandula Plant	Description of Patent	Applicant and Inventor	Publication Date
4.	20190269059	'FW Whimsical,' 'FW Spellbound,' 'FW Radiance'	A new and distinct cultivar of Lavandula plant characterized by its compact and broadly upright plant habit; freely branching growth habit, dense, and bushy appearance; round the year flowering, blooms hue ranges from purple-red color of sterile flowers slightly differing from the fertile one. Sepals of sterile flowers are arranged on dwarf terminal spike. These varieties are highly appropriate for garden performance.	Plant Growers Australia  By Steven Eggleton	August 29, 2019
5.	20190124815	'LA007'	This new cultivar is taxonomically characterized for its silver hued foliage, light purple-colored blooms, erect, pyramidal, and well-branched habit.	Rodney Bierhuizen	April 25, 2019
6.	20190029161, 20190029162, 20180014448	'KLELV16119,' 'KLELV16122,' **KLELV15115'	Early blooming and unique branching habit are the distinguishing features of this new cultivar. It possesses dark purple colored terminal bracts.	Klemm+Sohn GmbH & Co. KG  By Ruijun Li	January 24, 2019  * January 11, 2018
7.	20190029163	IBPRU 41016	Compact growth habit, dark violet-blue colored fertile flowers arranged in terminal spike inflorescence with dark purple sterile bracts with undulating margins. It is propagated asexually by stem cuttings which results in development of off spring with uniform features.	Plant Growers Australia  By Steven Eggleton	January 24, 2019
8.	20190021205	LAAZ 0006	This new cultivar is characterized for its flower hue (purple-blue) and extended blooming season, dark green greyish foliage, compact, well-branched, and upright habit and cold resistance.	Syngenta Participations AG  By Henricus Godefridus Wilhelmus Stemkens	January 17, 2019
9.	20180110169	LAMPU31-0	This new cultivar is characterized by its long inflorescence. Its inflorescence consists of dark purple-colored flowers and light purple-colored infertile bracts. By habit it is erect and resist lodging. It is especially suitable as pot plant.	John Robb	April 19, 2018

(Continued...)

Sl. No.	Patent/ Publication No.	Title/Name of Lavandula Plant	Description of Patent	Applicant and Inventor	Publication Date
10.	20180027721	'BKLVSSTFPU'	Compact and broad upright habit are its distinct feature. Apart from these, branching habit, early, and free blooming pattern, flower hue (purple colored), arrangement pattern of blooms on terminal spike and its good garden performance are the key distinguishing features.	Beekenkamp Plants B.V. By Annie Cornelia Beekenkamp	January 25, 2018
11.	20170290248, 20170290250, 20170290249	'Anouk Deluxe 1312' *'Anouk Deluxe 173' 'Anouk Deluxe 169'	These new cultivars are characterized by its compact growth habit, branching pattern, silvery grey-colored foliage, blooming habit, violet-blue to purple-blue colored flowers, durability of plants and peduncle, garden performance and re-flowering habit.	L. Koning Beheer B.V. By Lammert Koning	October 5, 2017
12.	20170290251	'Annet'	Compact growth pattern, upright habit, quick growth rate, durability, free blooming habit, unique flower hue and its arrangements are key distinguishing features.	L. Koning Beheer B.V. By Lammert Koning	October 5, 2017
13.	20170064898	'Riverina Margaret'	It is featured for its purple flowers with light pink infertile bracts and green foliage.	Nigel Alexander Russell Urwin	March 2, 2017
14.	20160338254	'Dowphscent'	It is a short statured plant with compact growth habit, long uniform spike inflorescence, basically used for growing in outdoor garden.	Simon Charlesworth and Fiona Wilson	November 17, 2016
15.	PP26814	'Riverina Gurli'	This is characterized by globose shaped, pink-red flowers with light pink sterile bracts and compact growth.	Nigel Alexander Russel Urwin	June 7, 2016
16.	PP27157	'LOWI2010-05'	Unique features are late commencing and prolonged blooming habit, significant shelf-life and resistant against downy mildew.	Wim Bergs	September 13, 2016
17.	PP27182	'Bridget Chloe'	It is characterized by its vivid purple bloom hue, round shape with mounding habit, multiscented fragrance and resistance against Septoria leaf spot and Alfalfa mosaic virus.	John Thomas Hendon, Jr.	September 20, 2016
18.	PP27398, PP27399,	'LABZ0005,' *'LABZ0006'	Its distinguishing features are its flower color. Its rose-pink blooms contain rose-pink infertile, large bracts and medium lengthed green foliage.	Henricus Godefridus Wilhelmus Stemkens	November 15, 2016

(Continued...)

Sl. No.	Patent/ Publication No.	Title/Name of Lavandula Plant	Description of Patent	Applicant and Inventor	Publication Date
19.	PP27447	'LABZ0005'	Its habit (erect, well-branched, and compact) and extended flowering season are key distinct features.	Do	December 6, 2016
20.	PP2749	'LABZ0004'	Innumerable deep purple-colored sterile bracts, durability, mounding habit and long blooming period are the unique features of this new cultivar.	Do	December 20, 2016
21.	PP27519	'LMARO32-0'	It is characterized for its long, red-purple colored terminal bracts.	John Robb	December 27, 2016
22.	PP27653	'DOWPHSCNT'	Dwarf, compact growth habit, wide flower spike and uniform inflorescence are its key features.	Simon Charlesworth, Fiona Wilson	February 7, 2017
23.	PP27768	'DLAVENLPOP'	It is characterized by its pink blooms and terminal bracts. Mostly used as container plant.	Gavriel Danziger	March 7, 2017
24.	PP28264	'Anouk Deluxe 1205'	Upright habit, free branching, durability, violet colored corolla, red bracts, erect peduncle – are its characteristics.	Lammert Koning	August 8, 2017
25.	PP28265	'Anouk Deluxe 1201'	Additional and repeated blooming habit and excellent garden performance are its features.	Lammert Koning	August 8, 2017
26.	PP2830	'Anouk Deluxe 1173'	The unique violet-blue colored flowers with new numerous white colored terminal bracts can tolerate full sunlight conditions which enhance its acceptability.	Lammert Koning	August 15, 2017

## 8.15 LAVENDER GENOMIC RESOURCES AND OPPORTUNITIES FOR MARKER ASSISTED LAVENDER IMPROVEMENT

The huge demand of lavender is imposing as compulsion on researchers to conduct cutting edge research on lavender breeding. To achieve the goal, selection of mutant clones or seed propagated lavender having improved traits are needed. Modern cutting-edge research is making the target-specific breeding program quite easy. Under such circumstances, use of marker assisted breeding (MAS) will be most appropriate to study the genetic relatedness of diversified floral volatiles in a comparative manner. Molecular characterization of major *Lavandula* members become imperative for acquiring in-depth knowledge on the diversity of its gene pool and also for achieving focused breeding objectives whereas molecular markers can be a reliable resort. The EST-SSR

marker model system was proposed by Lane et al. (2010) to study the molecular regulation of essential oil biosynthesis supported by adequate genomic resources. According to Adal et al. (2015), the use of EST-SSR markers is enough useful to test the transmittance potential of genetic traits of *Lavandula* species which may contribute to develop unique genetic markers for targeted breeding. Use of genetic markers for *Lavandula* species were mostly noted for their biodiversity study and phylogenetic relationship establishment although the application is quite finite (Chunshan et al., 2009; Bräuchler et al., 2010). Zagorcheva et al. (2020) had revealed that SRAP (Sequence-related amplified polymorphism) markers (Li & Quiros, 2001) could be considered as affordable genome wide markers to achieve the breeding objectives including diversity analysis. The wide use of SRAP marker is basically due to its simplicity, reliability, effectiveness, and genome-wide coverage (Aneja et al., 2012; Roberts & Wolfe, 2014). Sometimes, the consequences of its application in taxonomic studies might get influenced by anthropogenic or other specific influencers (Roberts & Wolfe, 2014). During the last decade SRAP markers had been used for diversity analysis of the species of Lamiaceae family. Zagorcheva et al. (2020) made inter and intraspecific and intergeneric studies using 51 SRAP primer pairs employing 10 Bulgarian and 5 other lavender varieties to characterize genetic resources and diversity. On one hand, they obtained high polymorphic scores (4697) and ratio (77.2%) and higher degree of genetic diversity (through molecular variance analysis) (96.6% of total variations), on other hand, at both interspecific and intergeneric level. Characterization of key genes responsible for biosynthesis of lavender essential oil could be also an effective step for targeted breeding program (Demissie et al., 2011, 2012; Landmann et al., 2007, 2011; Jullien et al., 2014; Sarker & Mahmoud, 2015; Sarker et al., 2012, 2013; Benabdelkader et al., 2015). Terpene synthase genes basically control the biosynthesis of lavender essential oil's constituents. Several authors studied the expression of terpene synthases gene of lavender and suggested its regulation at transcriptional level in lavender inflorescences (Lane et al., 2010; Guitton et al., 2010; Tholl, 2006). Based on this knowledge, it is feasible enough to improve lavender essential oils qualitatively like other agronomic traits and also to conduct biosynthesis of metabolically engineered target-specific essential oils by manipulating key essential oil genes. The instant identification of gene or allele of lavender varieties using specific SNP markers is possible if gene sequencing data is in hand. Sequenced trans-alpha-bergamotene synthase DNA fragments obtained from 7 Bulgarian varieties could be useful to identify the diversity between tested lavender varieties and also to analyze SNP allele configurations of

parent plant which can exemplify the above statement (Curto et al., 2018). Hence, EST-SSR, SRAP, and gene specific SNP could be effective enough to initiate target specific breeding programs. Except cloning and characterization of major genes of lavender, genetic marker's development and its subsequent application will be more impactful although it's very finite. Curto et al. (2018) developed molecular markers using single-copy nuclear genes at inter-specific level of *Lamiaceae* family while Hind et al. (2019) based on that data distinguished *L. latifolia* from *L. angustifolia* and *L. x intermedia* hybrid. Hnia et al. (2017) characterized *L. multifida* using RAPD markers. The EST database of *L. angustifolia* and *L. x intermedia* hybrid aided Adal et al. (2019) to develop set of SSR markers for *Lavandula* sp. which had proved its significant efficacy. Thus, to evaluate the genetic authenticity and homogeneity of commercial lavender cultivars, development of reliable molecular markers is highly important (Zagorcheva et al., 2020).

Comparative chemical analysis of wide range of extracted floral volatiles is another target for further lavender breeding program. As of now, selection of promising lavender varieties is made depending on outcomes of lavender oil analysis but direct analysis of flower volatiles (Kara & Baydar, 2013; Baser et al., 2005; Staikov & Boyadzhieva, 1989; Laurence, 1988; Raev & Boyadzhieva, 1988; Munoz-Bertomeu et al., 2007) involves accurate comparison of volatile compositions could be more significant. Furthermore, procedural routine application needed for chemical characterization of essential oils of tested materials make the procedure more complicated and less precise (Duskova et al., 2016; Cassel et al., 2006, 2009; Angioni et al., 2016; Hassiotis et al., 2014; Zheljazkov et al., 2013). According to Zagorcheva et al. (2013) the milling and successive extraction of oils from frozen inflorescences generally cause huge variations in chemical compounds quantitatively (during replica analyses) which nullify its application. The direct GC-MS analysis of lavender extracts found suitable in this regard (Zheljazkov et al., 2020).

Adal et al. (2019) demonstrated 3 major aspects namely development of unique genetic markers, identification, and characterization of geranyl pyrophosphate synthase (GPPS) genes and cloning of cDNA encoding monoterpene synthase genes which seems essential for further lavender improvement program. Firstly, they developed 250 simple sequence repeat (SSR) markers ( $\geq 18$  bp) from *L. angustifolia* and *L. x intermedia* ESTs (Expressed Sequence Tags). Among 31 valid SSR-ESTs, 24 only showed discriminatory power. GPPS (a heterodimeric protein consists of small subunit [LiGPPS.SSU1] and large subunit [LiGPPS.LSU]) produces GPP, precursor for all

common monoterpenes. Finally, catalyzing the condensation procedure of IPP (isopentenyl pyrophosphate) and DMAPP (dimethylallyl pyrophosphate) by recombinant GPPS produces GPP. Authors also identified and characterized cDNAs encoding GPPS. Interestingly, *N. benthamiana* based GGPPS (geranylgeranyl pyrophosphate synthase, precursor of diterpenes) can also produce GPP due to modification made by recombinant LiGPPS. SSU1 through interaction. Concentrations of monoterpenes determine the accumulation of lavender essential oils. Finally, they cloned and characterized 2 cDNA encoding monoterpene synthase genes (viz. 3-carene synthase [Li3CARS] and S-linalool synthase [LiSLINS]) of lavender *in-vitro*.

## 8.16 CONCLUSION

Elevated demands of lavender plants throughout the world, motivating entire scientific community for its further improvement. The asexually propagated crops are in high demand than seed derived populations due to the high oil yielding potential of the former one. Further adoption of upgraded harvesting procedures and more advanced targeted breeding programs (using MAS and direct analysis of floral volatiles) should be taken into consideration. Available genomic and molecular marker databases could assist to identify the major bottlenecks of lavender improvements. In fact, SRAP markers as a powerful and efficient tool could be utilized for detailed diversity analysis (like characterization of gene pools and segregating populations, genetic mapping and MAS) of lavender. Moreover, tested SRAP markers could be employed for quality testing of asexually propagated lavender planting materials. It could be suggested that the currently available genetic resources could be used as solid ground for initiation of long-term lavender breeding program.

## KEYWORDS

- antimicrobial agent
- aromatic
- electroencephalography
- essential oils
- herb
- *Lavandula*
- phytochemicals
- SRAP
- therapeutic

## REFERENCES

- Adal, A. M., (2019). *Development of Molecular Markers and Cloning of Genes Involved in the Biosynthesis of Monoterpenes in Lavandula* (pp. 1–201). PhD Thesis. Retrieved from: <https://open.library.ubc.ca/cIRcle/collections/ubctheses/24/items/1.0380463> (accessed on 31 August 2023).
- Adal, A., Demissie, Z., & Mahmoud, S., (2015). Identification, validation and cross-species transferability of novel *Lavandula* ESTSSRs. *Planta*, 241(4), 987–1004.
- Adam, K. L., (2006). *Lavender Production, Products, Markets, and Entertainment Farms*. A publication of ATTRA-National Sustainable Agricultural Information Service, Article No. 1-800-346-9140.
- Adam, K. L., (2006). *Lavender Production, Products, Markets, and Entertainment Farms* (pp. 1–12). Published by: ATTRA – National Sustainable Agriculture Information Service. Accessed from: <https://www.agri4africa.com/wp-content/uploads/2020/09/Lavender-Production-Products-Markets-and-Entertainment-Farms.pdf> (accessed on 30 September 2023).
- Agnel, R., & Ticsseirc, P., (1984). Essential oil of French lavender oils composition and adulteration. *Perf Flavor*, 9, 53–56.
- AgriFutures, (2017). *AgriFutures Australia, Rural Industries Research and Development Corporation*. Retrieved from: <https://www.agrifutures.com.au/farm-diversity/lavender-oil/> (accessed on 31 August 2023).
- Akhondzadeh, S., Kashani, L., & Fotouhi, A., (2003). Comparison of *Lavandula angustifolia* Mill. tincture and imipramine in the treatment of mild to moderate depression: A double-blind, randomized trial. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, 27(1), 123–127.
- Alaoui-Ismaili, O., Vernet-Maury, E., Dittmar, A., Delhomme, G., & Chanel, J., (1997). Odor hedonics: Connection with emotional response estimated by autonomic parameters. *Chemical Senses*, 22, 237–248.
- Anderson, C., Lis-Balchin, M., & Krik-Smith, M., (2000). Evaluation of massage with essential oils on childhood atopic eczema. *Phytotherapy Research*, 14, 452–456.
- Aneja, B., Yadav, N. R., & Chawla, V., (2012). Sequence-related amplified polymorphism (SRAP) molecular marker system and its applications in crop improvement. *Molecular Breeding*, 30(4), 1635–1648.
- Angioni, A., Barra, A., Coroneo, V., Dessi, S., & Cabras, P., (2006). Chemical composition, seasonal variability, and antifungal activity of *Lavandula stoechas* L. ssp. ‘Stoechas’ essential oils from stem or leaves and flowers. *Journal of Agricultural and Food Chemistry*, 54(12), 4364–4370.
- Anonymous, (2001). *The Wealth of India, Raw Materials, Part 2* (pp. 44–47). CSHv, Delhi.
- Anonymous, (2009). *Essential Oil Crops Production Guidelines for Lavender* (pp. 1–20). In: Lavender Production, Pretoria, South Africa.
- Anonymous, (2015). *Elementary Essential Oils*. Retrieved from: <https://www.healthline.com/health/9-ways-eucalyptus-oil-can-help> (accessed on 30 September 2023).
- Anonymous, (2018a). *The Plant List*. Retrieved from: <http://www.theplantlist.org/browse/A/Lamiaceae/> (accessed on 31 August 2023).
- Anonymous, (2018b). *Ultra International, Market Reports of 2015–2018*. Retrieved from: <http://ultranl.com/market/34> (accessed on 31 August 2023).

- Anonymous, (2018c). *Market Price Information on Essential Oils and Oleoresins, International Trade Centre*. Retrieved from: <https://www.marketsandmarkets.com/Market-Reports/essential-oil-market-119674487.html> (accessed on 30 September 2023).
- Antonov, A., Stewart, A., & Walter, M., (1997). Inhibition of conidium germination and mycelial growth of *Botrytis cinerea* by natural products. *Proceedings of the 1997 New Zealand Plant Physiology Society Conference*. Retrieved from: [https://nzpps.org/\\_journal/index.php/pnzppc/article/view/11289](https://nzpps.org/_journal/index.php/pnzppc/article/view/11289) (accessed on 30 September 2023).
- Aoshimaand, H., & Hamamoto, K., (1999). Potentiation of GABAA receptors expressed in *Xenopus* oocytes by perfume and phytoncid. *Bioscience, Biotechnology and Biochemistry*, 63(4), 743–748.
- Bailey, L. H., (1949). *Manual of Cultivated Plants*. MacMillan Publishing Company.
- Barazandeh, M. M., (2002). Essential oil composition of *Lavandula latifolia* Medik from Iran. *Journal of Essential Oil Research*, 14, 103, 104.
- Barocelli, E., Calcina, F., Chiavarini, M., Impicciatore, M., Bruni, R., Bianchi, A., & Ballabeni, V., (2004). Antinociceptive and gastroprotective effects of inhaled and orally administered *Lavandula hybrida* reverchon ‘grosso’ essential oil. *Life Science*, 76, 213–223.
- Baser, K., Özek, T., & Konakchiev, A., (2005). Enantiomeric distribution of linalool, linalyl acetate and camphor in Bulgarian lavender oil. *Journal of Essential Oil Research*, 17(2), 135–136.
- Benabdelkader, T., Guitton, Y., Pasquier, B., Magnard, J., Jullien, F., Kameli, A., & Legendre, L., (2015). Functional characterization of terpene synthases and chemotypic variation in three lavender species of section *Stoechas*. *Physiologia Plantarum*, 153(1), 43–57.
- Benito, M., Jorro, G., Morales, C., Pelaez, A., & Fernandez, A., (1996). Labiatea allergy: Systematic reactions due to ingestion of oregano and thyme. *Annals of Allergy Asthma and Immunology*, 76, 416–418.
- Boelens, M. H., (1995). Chemical and sensory evaluation of *Lavandula* oils. *Perf Flavor*, 20, 23–51.
- Bozkiran, S., & Giray, F. H., (2016). *Structural Analysis of Lavender Farms*. XII Agricultural Economists Congress, Isparta, Turkey.
- Braden, R., Reichow, S., & Halm, M. A., (2009). The use of the essential oil lavandin to reduce preoperative anxiety in surgical patients. *Journal of Perianesthesia Nursing*, 24(6), 348–355.
- Bradley, B. F., Brown, S. L., Chu, S., & Lea, R. W., (2009). Effects of orally administered lavender essential oil on responses to anxiety provoking film clips. *Human Psychopharmacology*, 24(4), 319–330.
- Bräuchler, C., Meimberg, H., & Heubl, G., (2010). Molecular phylogeny of menthinae (*Lamiaceae*, *Nepetoideae*, *Menthae*)—taxonomy, biogeography and conflicts. *Molecular Phylogenetics and Evolution*, 55(2), 501–523.
- Brown, S. A., (1965). Biosynthesis of the coumarins-VI further studies on herniarin formation in lavender. *Canadian Journal of Biochemistry*, 43(2), 199–207.
- Buchbauer, G., Jirovetz, L., Jäger, W., Dietrich, H., & Plank, C., (1991). Aromatherapy: Evidence for sedative effects of the essential oil of lavender after inhalation. *Zeitschrift für Naturforschung*, 46(11, 12), 1067–1072.
- Buchbauer, G., Jirovetz, L., Jaeger, W., Dietrich, H., Plank, C., & Karamat, E., (1991). Aromatherapy: Evidence for sedative effects of the essential oil of lavender after inhalation. *Zeitschrift Für Naturforschung Section C Biosciences*, 46(11, 12), 1067–1072.



- Bumett, K. M., Solterbeck, L. A., & Strapp, C. M., (2004). Scent and mood state following an anxiety-provoking task. *Psychological Reports*, *95*, 707–722.
- Campenni, C. E., Crawley, E. J., & Meier, M. E. (2004). Role of suggestion in odor-induced mood change. *Psychological Reports*, *94*(3\_suppl), 1127–1136.
- Carrasco, J., Barranco, R., Martin, E., & Frasquet, F., (1980). *Investigation Analytique sur Huile Essentielle d'Aspic Cultive*. VIII International Congress of Essential Oils, Cannes, France.
- Cassel, E., Vargas, R., Martinez, N., Lorenzo, D., & Dellacassa, E., (2009). Steam distillation modelling for essential oil extraction process. *Industrial Crops and Products*, *29*(1), 171–176.
- Cavanagh, H. M. A., & Wilkinson, J. M., (2002). Biological activities of lavender essential oil. *Phytotherapy Research*, *16*, 301–308.
- Cavanagh, H., & Wilkinson, J., (2005). Lavender essential oil: A review. *Healthcare Infection*, *10*(1), 35–37.
- Chanamai, R., Horn, G., & McClements, D. J., (2002). Influence of oil polarity on droplet growth in oil-in-water emulsions stabilized by a weakly adsorbing biopolymer or a nonionic surfactant. *Journal of Colloid and Interface Science*, *247*(1), 167–176. doi: 10.1006/jcis.2001.8110.
- Chaytor, D. A., (1937). *A Taxonomic Study of the Genus Lavandula*, *51*(338), 153–204. doi: <https://doi.org/10.1111/j.1095-8339.1937.tb01906.x>.
- Chunshan, C., Guojun, C., Baoru, M., Tianfu, Z., & Juan, L., (2009). Introduction and breeding & cultivation techniques of lavender (*Lavandula* spp.). *Chinese Wild Plant Resources*, *6*, 20–25.
- Clinical, (2000). Natural cosmetics may cause dermatitis, say dermatologists. *Journal of Pharmacology*, *264*, 503.
- Conrad, P., & Adams, C., (2012). The effects of clinical aromatherapy for anxiety and depression in the high-risk postpartum woman—A pilot study. *Complementary Therapies in Clinical Practice*, *18*(3), 164–168.
- Coulson, I. H., & Khan, A. S., (1999). Facial ‘pillow’ dermatitis due to lavender oil allergy. *Contact Dermatitis*, *41*, 1–11.
- Cristea, S., & Boros-Iacob, G., (2017). Culture of lavender: Investment for health, beauty, and food. Lumen Proceedings, International Scientific Conference Risk in Contemporary Economy, Galati, Romania, pp.347–355.
- Culpeper, N., (1952). Lavender. *The English Physician: Or an Astrologo-Physical Discourse of the Vulgar Herbs of this Nation*. Peter Cole, London. Yale Medical Library. Retrieved from: [www.med.yale.edu/library/historical/culpeper/culpeper.htm](http://www.med.yale.edu/library/historical/culpeper/culpeper.htm) (accessed on 31 August 2023).
- Daferera, D. J., Ziogas, B. N., & Polissiou, M. G., (2000). GC-MS analysis of essential oils from some Greek aromatic plants and their fungitoxicity on *Penicillium digitatum*. *Journal of Agricultural Food Chemistry*, *48*, 2576–2581.
- Dale, A., & Cornwell, S., (1994). The role of lavender oil in relieving perianal discomfort following childbirth: A blind randomized clinical trial. *Journal of Advanced Nursing*, *19*(1), 89–96.
- Degel, J., & Koster, E. P., (1999). Odors: Implicit memory and performance effects. *Chemical Senses*, *24*(3), 317–325.

- Demissie, Z., Cella, M., Sarker, L., Thompson, L., Rheault, M., & Mahmoud, S., (2012). Cloning, functional characterization and genomic organization of 1, 8-cineole synthases from *Lavandula*. *Plant Molecular Biology*, 79(4, 5), 393–411.
- Demissie, Z., Sarker, L., & Mahmoud, M., (2011). Cloning and functional characterization of  $\beta$ -phellandrene synthase from *Lavandula angustifolia*. *Planta*, 233(4), 685–696.
- DePascual, T. J., Ovejero, J., Anaya, J., Caballero, E., Hernandez, J. M., & Caballero, M. C., (1989). Chemical composition of the Spanish spike oil. *Planta Medicina*, 55, 398.
- DeSousa, D. P., Nobrega, F. F. F., Santos, C. C. M. P., & deAlmeida, R. N., (2010). Anticonvulsant activity of the linalool enantiomers and racemate: Investigation of chiral influence. *Natural Product Communications*, 5(12), 1847–1851.
- Diego, M. A., Jones, N. A., Field, T., Hernandez-Reif, M., Schanberg, S., Kuhn, C., McAdam, V., et al., (1998). Aromatherapy positively affects mood, EEG patterns or alertness and math computations. *International Journal of Neuroscience*, 96, 217–224.
- Dimitrova, E., (1959). Nature of inheritance during seed propagation of *Lavandula vera* L. use of seedling generation obtained by free pollination in selection and seed production. *Compte Rendu of the Institute of Horticulture*, 8, 12–23.
- DiNardo, W., DiGirolamo, S., Galli, A., Meduri, G., Paludetti, G., & De Rossi, G., (2000). Olfactory function evaluated by SPECT. *American Journal of Rhinology*, 14(1), 57–61.
- Duan, X., Tashiro, M., & Wuetal, D., (2007). Autonomic nervous function and localization of cerebral activity during lavender aromatic immersion. *Technology and Health Care*, 15(2), 69–78.
- Dunn, C., Sleep, J., & Collett, D., (1995). Sensing an improvement: An experimental study to evaluate the use of aromatherapy, massage, and periods of rest in an intensive care unit. *Journal of Advanced Nursing*, 21(1), 34–40.
- Dušková, E., Dušek, K., Indrák, P., & Smékalová, K., (2016). Postharvest changes in essential oil content and quality of lavender flowers. *Industrial Crops and Products*, 79, 225–231.
- Elshafie, H. S., & Camele, I., (2017). An overview of the biological effects of some Mediterranean essential oils on human health. *Bioactive Natural Products*, 2017, 1–14. doi: <https://doi.org/10.1155/2017/9268468>.
- Ernst, M., (2017). *Lavender*. Lexington, Kentucky. Accessed from: [www.uky.edu/ccd/production/crop-resources/nursery-ornamental/lavender](http://www.uky.edu/ccd/production/crop-resources/nursery-ornamental/lavender) (accessed on 31 August 2023).
- Farooqi, A. H. A., Sharma, S., Kumar, V. S., & Kumar, S., (1996). Aromatherapy – A promising holistic system. *CIMAP News Letter*, 23, 39–41.
- Ferley, J. P., Poutignet, N., Zmiron, D., Azzoparrdi, Y., & Balducci, F., (1998). Prophylactic aromatherapy for supervening infection in patients with chronic bronchitis: Statistical evaluation conducted in clinics against a placebo. *Phytotherapy Research*, 3, 97–100.
- Fismer, K. L., & Pilkington, K., (2012). Lavender and sleep: A systematic review of the evidence. *European Journal of Integrative Medicine*, 4(4), 436–447. doi: 10.1016/j.eujim.2012.08.001.
- Forney, J. M., (n.d.). *Outdoor Flowering Plants-Mona Lavender*. Retrieved from: <https://www.hgtv.com/outdoors/flowers-and-plants/houseplants/mona-lavender> (accessed on 31 August 2023).
- FranceAgriMer, (2013). *Production et Marchés des Huiles Essentielles de Lavandes et Lavandins* (Vol. 1).
- Gedney, J. J., Glover, T. L., & Fillingim, R. B., (2004). Sensory and affective pain discrimination after inhalation of essential oils. *Psychosomatic Medicine*, 66, 599–606.

- Georgiev, K., (1964). History of the experimental station for roses and essential oil-bearing plants in Kazanlak. *Bulletin of the Development of the Essential Oil Industry*, 8, 1–25.
- Giray, F. H., (2018). An analysis of world lavender oil markets and lessons for Turkey. *Journal of Essential Oil-Bearing Plants*, 21(6), 1612–1623. doi: 10.1080/0972060X.2019.1574612.
- Gorjiand, A., & Ghadiri, M. K., (2002). History of headache in medieval Persian medicine. *Lancet Neurology*, 1(8), 510–515.
- Graham, P. H., Browne, L., Cox, H., & Graham, J., (2003). Inhalation aromatherapy during radiotherapy: Results of a placebo-controlled double-blind randomized trial. *Journal of Clinical Oncology*, 21, 2372–2376.
- Grebenicharski, S., (2016). In: Nikolay, V., & Bozhinov, B., (eds.), *Lavender Production in Bulgaria: Market and Opportunity Analysis*. InteliAgro, Sofia.
- Groom, N., (1997). *The New Perfume Handbook* (2<sup>nd</sup> edn.). Blackie Academic & Professional. ISBN 978-0-7514-0403-6.
- Guenther, E., (1972). *The Essential Oils* (Vol. 1). Reprint: History, Origin of plants, production, analysis. Kreiger Publishing Co., Huntington, New York.
- Guitton, Y., Nicolè, F., Moja, S., Valot, N., Legrand, S., Jullien, F., & Legendre, L., (2010). Differential accumulation of volatile terpene and terpene synthase mRNAs during lavender (*Lavandula angustifolia* and *L. x intermedia*) inflorescence development. *Physiologia Plantarum*, 138(2), 150–163.
- Gül, M., Kart, M. Ç. O., & Sirikci, B. S., (2016). Determining costs and profitability of lavender farms in Isparta province of Turkey. *Journal of Essential Oil-Bearing Plants*, 19(3), 686–692.
- Hammer, K., Carson, C., & Riley, T., (1999). Antimicrobial activity of essential oils and other plant extracts. *Journal of Applied Microbiology*, 86, 985–990.
- Handa, K. L., Chopra, I. C., & Abrol, B. K., (1957). Introduction of some of the important exotic aromatic plants in Jammu and Kashmir. *Indian Perfumer*, 1, 1–44.
- Hassiotis, C., Ntana, F., Lazari, D., Poullos, S., & Vlachonasios, K., (2014). Environmental and developmental factors affect essential oil production and quality of *Lavandula angustifolia* during flowering period. *Industrial Crops and Products*, 62, 359–366.
- Hay, I. C., Jamieson, M., & Ormerod, A. D., (1998). Randomized trial of aromatherapy, successful treatment for alopecia areata. *Archives of Dermatology*, 134, 1349–1352.
- Henley, D. V., Lipson, N., Korach, K. S., & Bloch, C. A., (2007). Prepubertal gynecomastia linked to lavender and tea tree oils. *The New England Journal of Medicine*, 356(5), 479–485. doi: 10.1056/NEJMoa064725.
- Heuberger, E., Redhammer, S., & Buchbauer, G., (2004). Transdermal absorption of (-)-linalool induces autonomic deactivation but has no impact on ratings of well-being in humans. *Neuropsychopharmacology*, 29, 1925–1932.
- Holmes, C., Hopkins, V., Hensford, C., MacLaughlin, V., Wilkinson, D., & Rosenvinge, H., (2002). Lavender oil as a treatment for agitated behavior in severe dementia: A placebo-controlled study. *International Journal of Geriatric Psychiatry*, 17(4), 305–308.
- Ignatowicz, S., (1997). Powdered herbs of the mint family (*Laminaceae*) as insect repellants for protection of stored wheat grain. *Polskie Pismo Entomologiczne*, 66(1, 2), 135–150.
- Inouye, S., Tsuruoka, T., Uchida, K., & Yamaguchi, H., (2001a). Effect of sealing and tween 80 on the antifungal susceptibility testing of essential oils. *Microbiology Immunology*, 45:201–208.

- Inouye, S., Tsuruoka, T., Watanabe, M., Takeo, K., Akao, M., Nishiyama, Y., & Yamaguchi, H., (2000). Inhibitory effect of essential oils on apical growth of *Aspergillus fumigatus*. *Mycoses*, 43(1, 2), 17–23.
- Inouye, S., Watanabe, M., Nishiyama, Y., Takeo, K., Akao, M., & Yamaguchi, H., (1998). Anti-sporulating and respiration-inhibitory effects of essential oils on filamentous fungi. *Mycoses*, 41, 403–410.
- Inouye, S., Yamaguchi, H., & Takizawa, T., (2001b). Screening of the antibacterial effects of a variety of essential oils on respiratory tract pathogens, using the modified dilution assay method. *Journal of Infection and Chemotherapy*, 7, 251–254.
- Itai, T., Amayasu, H., & Kuribayashietal, M., (2000). Psychological effects of aromatherapy on chronic hemodialysis patients. *Psychiatry and Clinical Neurosciences*, 54(4), 393–397.
- Jager, W., Buchbauer, G., Jirovetz, L., & Fritzer, M., (1992). Percutaneous absorption of lavender oil from a massage oil. *Journal of the Society of Cosmetic Chemists*, 43, 49–54.
- Jimbo, D., Kimura, Y., Taniguchi, M., Inoue, M., & Urakami, K., (2009). Effect of aromatherapy on patients with Alzheimer's disease. *Psychogeriatrics*, 9(4), 173–179.
- Jullien, F., Moja, S., Bony, A., Legrand, S., Petit, C., Benabdelkader, T., Poirot, K., ET AL., (2014). Isolation and functional characterization of a  $\tau$ -cadinol synthase, a new sesquiterpene synthase from *Lavandula angustifolia*. *Plant Molecular Biology*, 84(1, 2), 227–241.
- Kains, M. G., (1912). American Agriculturist, (ed.), *Culinary Herbs: Their Cultivation Harvesting Curing and Uses Orange Judd Company*. Retrieved from: [http://www.gutenberg.org/files/21414/21414-h/21414-h.htm#Page\\_97](http://www.gutenberg.org/files/21414/21414-h/21414-h.htm#Page_97) (accessed on 31 August 2023).
- Kaiser, R., & Lamparsky, D., (1983b). New carbonyl compounds in the high-boiling fraction of lavender oil. *Inorganica Chimica Acta*, 66(6), 1843–1849.
- Kaiser, R., & Laraparsky, D., (1983a). New carbonyl compounds in the high-boiling fraction of lavender oil. *Inorganica Chimica Acta*, 66(6), 1835–1842.
- Kara, N., & Baydar, H., (2013). Determination of lavender and lavandin cultivars (*Lavandula* sp.) containing high quality essential oil in Isparta, Turkey. *Turkish Journal of Field Crops*, 18, 58–65.
- Kashani, M., Tavirani, M., Talaei, S., & Salami, M., (2011). Aqueous extract of lavender (*Lavandula angustifolia*) improves the spatial performance of a rat model of Alzheimer's disease. *Neuroscience Bulletin*, 27(2), 99–106.
- Kasper, S., Gastpar, M., & Muller, W. E., (2010). Silexan, an orally administered *Lavandula* oil preparation, is effective in the treatment of 'subsyndromal' anxiety disorder: A randomized, double-blind, placebo-controlled trial. *International Clinical Psycho Pharmacology*, 25(5), 277–287.
- Kim, H. M., & Cho, S. H., (1999). Lavender oil inhibits immediate type allergic reaction in mice and rats. *Journal of Pharmaceutical Pharmacology*, 51, 221–226.
- Koulivand, P. H., Ghadiri, M. K., & Gorji, A., (2012). Lavender and the nervous system. *Evidence Based Complementary and Alternative Medicine*, 2013, 1–10. ArticleID681304, doi: <http://dx.doi.org/10.1155/2013/681304>.
- Kritsidima, M., Newton, T., & Asimakopoulou, K., (2010). The effects of lavender scent on dental patient anxiety levels: A cluster randomized-controlled trial. *Community Dentistry and Oral Epidemiology*, 38(1), 83–87.
- Laget, F., (2005). From its birthplace in Egypt to Marseilles, an ancient trade: Drugs and spices. *Diogenes*, 52(3), 131–139. doi: 10.1177/0392192105055941. doi: <https://doi.org/10.1177%2F0392192105055941>.

- Landmann, C., Fink, B., Festner, M., Dregus, M., Engel, K. H., & Schwab, W., (2007). Cloning and functional characterization of three terpene synthases from lavender (*Lavandula angustifolia*). *Archives of Biochemistry and Biophysics*, 465(2), 417–429.
- Landmann, C., Hücherig, S., Fink, B., Hoffmann, T., Dittlein, D., Coiner, H., & Schwab, W., (2011). Substrate promiscuity of a rosmarinic acid synthase from lavender (*Lavandula angustifolia* L.). *Planta*, 234(2), 305–320.
- Lane, A., Boecklemann, A., Woronuk, G., Sarker, L., & Mahmoud, S., (2010). A genomics resource for investigating regulation of essential oil production in *Lavandula angustifolia*. *Planta*, 231(4), 835–845.
- Laurence, B., (1988). Progress in essential oils. Lavender oil. *Perfume and Flavor*, 12(6), 64–70.
- Lawrence, B. M., (1985). A review of the world production of essential oils. *Perfumer Flavourist*, 10, 1–20.
- Lawrence, B. M., (1985). Progress in essential oils. *Perf Flavor*, 10, 43–53.
- Lawrence, B. M., (1994). Progress in essential oils. *Perf Flavor*, 19, 36, 37.
- Lawrence, B. M., (1996). Progress inessential oils. *Perf Flavor*, 21, 67, 68.
- Lee, K. A., Harnett, J. E., & Cairns, R., (2019). Essential oil exposures in Australia: Analysis of cases reported to the NSW poisons information center. *The Medical Journal of Australia*. doi: 10.5694/mja2.50403.
- Lesage-Meessen, L., Bou, M., Sigoillot, J. C., Faulds, C., & Lomascolo, A., (2015). Essential oils and distilled straws of lavender and lavandin: A review of current use and potential application in white biotechnology. *Applied Microbiology and Biotechnology*, 99(8), 3375–3385.
- Lewith, G. T., Godfrey, A. D., & Prescott, P., (2005). A single-blinded, randomized pilot study evaluating the aroma of *Lavandula angustifolia* as a treatment for mild insomnia. *Journal of Alternative and Complementary Medicine*, 11(4), 631–637.
- Li, G., & Quiros, C. F., (2001). Sequence-related amplified polymorphism (SRAP), a new marker system based on a simple PCR reaction: Its application to mapping and gene tagging in Brassica. *Theoretical and Applied Genetics*, 103(2, 3), 455–461.
- Lis-Balchin, M., & Hart, S., (1999). Studies on the mode of action of the essential oil of lavender (*Lavandula angustifolia* Mill.). *Phytotherapy Research*, 13(6), 540–542.
- Lis-Balchin, M., (2002). *Lavender: The Genus Lavandula* (p. 283). Taylor and Francis, London. ISBN 9780203216521.
- Lis-Balchin, M., Deans, S. G., & Eaglesham, E., (1998). Relationship between bioactivity and chemical composition of commercial essential oils. *Journal of Flavor and Fragrance*, 13, 98–104.
- Liston, B. W., Nines, R., Carlton, P. S., Gupta, A., Aziz, R., Frankel, W., & Stoner, G. D., (2003). Perillyl alcohol as a chemopreventive agent in N-nitroso methyl benzylamine-induced rat esophageal tumorigenesis. *Cancer Research*, 63, 2399–2403.
- Louzina, L., (1968). *Lavender Selection* (Vol. 1, pp. 128–134). Works of the All-Union Institute of Essential Oil-Bearing Crops.
- Maclain, B., (2015). *Lavender Marshmallows – Havoc in the Kitchen*. <https://en.wikipedia.org/wiki/Lavandula> (accessed on 30 September 2023).
- Mambri, A. P. S., Jerônimo, L. A., Melânia, P. M., Suany, M. G. P., Cardoso, F. L., & Neves, M. G., (2018). Yield and composition of lavender essential oil grown in substrate. *Horticultura Brasileira*, 36, 1–8.

- Masago, R., Matsuda, T., Iokuchi, Y., Miyazaki, Y., Iwanaga, K., Harada, H., & Katsura, T., (2000). Effects of inhalation of essential oils on EEG activity and sensory evaluation. *Journal of Physiology and Anthropology Applied Human Science*, 19, 35–42.
- Masango, P., (2005). Cleaner production of essential oils by steam distillation. *Journal of Cleaner Production*, 13(8), 833–839. doi: 10.1016/j.jclepro.2004.02.039.
- Matthieu, L., Meuleman, L., Van, H. E., Blondeel, A., Dezfoulian, S., Constandt, L., & Goossens, A., (2004). Contact and photocontact allergy to ketoprofen: The Belgian experience. *Contact Dermatitis*, 50, 238–241.
- McCoy, J. A., (1999). *Lavender: History, Taxonomy, and Production*. PhD Thesis.
- Millot, J. L., & Brand, G., (2001). Effects of pleasant and unpleasant ambient odors on human voice pitch. *Neuroscience Letters*, 29, 61–63.
- Möller, H. J., Volz, H. P., Dienel, A., Schläfke, S., & Kasper, S., (2019). Efficacy of silexan in sub-threshold anxiety: Meta-analysis of randomized, placebo-controlled trials. *European Archives of Psychiatry and Clinical Neuroscience*, 269(2), 183–193. doi: 10.1007/s00406-017-0852-4.
- Moon, T., Cavanagh, H. M. A., & Wilkinson, J. M., (2004). *Lavender as an Antibacterial Essential Oil – Are All Lavenders Equal?* (p. 46). AICA National Conference, 2004, Abstracts.
- Moscovitch, D. A., Santesso, D. A., & Miskovic, V., (2011). Frontal EEG asymmetry and symptom response to cognitive behavioral therapy in patients with social anxiety disorder. *Biological Psychology*, 87(3), 379–385.
- Muñoz-Bertom, J., Arrillaga, I., & Segura, J., (2007). Essential oil variation within and among natural populations of *Lavandula latifolia* and its relation to their ecological areas. *Biochemical Systematics and Ecology*, 35(8), 479–488.
- Naef, R., & Morris, A. F., (1992). *Lavender–Lavandin: A Comparison* (pp. 364–377). Rivista Ital. EPPOS, (Numero Speciale).
- Naf, R., Jaquier, A., & Velluz, A., (1997). A new natural furan anti stMiic related compounds. *Journal of Flavor Fragrance*, 12(6), 377–380.
- Nelson, R. R. S., (1997). *In-vitro* activities of five plant essential oils against methacil-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus faecium*. *Journal of Antimicrobial Chemotherapy*, 40, 305, 306.
- Nurzyńska-Wierdak, R., & Zawiślak, G., (2016). Chemical composition and antioxidant activity of lavender (*Lavandula angustifolia* mill.) aboveground parts. *Acta Scientiarum Polonorum Hortorum Cultus*, 15(5), 225–241.
- Pattnaik, S., Subramanyam, V. R., Bapaji, M., & Kole, C. R., (1997). Antibacterial and antifungal activity of aromatic constituents of essential oils. *Microbios*, 8, 39–46.
- Peco, E., Milic, D., & Sredojevic, Z., (2015). *Economic Analysis of Oil Production from Organic Lavender*, VI (pp. 1112–1117). International Scientific Agricultural Symposium (Agrosym 2015).
- Perucci, S., (1995). Acaricidal activity of some essential oils and their constituents against *Tyrophagus longior*, a mite of stored food. *Journal of Food Protection*, 58, 560–563.
- Perucci, S., Macchioni, G., Cioni, P. C., Flamini, G., Morelli, I., & Taccini, F., (1996). The activity of volatile compounds from *Lavandula angustifolia* against *Psoroptes cuniculi*. *Phytotherapy Research*, 10, 5–8.
- Petkova, M., Tahsin, N., Yancheva, S., & Yancheva, H., (2018). *Development of the Production of Aromatic oil Crops in Bulgaria* (Vol. 2, pp. 71–86) China-Bulgaria Rural Revitalization Development Cooperation Forum, Sofia.

- Pohrib, E. L., & Nistor, E., (2012). Spikes of azure bloom: Lavender – history and stories. *Scientific Papers. Series A. Agronomy*, 55, 397–405.
- PolyDeonny, V. I., Sotnik, V. F., & Dhillapzew, E. E., (1979). *Medicinal and Aromatic Plants*. Moscow: Kolos Press.
- Porter, N. G., Shaw, M. L., & Hurndell, L. C., (1982). Preliminary studies of lavender as an essential oil crop of New Zealand. *NZJ Agricultural Research*, 25(3), 389–394.
- Prashar, A., Locke, I. C., & Evans, C. S., (2004). Cytotoxicity of lavender oil and its major components to human skin cells. *Cell Proliferation*, 37(3), 221–229.
- Proenca Da, C. A., Queiros, M., & Roque, O. R., (1985). Estudio cariologicoe determinacao da composicao quimica do oleo essencial de lavandula latifolia medicus da regioa Leira. *Boletim da Faculdade de Direito da Universidade de Coimbra*, 9(1), 25–35.
- Raev, R., & Boyadzhieva, B., (1988). Newly developed lavender cultivars ‘septopolis’ and ‘yubilejna.’ *Proceedings of Scientific Conference, Stara Zagora, Bulgaria*.
- Ramie, S., Miirko, I., & Dlic, F., (1982). Investigation of chemical composition of natural and synthetic lavender essential oils by means of thin-layer chromatography. *Herba-Polonica*, 28(1, 2), 15–20.
- Reid, A., (2000). *Growing Lavender in Western Australia*. Department of Agriculture and Food, Western Australia, Perth. Bulletin 4454.
- Revrchon, E., Della-Porta, G., Senatore, F., & Porta, F. D., (1995). Supercritical CO<sub>2</sub> extraction and fractionation of lavender essential oil and waxes. *Journal of Agricultural Food Chemistry*, 43(6), 1654–1658.
- Roberts, D. W., & Wolfe, A. D., (2014). Sequence-related amplified polymorphism (SRAP) markers: A potential resource for studies in plant molecular biology. *Applied Plant Science*, 2(7), 140–170.
- Romanenko, L., (1973). *Combining Ability of Lavender Lines* (Vol. 6, pp. 38–42). Works of the All-Union Institute of Essential Oil-Bearing Crops.
- Saadatian, M., Aghaei, M., Farahpour, M., & Balouchi, Z., (2013). Chemical composition of lavender (*Lavandula officinallis* L.) extraction extracted by two solvent concentrations. *Global Journal of Medicinal Plant Research*, 1(2), 214–217.
- Sakurada, H., Kuwahata, S., & Katsuyama, T., (2009). Intra plantar injection of bergamot essential oil into the mouse hind paw. In: *Effects on Capsaicin-Induced Nociceptive Behaviors: International Review of Neurobiology*, 85, 237–248.
- Salah, S. M., & Jager, A. K., (2005). Screening of traditionally used Lebanese herbs for neurological activities. *Journal of Ethnopharmacology*, 97(1), 145–149.
- Samaila, D., Ezekwudo, D. E., Yimam, K. K., & Elegbede, J. A., (2004). Bioactive plant compounds inhibited the proliferation and induced apoptosis in human cancer cell lines, *in vitro*. *Journal of Transactions of the Integrated Biomedical Informatics & Enabling Technologies Symposium*, 1, 34–42.
- Sanders, C., Diego, M., Fernandez, M., Field, T., HernandezReif, M., & Roca, A., (2002). EEG asymmetry responses to lavender and rosemary aromas in adults and infants. *International Journal of Neuroscience*, 112(11), 1305–1320.
- Sarker, L., & Mahmoud, S., (2015). Cloning and functional characterization of two monoterpene acetyltransferases from glandular trichomes of *L. x intermedia*. *Planta*, 242(3), 709–719.
- Sarker, L., Demissie, Z., & Mahmoud, S., (2013). Cloning of a sesquiterpene synthase from *Lavandula x intermedia* glandular trichomes. *Planta*, 238(5), 983–989.

- Sarker, L., Galata, M., Demissie, Z., & Mahmoud, S., (2012). Molecular cloning and functional characterization of borneol dehydrogenase from the glandular trichomes of *Lavandula x intermedia*. *Archives of Biochemistry and Biophysics*, 528(2), 163–170.
- Sarkic, A., & Stappen, I., (2018). Essential oils and their single compounds in cosmetics – A critical review. *Cosmetics*, 5, 1–11.
- Schweisheiner, W., (1960). Laveiicler anti lavender oil. *Perfumery Essential Oil Record*, 51, 124–126.
- Seidler-àIykowska, K., Mordalski, R., Kucharski, W., Kędzia, B., & Bocianowski, J., (2014). Yielding and quality of lavender flowers (*Lavandula angustifolia* mill.) from organic cultivation *Acta Scientiarum Polonorum Hortorum Cultus*, 13(6), 173–183.
- Sharma, R., Gupta, A., Patwardhan, S., Hebbalkar, D., Tare, V., & Bhone, S., (1992). Bioactivity of *Lamiaceae* plants against insects. *Indian Journal of Experimental Biology*, 30(3), 244–246.
- Shawl, A. S., & Kumar, S., (2000). Potential of lavender oil industry in Kashmir. *Journal of medicinal and Aromatic Plant Sciences*, 22, 319–322.
- Sheikhan, F., Jahdi, F., & Khoietal, E. M., (2012). Episiotomy pain relief: Use of lavender oil essence in primiparous Iranian women. *Complementary Therapies in Clinical Practice*, 18(1), 66–70.
- Shellie, R., Mondello, L., Marriott, P., & Dugo, G., (2002). Characterization of lavender essential oils by using gas chromatography-mass spectrometry with correlation of linear retention indices and comparison with comprehensive two-dimensional gas chromatography. *Journal of Chromatography*, 970(1, 2), 225–234. doi: 10.1016/S0021-9673(02)00653-2.
- Shen, J., Nijima, A., Tanida, M., Horii, Y., Nakamura, T., & Nagai, K., (2007). Mechanism of changes induced in plasma glycerol by scent stimulation with grapefruit and lavender essential oils. *Neuroscience Letters*, 416(3), 241–246.
- Sienkiewicz, M., Kowalczyk, E., & Wasiela, M., (2012). Recent patents regarding essential oils and the significance of their constituents in human health and treatment. *Recent Patents on Anti-Infective Drug Discovery*, 7(2), 1–8.
- Sienkiewicz, M., Lysakowska, M., Cieciewicz, J., Denys, P., & Kowalczyk, E., (2011). Antibacterial activity of thyme and lavender essential oils. *Medicinal Chemistry*, 7(6), 674–689.
- SilvaBrum, L. F., Elisabetsky, E., & Souza, D., (2001). Effects of linalool on [3H] MK801 and [3H] muscimol binding in mouse cortical membranes. *Phytotherapy Research*, 15(5), 422–425.
- Singh, A., Singh, J., & Sharma, S., (1989). Multivariate analysis in relation to genetic improvement in lavender, *Lavandula officinalis* Chaix. *Plant Breeding*, 102(4), 302–305.
- Singh, S., Singh, V., Babu, G. D. K., Kaul, V. K., & Ahuja, P. S., (2007). Economics of lavender (*Lavandula officinalis* L.) in Himachal Pradesh. *Journal of Non-Timber Forest Products*, 14(2), 97–100.
- Snow, L. A., Hovanec, L., & Brandt, J. A., (2004). Controlled trial of aromatherapy for agitation in nursing home patients with dementia. *Journal of Alternative and Complementary Medicine*, 10, 431–437.
- Soden, K., Vincent, K., Craske, S., Lucas, C., & Ashley, S., (2004). A randomized controlled trial of aromatherapy massage in a hospice setting. *Palliative Medicine*, 18, 87–92.
- Soltani, R., Soheilipour, S., Hajhashemi, V., Asghari, G., Bagheri, M., & Molavi, M., (2013). Evaluation of the effect of aromatherapy with lavender essential oil on post-tonsillectomy



- pain in pediatric patients: A randomized controlled trial. *International Journal of Pediatric Otorhinolaryngology*, 77(9), 1579–1581.
- Staikov, V., & Boyadzhieva, B., (1989). ‘Hemus’ Newly developed highly productive lavender cultivar. *Horticultural Sciences*, 26(1), 31–34.
- Stanev, S., (2007). *Alternative Approach for Vegetative Propagation of Lavender* (pp. 206–210). Scientific conference: 100 Years of experimental and scientific work with essential oil bearing and medicinal crops in Bulgaria, Kazanlak.
- Stanev, S., (2010). Evaluation of the stability and adaptability of the Bulgarian lavender (*Lavandula angustifolia* Mill.) sorts yield. *Agricultural Science and Technology*, 2(3), 121–123.
- Stanev, S., Zagorcheva, T., & Atanassov, I., (2016). Lavender cultivation in Bulgaria – 21<sup>st</sup> century developments, breeding challenges and opportunities. *Bulgarian Journal of Agricultural Science*, 22, 584–590.
- Stradley, L., (2015). *Lavender Scones*. Whats Cooking America. Retrieved from: <https://whatscookingamerica.net/EllenEaston/LavenderScones.htm> (accessed on 31 August 2023).
- Sturdivant, L., & Blakley, T., (1999). *The Bootstrap Guide to Medicinal Herbs in the Garden, Field, and Marketplace* (pp. 210, 211). San Juan Naturals, WA.
- Sugiura, M., Hayakawa, R., Kato, Y., Sugiura, K., & Hashimoto, R., (2000). Results of patch testing with lavender oil in Japan. *Contact Dermatitis*, 43, 157–160.
- Tewari, R., & Sharma, A., (1987). Chemistry of lavender oil: A Review. *Current Research on Medicinal and Aromatic Plants*, 9, M04.
- Tholl, D., (2006). Terpene synthases and the regulation, diversity, and biological roles of terpene metabolism. *Current Opinion in Plant Biology*, 9(3), 297–304.
- Thomson, K. F., & Wilkinson, S. M., (1998). Positive patch tests to plant extracts in patients with cosmetic dermatitis. *British Journal of Dermatology*, 139, 1–90.
- Tisserand, R., & Balacs, T., (1999). *Essential Oil Safety*. A guide for Health Care Professionals. Harcourt: Glasgow.
- Tomi, M., Kitao, M., Murakami, H., Matsumura, Y., & Hayashi, T., (2018). Classification of lavender essential oils: Sedative effects of *Lavandula* oils. *Journal of Essential Oil Research*, 30(1), 56–68.
- Topalov, V., (1962). On the diversity of lavender population. *Agricultural Science*, 6, 623–630.
- Topalov, V., (1969). Newly developed lavender cultivar ‘Venetsh’ *Scientific Works of the High Agricultural Institute, V Kolarov, Plovdiv*, 18(1), 47–50.
- Tucker, A., & DeBaggio, T., (1984). ‘Irene Doyle’ lavender. *Hortscience*, 19(4), 595.
- Tucker, A., & Hensen, K., (1985). The cultivars of lavender and lavandin (Labiatae). *Baileya*, 22(4), 168–177.
- TURKSTAT, (2018). *Agricultural Product Statistics*. Turkish Statistical Institute. Retrieved from: <https://biruni.tuik.gov.tr/medas/?kn=92&locale=tr> (accessed on 31 August 2023).
- Tysoe, P., (2000). The effect on staff of essential oil burners in extended care settings. *International Journal of Nursing Practice*, 6, 110–112.
- Uehleke, B., Schaper, S., Dienel, A., Schlaefke, S., & Stange, R., (2012). Phase II trial on the effects of Silexan in patients with neurasthenia, post-traumatic stress disorder or somatization disorder. *Phytomedicine*, 19(8, 9), 665–671.
- Umezu, T., (2000). Behavioral effects of plant-derived essential oils in the Geller type conflict test in mice. *Japanese Journal of Pharmacology*, 83(2), 150–153.
- Upton, T., & Andrews, S., (2004). *The Genus Lavandula*. Royal Botanic Gardens, Kew. ISBN 9780881926422.

- Van, D. D. H., & Kratz, D. J., (1963). A generalization of the retention index system including liner temperature programmed gas-liquid partition chromatography. *Journal of Chromatography*, *11*, 463–467.
- Venskutonis, P. R., Dapkevicius, A., & Baranauskiene, M., (1997). Composition of the essential oil of lavender (*Lavandula angustifolia* Mill) from Lithuania. *Journal of essential Oil Research*, *9*(1), 107–110.
- Vokou, D., Varelizidou, S., & Katinakis, P., (1993). Effects of aromatic plants on potato storage: Sprout suppression and antimicrobial activity. *Agricultural Ecosystem and Environment*, *47*(3), 223–235.
- Walsh, D., (1996). Using aromatherapy in the management of psoriasis. *Nursing Standard*, *11*, 53–56.
- Walsh, E., & Wilson, C., (1999). Complementary therapies in long-stay neurology in-patients settings. *Nursing Standard*, *13*, 32–35.
- Wang, J., Eslinger, P. J., Smith, M. B., & Yang, Q. X., (2005). Functional magnetic resonance imaging study of human olfaction and normal aging. *Journals of Gerontology: Series A*, *60*(4), 510–514.
- Ward, G. W., (2008). *The Grove Encyclopedia of Materials and Techniques in Art* (pp. 605–606). Oxford University Press. ISBN 978-0-19-531391-8.
- Williams, T. I., (2006). Evaluating effects of aromatherapy massage on sleep in children with autism: A pilot study. *Evidence-Based Complementary and Alternative Medicine*, *39*(3), 373–377.
- Woelk, H., & Schlafke, S., (2010). A multi-center, double-blind, randomized study of the lavender oil preparation silexan in comparison to lorazepam for generalized anxiety disorder. *Phytomedicine*, *17*(2), 94–99.
- Woronuk, G., Demissie, Z., Rheault, M., & Mahmoud, S., (2011). Biosynthesis and therapeutic properties of *Lavandula* essential oil constituents. *Planta Medica*, *77*(1), 7–15.
- Yip, Y. B., & Tse, S. H., (2004). The effectiveness of relaxation acupoint stimulation and acupressure with aromatic lavender essential oil for non-specific low back pain in Hong Kong: A randomized controlled trial. *Complementary Therapies in Medicine*, *12*, 28–37.
- Zagorcheva, T., Stanev, S., Rusanov, K., & Atanassov, I., (2020). SRAP markers for genetic diversity assessment of lavender (*Lavandula angustifolia* mill.) varieties and breeding lines. *Biotechnology & Biotechnological Equipment*, *34*(1), 303–308. doi: 10.1080/13102818.2020.1742788.
- Zheljazkov, V., Cantrell, C., Astatkie, T., & Jeliazkova, E., (2013). Distillation time effect on lavender essential oil yield and composition. *Journal of Oleo Science*, *62*(4), 195–199.

# Index

---

## $\alpha$

$\alpha$ -acoradiene, 47  
 $\alpha$ -asarone, 39, 59, 60  
 $\alpha$ -bisabolol, 44  
 $\alpha$ -cadinol, 44  
 $\alpha$ -calacorene, 43, 44  
 $\alpha$ -caryophyllene, 39  
 $\alpha$ -cedrene, 43  
 $\alpha$ -cubebene, 89, 229  
 $\alpha$ -pinene, 46, 246, 248  
 $\alpha$ -selinene, 44  
 $\alpha$ -terpineol, 47

## $\beta$

$\beta$ -acoradiene, 47  
 $\beta$ -asarone, 40, 56, 59, 60  
 $\beta$ -cedrene, 43  
 $\beta$ -elemene, 43  
 $\beta$ -gurjunene, 43  
 $\beta$ -pinene, 39, 46, 185, 225, 228

## $\gamma$

$\gamma$ -asarone, 39  
 $\gamma$ -terpinene, 47  
 $\gamma$ -terpinenemay, 120

## A

Abdominal pain, 23, 286  
Acetate-chloroform extract, 59  
Acetic acid, 121, 125, 315, 359  
*Achillea*, 1, 3, 4, 6–12  
    *millefolium* L., 5, 6, 8–10  
Acoraceae, 21, 22, 35  
Acorine, 39  
Acoro, 34  
*Acorus*, 21, 22, 24, 28, 34–36, 39, 55, 56,  
    58–60, 72–75  
    *americanus*, 28, 34  
    *calamus*, 21, 22, 24, 28, 34–36, 39,  
    55–62, 72–75  
Adipocyte, 59, 60, 177, 178, 273

Adipose tissues, 59, 177  
Adoption, 223, 344, 376  
Adverse effects, 57, 59, 317, 338, 367  
Agroforestry systems, 298  
Ailments, 1, 2, 11, 21, 22, 24, 95, 96, 133,  
    136, 165, 192, 247, 285, 286, 338, 358  
Alcohols, 40, 119, 189, 263  
Aldehydes, 40, 116, 119, 226  
Alkaloids, 24, 39, 40, 116, 171, 228, 304  
Alkamid database, 5, 6  
Alkylamides, 5, 6  
Allantoin, 171, 172  
*Allium sativum*, 2  
Alpha-asarone, 39, 62  
Alzheimer's disease, 121, 360, 361  
Amino acids, 40, 263  
Analgesic, 27, 89, 96, 121, 166, 189, 190,  
    195, 232, 247, 290, 306, 335, 359, 360, 366  
Anodyne, 27, 189  
Anthelmintic, 23, 59, 166  
Anthemideae, 4–6  
Antibacterial properties, 57, 357  
Antibiotics, 2, 57, 176  
Anticancer, 56, 89, 96, 108, 174, 185, 195,  
    235, 265, 271, 272, 276, 291, 360  
    activity, 56, 126, 173, 271  
Anticholinergic, 361, 363  
Antidiabetic, 56, 121, 272  
    activity, 56, 177, 272  
    effect, 242  
    study, 56  
Antidiarrheal activity, 58, 74  
Antifungal, 11, 57, 120, 189, 190, 222, 238,  
    240, 250, 283, 288, 304, 358, 368  
    activity, 57, 367, 368  
Anti-HIV activity, 178, 181  
Anti-inflammatory, 4, 5, 8, 10, 12, 57, 58,  
    89, 96, 118, 120, 121, 165, 166, 171, 176,  
    177, 181, 185, 189, 190, 195, 231, 247,  
    250, 268, 270, 276, 283, 287, 289, 290,  
    335, 369  
    activity, 8, 57, 121, 118, 268

- drugs, 57
  - properties, 4, 289, 290
  - Antimicrobial, 11, 57, 89, 91, 93, 96, 119, 120, 124, 175, 176, 185, 188, 195, 237–239, 247, 248, 288, 289, 368, 369, 376
  - action, 57
  - activity, 57, 120, 124, 175, 176, 237, 238, 368, 369
  - agent, 239, 367, 376
  - bioassay, 57
  - effect, 237
  - Antioxidant, 2, 11, 12, 56, 89, 91, 93, 94, 96, 107, 108, 118, 120, 122, 123, 126–128, 166, 171, 172, 175, 178, 179, 181, 185, 189, 192, 195, 232–234, 273, 274, 287, 302, 305
  - activity, 91, 94, 108, 127, 128, 178, 179, 181, 233, 234, 273
  - effect, 232
  - Anti-pancreatitis, 179
  - Antiparasitic, 125, 235
  - activity, 125
  - Antiproliferative, 171, 175, 234
  - Anti-secretory impacts, 122
  - Antispasmodic, 8, 10, 23, 72, 335
  - Antiulcerogenic, 89, 96
  - Anxiety, 362
  - Apex, 97, 99, 112, 168, 292, 317
  - Aphrodisiac, 27, 166, 268, 318
  - Apigenin, 9, 118, 125, 303
  - Apoptotic action, 271, 272
  - Aqueous extract, 95, 116, 122, 124–126, 128, 129, 131, 133, 176, 236, 238, 241, 272
  - Arachidonic acid (AA), 231
  - Aromatic, 7, 8, 23, 27, 34, 39, 40, 58, 89, 91, 93, 95, 96, 98, 100, 101, 105, 115, 118, 119, 136, 189, 195, 223–225, 262, 283, 284, 292, 306, 315, 316, 318, 320, 326, 335, 336, 366, 376
  - odor, 23, 262
  - plants, 7, 119, 136, 302, 304, 306, 326
  - Artemisia*, 4
    - dracunculus*, 5
  - Arthritis, 21, 28, 196, 268, 269, 287
  - Articular cartilage deterioration, 176
  - Asarone, 24, 39, 40, 57, 59, 60, 62
  - Asexual propagation, 187, 244, 351
  - Aspirin, 95, 121, 122, 290
  - Asteraceae*, 1, 3–5, 12
    - family, 3, 5
  - Asthma, 3, 4, 21, 27, 167, 196, 231, 247, 286, 287
  - Asthmatic symptoms, 97, 133
  - Astringent, 10, 185, 189, 262
  - Atomic force microscopy (AFM), 241
  - Axillary fascicles, 168, 292
  - Ayurveda, 23, 73, 74, 89, 106, 116, 136, 262, 275
  - Ayurvedic, 24, 27, 58, 72, 74, 135, 153, 261, 262, 268, 276, 284, 287, 305
  - Azadirachtin, 112, 113
- ## B
- Bacterial infection, 57, 242
  - Basil, 89–102, 104–114, 116, 118–136, 153, 237, 365
    - leaf extracts, 96, 97
    - plants, 91, 98, 113, 124
    - species, 103
  - Basilica*, 90, 91
  - Bile salt export pump (BSEP), 271
  - Bioactive
    - compounds, 5, 61, 62, 175
    - constituents, 1, 2, 5, 263
  - Bio-prospection, 121, 230, 304
  - Bleeding on probing (BOP), 241
  - Blood
    - glucose level, 56, 57
    - pressure (BP), 132, 247, 366
  - Blue gum chalcid (BGC), 175, 220
  - Body mass index (BMI), 132
  - Bornyl acetate, 263, 304
  - Botanicals, 9, 10, 224, 225
  - Botany, 34, 98, 199, 291, 339
  - Botryosphaeria* sp., 221
  - Brassica oleracea* L., 2
  - Breeding programs, 186, 187, 243, 244, 375, 376
  - Bronchitis, 3, 11, 21, 24, 27, 28, 96, 167, 196, 247
  - Bruises, 11, 335
  - Bug, 113, 221
  - Bulked segregant analysis (BSA), 246
  - Burgeoning demand, 187, 192, 344

## C

Caffeate/5-hydroxyconiferaldehyde O-methyltransferase 1 (COMT1), 245  
 Caffeoyl coenzyme A O-methyltransferase (CCoAOMT), 245  
 Calamus, 22–24, 27–29, 34–41, 56–63, 68, 72–74  
   rhizome, 56, 61, 62  
   root, 27, 58, 61, 73  
   vapors, 24  
 Campanulate, 206, 212  
 Camphene, 39, 225, 228, 285, 288, 303, 329  
 Camphor, 39, 94, 100, 101, 103, 116, 120, 190, 248, 286, 304, 315, 317, 324, 329, 335, 338, 354  
 Cancer  
   cell, 174, 235, 271, 272  
   lines, 126, 234, 235, 271  
 Cardioprotective activity, 273, 276  
 Carminative, 23, 27, 286, 335, 337  
 Caryophyllene, 39, 116, 118, 120, 227, 229, 315, 329, 335  
*Catharanthus roseus*, 97  
 Central  
   Drug Research Institute (CDRI), 270  
   Institute of Medicinal and Aromatic Plants (CIMAP), 131, 275, 317, 320, 349  
   nervous system (CNS), 24, 60, 89, 96, 123, 177, 231, 303, 362  
 Cerebrospinal FLUID (CSF), 236  
 Chemical  
   components, 35, 40, 125, 222, 226, 358  
   constituents, 100, 103, 131, 145, 170, 188–190, 195, 196, 226, 246, 248, 263, 349, 354, 368  
 Chemomodulatory, 89, 96  
 Chlorhexidine (CLX), 134, 239, 241  
 Cholesterol, 122, 128, 170, 171, 175, 263, 270–273, 290  
 Cineole, 39, 94, 120, 146, 185, 189, 190, 194–197, 210, 211, 225–228, 230–232, 234, 237, 238, 242, 246–248, 285, 294, 303, 315, 317, 329, 335  
 Cinnamate 4-hydroxylase (C4H), 245  
 Cinnamon, 22, 23, 27, 90, 119, 368  
*Citrus*  
   *limonum*, 2  
   *sinensis*, 2

Clinical attachment level (CAL), 241  
 Clonal propagation, 215, 295, 296  
*Commiphora wightii*, 261, 262, 276  
 Composition, 24, 93, 195, 285, 329  
 Conical, 205, 206, 211, 212  
 Conjunction, 59, 62  
 Constipation, 27, 287  
 Continuous passive motion (CPM), 247  
 Convention on international trade in endangered species (CITES), 274  
 Convulsions, 28, 123  
 Coronary, 62, 273  
 Corymbia, 204, 205, 208, 211  
 Cosmetic, 91, 93, 96, 185, 276, 283, 304, 305, 318, 325, 335, 337, 344, 370  
 Cough, 21, 24, 96, 97, 196  
 Coumarins, 1, 329  
 C-reactive protein (CRP), 247  
*Cucumis melo*, 2  
 Cuisines, 91, 119, 286, 336  
 Culinary, 7, 89–91, 93, 94, 96, 100, 102–107, 115, 116, 118, 129, 187, 243, 283, 285, 286, 293, 301, 302, 306, 316, 317, 319, 325, 327, 336, 338, 342–344, 348, 351, 353, 372, 375  
   lavender, 336  
   use, 336  
 Cultivars, 35, 103, 209, 211, 292  
 Cultivation, 7, 12, 24, 37, 91, 98, 107, 112, 116, 187, 189, 213–215, 250, 275, 284, 315, 316, 319–323, 325–327, 344–350  
 Cyclin-dependent kinase (CDK), 272  
 Cyclooxygenase-2 (COX-2), 177, 269, 270  
 Cyclopropyl, 315, 330  
 Cylindrical, 22, 34, 35, 206, 207, 213, 292  
   rhizome, 34  
   shaped, 34  
 Cymose nature, 204  
 Cytological features, 103  
 Cytotoxic effect, 234  
 Czech, 24–26

## D

Days after planting (DAP), 37, 114, 353, 354  
 Decoction, 10, 95–97, 286  
 Decussate, 201, 204  
 Delayed-type hypersensitivity (DTH), 127  
 Depression, 62, 97, 133, 288, 303, 358–360, 362, 363, 366

- Deteriorate, 28, 131, 224, 302, 354  
 Diabetes, 56, 272  
 Diaphoretic, 10, 27, 189  
 Diarrhea, 10, 11, 21, 28, 58, 166, 177  
 Digestive  
   problems, 11, 27  
   system, 2, 24  
 Dimension, 202, 217  
 Dimethylallyl pyrophosphate (DMAPP), 376  
 Dimethylamin, 315, 330  
*Dioscorea*, 165–172, 174, 178–181  
 Diosgenin, 165, 166, 171, 172, 174–178, 180  
 Diseases, 113, 220, 221  
 Dispersed, 23, 91  
 Dispersion, 170, 370  
 Distillate water, 224, 358  
 Distillation  
   procedure, 225, 321  
   process, 115, 130, 224, 225, 354, 358  
 Distinctive, 23, 170, 194  
 Distribution, 5, 91, 92, 165, 180, 181, 188,  
   192, 193, 198, 243, 315, 326, 327, 351  
 Diterpenes, 1, 270  
 Diterpenoids, 172, 263  
 Diuretic, 10, 166, 268, 286, 335  
 Diverse, 3, 11, 23, 40, 56, 116, 119, 294, 304  
 Diversity, 1, 3, 90, 100, 116, 120, 181, 199,  
   214, 243, 244, 292, 323, 373, 374, 376  
 DNA fragmentation, 127, 234, 235  
 Dorsal, 90, 200, 221, 342  
   surface, 342  
 Douche, 10  
 Doxorubicin, 174  
 Dried buds, 336  
   flowers, 355  
 Drip irrigation system, 216  
 Drought tolerant, 216  
 Drug resistance, 57, 59  
 Dysentery, 23, 58, 96, 97, 166  
 Dysmenorrhea, 11, 366  
 Dyspepsia, 1, 11, 21, 24, 28, 167, 286, 367
- E**
- Echinacea*, 3–5, 9  
   *angustifolia*, 5  
   extracts, 4  
   *pallida*, 5  
   *purpurea*, 5  
   species, 3  
 Eco-friendly nature, 193, 225  
 Economic measures, 224  
 Eczema, 21, 363, 364  
 Edema, 27, 246  
 Ehrlich ascites carcinoma (EAC), 235  
 Electroencephalography (EEG), 123, 359,  
   365, 376  
 Embryo, 170  
 Emmenagogic agents, 10  
 Enclosed valves, 207  
 Endocannabinoid system (ECS), 5  
 Endodermal cells, 23  
 Endothelial tyrosine kinase, 177  
 Enormous, 3, 21, 23, 90  
 Enzyme, 4, 126, 128, 174, 178, 246,  
   270–272, 284  
 Epilepsy, 24, 28, 60, 286, 336, 365  
 Epistasis, 244  
 Erect, 34, 100, 106, 206, 211, 342, 350, 371,  
   373  
 Ergostanol, 170  
*Erysiphe cichoracearum*, 221  
*Escherichia coli*, 124, 145, 175, 237–240,  
   288, 357, 369  
 Essential oil (EO), 9, 24, 27, 39, 56, 61,  
   62, 72, 73, 89, 91, 93–98, 104, 106,  
   107, 114–116, 118, 120, 121, 123–126,  
   129, 130, 133, 135, 137, 145, 153, 185,  
   186, 188–196, 210, 222–228, 232–235,  
   237–240, 248, 250, 263, 284, 285, 293,  
   295, 300, 302–305, 315–328, 330, 334,  
   335, 338, 342–345, 348–370, 374–376  
 Esters, 40, 119, 189, 196, 227, 315, 329  
 Ethnobotanical  
   records, 3, 4  
   reports, 3, 4  
   uses, 285  
 Ethnomedical uses, 286  
 Ethnomedicinal, 1, 3, 12, 97, 186  
   uses, 1, 3, 12  
 Ethnopharmacological, 286  
 Ethyl, 59, 124, 173, 178, 179, 229, 235,  
   236, 269, 270, 283, 285, 288–291, 294,  
   296, 303, 304, 306  
   cinnamate, 283, 288, 289, 304, 306  
   p-methoxy-cinnamate, 283, 288, 304, 306  
 Eucalypt trunks, 201

*Eucalyptus*, 185–194, 197–200, 204, 206, 208–211, 213–222, 224, 225, 227, 228, 230, 233–235, 237, 240, 246, 249, 250  
*bicolor*, 211  
*camaldulensis*, 209–211, 227, 230, 233–235, 237  
*coolabah*, 213  
 farming, 213, 215  
 globulus, 195, 196  
*griffithsii*, 212, 227  
*incrassata*, 209, 212, 227  
 oil, 194, 196, 197  
 plantation, 198, 215  
 progenies, 243  
*torquata*, 209, 213  
 tree, 218

Eugenol, 39, 40, 62, 89, 91, 93, 94, 103, 104, 116, 118, 120, 131, 143, 145, 146, 263  
 basil, 100

Eukaryota, 35

European  
 Chemical Agency (ECHA), 305  
 triploid type, 24

Evolutionary components, 5

Exhaustion, 27

Expectorant, 23, 27, 58, 189, 286, 287

Expressed sequence tag (EST), 188, 373–375

Exsert valves, 207

Extracellular, 176

Extraction  
 methods, 224  
 procedure, 223

**F**

Farmyard, 36, 299–301

Farnesoid X receptor (FXR), 271–273

Fatigue, 27, 96

Fatty acids, 39, 40, 116, 118, 129, 196, 222

Febrifuge, 27, 189

Feminine, 10

Fenofibrate treatments, 122

Fertility, 128

Fertilization, 346

Feruloyl, 9  
 caffeoylquinic acid, 9

Fiber patches, 23

Fibrous  
 roots, 39, 292  
 texture, 201

Field culture, 352

Fingerprinting, 244

Flatulence, 1, 28, 95

Flavonoids, 1, 8, 24, 123, 128, 170, 185, 222, 225, 226, 263, 267, 291, 304

Flotation, 197

Foliage, 96, 105, 107, 125, 189, 202, 217, 219, 221, 316, 343, 344, 352, 369, 371, 372

Food preparations, 27, 93

Fragrant, 27, 99, 107, 120, 197, 248, 317, 336–338

Free radicals, 56, 91, 93

Furostarol, 170

## G

Gall bladder disorders, 28

Garlic, 2, 97, 106, 119

Gastritis, 246

Gastrointestinal, 10–12, 58, 95, 286, 367  
 effects, 230  
 issues, 10

Gene bank collection, 24

Generally recognized as safe (GRAS), 95

Genetic  
 diversity, 243  
 dominance, 244

Genus, 4, 6, 8, 9, 90–92, 102, 165, 167, 168, 170, 185, 188, 190, 225, 244, 283, 292, 316, 339, 340  
*Achillea*, 6

Geographical source, 103, 168

Geraniol, 94, 120, 225, 263, 329

Geranyl pyrophosphate synthase (GPPS), 375

Geranylgeranyl pyrophosphate synthase (GGPPS), 376

Germination, 7, 108, 275, 343, 351, 352, 367, 368

Gingival index (GI), 241

Global  
 biodiversity information facility, 34  
 trade, 8

Globose, 102, 168, 372

Globular, 206, 212, 292

Glucokinase (GK), 122, 178

Glucose, 171  
 Glutathione S-transferase-pi (GSTP1), 126  
 Glycomimetics, 174  
 Glycoside, 27, 39, 40, 116, 170, 171, 225, 226, 267  
 Golden pheasant, 36  
 Gonorrhea, 176  
 Gouging, 217  
 Grading, 355  
*Gramineus*, 35, 36  
 Gram-positive, 175  
 Green hue, 217  
 Grey-green foliage, 343  
*Grindelia*, 3  
 Guggul, 74, 261–276  
 Guggulipid, 270, 273  
 Guggulsterones, 269–274, 276

## H

Hakuro-nishiki, 36  
 Hallucinogenic, 27  
 Hardy lavenders, 342  
 Harvest, 28, 37, 108, 114, 115, 130, 222, 299, 301, 302, 321, 349  
 Hazardless construction, 224  
 Headache, 1, 27, 96, 97, 196, 287, 290, 319, 337  
 Healthy volunteers, 62  
 Heavy metal accumulators, 8  
 Heleniums, 3  
 Helminthiasis, 59  
 Hemagglutination (HA), 127  
 Hemispherical, 206, 211–213  
 Hemorrhage, 10  
 Hemorrhoids, 11, 166  
 Hepatitis C virus (HCV), 175  
 Hepatocellular carcinoma (HCC), 174, 175  
 Hepatoma-derived cell line (HepG2), 127  
 Heptanoic acid, 315  
 Herb, 7, 21–23, 27, 35–38, 57, 60, 89–96, 98, 100, 106, 112, 114, 115, 118, 129, 130, 153, 167, 283, 291, 315, 317, 336, 338, 376  
 Herbaceous perennial plant, 74  
 Herbal drug, 12, 27  
 Herbivorous, 5  
 Heredity materials, 214  
 Herniarine, 315

Heterozygosity, 244  
 Hexane, 124, 146, 223, 236, 289, 354, 370  
 Hexokinase (HK), 122  
 Hexose, 171  
 High-density  
   lipoproteins (HDL), 290  
   plantations, 217  
 Histopathological improvements, 122  
 Historical uses, 318  
 Homeopathic cure, 28  
 Homo-neanderthalensis grave, 10  
 Hues, 90, 99, 103, 114, 200, 201, 324  
 Human  
   chronic myeloid leukemia, 175  
   colorectal cell lines, 56  
   studies, 362  
   tumors, 175  
 Hybrid cultivation, 213  
 Hybridization, 102, 244, 325, 348  
 Hydro-distillation, 224  
 Hydroxycinnamoyl, 9  
 Hypanthium, 204–207, 211–213  
 Hypertension, 11, 192, 247, 287  
 Hyphal growth, 367  
 Hypoglycemic, 56, 171, 178, 185  
   action, 56, 185  
 Hypolipidemic, 59, 60, 89, 96, 171, 178, 270, 273, 276  
   activity, 59, 270, 273  
   efficacy, 59  
 Hypotensive, 27, 335  
 Hypothesized, 5, 171

## I

Immunoglobulin, 362  
 Immunological  
   activity, 176, 181  
   exercises, 9  
 Immunomodulation, 133  
 Immunomodulatory, 5, 12, 61, 127, 176, 262  
   activity, 127  
 Immunosuppressant, 61  
 Importers, 24, 93, 194  
 Individual drug, 175  
 Indomethacin, 122, 178  
 Industrial uses, 337  
 Inebriated, 10  
 Inexpensive, 166, 224



- Inferior quality timber, 214  
 Inflammation, 1, 3, 57, 58, 133, 177, 178, 231, 246, 261  
 Inflorescence, 97, 99, 204, 211–213, 317  
 Inhibitory  
   concentration (IC), 126, 178, 179, 233–236, 239  
   effect, 4, 121, 176, 179, 238, 240, 288, 300  
 Insect repelling activity, 24  
 Insecticidal, 61, 235, 289  
   activity, 61, 62, 74  
 Insect-pests, 220  
*In-situ*, 131, 275, 321  
 Institute of Roses and Aromatic Plants (IRAP), 348, 351  
 Insulin, 56, 121, 122, 132, 178, 272  
 Intellectual property rights (IPRs), 136  
 Intercrop, 112, 215, 298  
 Intermediate leaves, 202  
 Internal market, 24  
 International  
   code of botanical nomenclature (ICBN), 102  
   market, 120, 284, 324, 326, 327  
   Union for Conservation of Nature (IUCN), 166, 261, 274  
 Internode, 203  
 Inter-specific hybridization, 244  
 Intoxicating scent, 197  
 Intracellular superoxide anion, 176  
 Intra-marginal vein, 203, 204  
 Intraperitoneal acetic acid, 231  
 Intra-peritoneal application, 361  
 Intra-plantar, 231, 360  
*In-vitro*, 1, 57, 61, 175, 180, 231, 360, 376  
*In-vivo*, 1, 180  
 Iris, 34  
 Iron phosphate, 37  
 Ironbark type, 201  
 Irrigation, 37, 109, 111, 298, 347  
   management, 216  
 Isolated, 4, 5, 9, 28, 59, 118, 179, 227, 235, 263, 265, 266, 268, 290, 303  
 Isomerization, 172  
 Isopentenyl pyrophosphate (IPP), 376  
 Isoprene, 40  
 Isothymonin, 118  
 Isothymusin, 118
- J**
- Jaccard's coefficient analysis method, 243  
 Jasmonic acid (JA), 94  
 Jungles, 3  
 Juniper, 119, 365  
 Juvenile  
   foliages develop, 202  
   leaves, 112, 201, 202, 212, 222, 227, 342, 336  
   stage, 202, 203, 211, 212
- K**
- Kaempferia galanga*, 283–285, 287–294, 299, 300, 302–306  
 Kaempferol, 172, 283, 288, 291, 293, 306  
 Ketones, 40, 119, 142, 196, 225, 315  
 Kidney, 11, 21, 95  
*Klebsiella*, 237  
   *pneumoniae*, 57, 238, 288
- L**
- Lactone rings, 40  
 Lamiaceae, 89, 90, 98, 101, 127, 130, 315, 316, 374, 375  
 Lamiales, 101  
 Lanceolate, 202, 212, 213  
 Land preparation, 110, 215  
 Landscaping industry, 217  
 Larvae, 113, 126, 220, 236, 237  
 Larvicidal, 125  
   activities, 89, 96  
 Lateral veins, 203, 204  
   diverge, 203  
*Lavandula*, 315, 316, 320, 324, 326, 328, 339, 353, 356–358, 363, 371, 374–376  
 Lavender, 315–324, 326–328, 330, 336–339, 342–346, 348, 349, 353–359, 361–367, 369, 373  
   blooms, 321, 327, 336, 344, 355  
   buds, 336, 337, 354  
   cultivation, 320, 321, 323, 326, 349, 350  
   essential oil, 356, 369  
   field, 336, 352  
   flower stalk, 321  
   genomic resources, 373  
   improvement, 348, 373  
   odor, 364–367

- oil, 317, 319–330, 335, 337, 338, 350, 357–370, 375
    - production, 357
    - plants, 319, 345, 346, 368, 376
    - species, 316, 323, 324, 339, 342, 344, 353
  - Leaf
    - edge, 203, 204
    - faces, 203
    - rollers, 112, 113
    - spot, 38, 113
  - Lemon essential oils, 366
  - Lepidocephalus*, 38
  - Lesbos, 105
  - Leucas indica*, 97
  - Leukotriene amalgamation, 4
  - Level valves, 207
  - Lignans, 266
  - Lignotuber, 201, 218
  - Liliaceae, 2
  - Limonene, 91, 93, 94, 105, 185, 195, 196, 211, 225, 248, 263, 315, 329
  - Linalool, 93, 94, 100, 103, 104, 106, 116, 118–120, 125, 146, 185, 195, 248, 263, 315, 317, 324, 325, 329, 334, 335, 338, 349, 354, 356, 359, 360, 362, 368, 369, 376
  - Linalyl
    - acetate, 315, 317, 325, 329, 335, 338, 348, 349, 355, 356, 359, 360, 362, 368
    - butyrate, 355
  - Lipid, 268
    - levels, 132, 270, 273
    - metabolism disorders, 270
  - Lipolysis, 59, 273, 361
  - Lipophilic, 9
  - Lipopolysaccharides (LPS), 61, 179, 180, 242
  - Locules, 168, 292
  - Long diosgenin therapy, 177
  - Long-fibred brown bark, 201
  - Longitudinal, 204
  - Loppers, 217
  - Lorazepam, 362
  - Low-density lipoprotein (LDL)-cholesterol, 122
  - Lower temperate latitudes, 3
  - Lozenges, 196, 230
  - Lung resistance, 4
  - Luteolin, 4
  - Lycopene, 2
- M**
- Macro-parasitic worm disease, 59
  - Magnoliopsida, 101
  - Malarial vector, 125
  - Malignant growth, 2
  - Mallees, 199
  - Malus domestica*, 2
  - Marjoram, 119, 365, 366
  - Marker-assisted selection (MAS), 242, 244–246, 350, 373, 376
  - Marshes, 28
  - Mast cells, 177, 361
  - Matrix metalloproteinase 9 (MMP-9), 175, 272
  - Maturing time, 354
  - Meagre quantity, 118, 315
  - Mealy bugs, 38
  - Medication, 2, 7, 10, 56, 125, 180, 318, 365
  - Medicinal
    - plant, 1, 2, 4, 5, 8, 58, 59, 136, 153, 166, 234, 366
    - uses, 286
    - value, 23
  - Menstrual
    - bleeding, 10
    - problems, 11
  - Meristems, 215
  - Metabolic
    - conditions, 62
    - disorders, 131
  - Metabolize pyrrolizidine alkaloids, 5
  - Metaldehyde, 37
  - Methanecarboxylic acid, 315, 330
  - Methanolic extract, 56, 58, 124, 125, 230, 232, 233, 236–238, 240, 290, 304, 360
  - Methicillin-resistant staphylococcus aureus (MRSA), 357, 367
  - Methyl
    - cinnamate, 91, 93, 94, 100, 103, 104, 120, 146, 190, 211, 225, 285
    - basil, 100
    - eugenol, 89, 116, 120
    - heptanone, 263
    - parathion, 38
    - thiazol tetrazolium (MTT), 127, 235, 236
  - Micropropagation, 187
  - Microsatellite, 244
    - markers, 243, 244

Midrib, 203, 204, 220  
 Mildly tonic, 27  
 Minimum inhibitory concentration (MIC),  
 125, 176, 230, 238–240, 357, 369  
*Minimus aureus*, 36  
 Mitogen-activated protein kinases (MAPK),  
 174, 176, 233, 271  
 Modern extraction technologies, 350  
 Molecular targets, 22, 276  
*Monocalyptus*, 204–206, 208  
 Monochasial, 204  
 Monocotyledonae, 35  
 Monocyclic, 40  
 Mono-floral honey, 336  
 Monoterpene, 1, 9, 39, 40, 120, 185, 195,  
 225, 226, 232, 376  
   alcohol linalool, 91, 93  
 Monoterpenoids, 263  
 Monotherapy, 62  
 Monsoon plantation, 215  
 Mood modulator, 366  
 Morphological, 24, 91, 102, 103, 119, 237,  
 292, 324  
   characteristics, 25  
 Mucous, 4  
 Mulching, 111, 112, 347, 353  
 Multi-branched, 342  
 Mustard, 119  
*Mycosphaerella* sp., 221  
 Myocardial infraction (MI), 122

## N

Narrow-lanceolate, 211  
 Nasal effect, 242  
 National  
   level data, 284  
   Medicinal Plants Board, 275, 284  
 Nematodes, 59, 306  
 Neoplasms, 290  
 Nerve growth factor (NGF), 179  
 Nervous system, 23, 27, 60, 361  
 Neuralgia, 21, 28, 196  
 Neuro  
   protection, 60  
   protective component, 361  
   toxic conditions, 60  
 Neurocognition, 132  
 Neuroimaging, 364

Neurological disorder, 365  
 Neuronal function, 60  
 Neuroprotection disorders, 62  
 Neuroprotective activity, 60, 179, 181  
 Nitric oxide (NO), 61, 121, 127, 128, 143,  
 179, 180, 270  
 Nitrogen, phosphorus, potassium (NPK), 37,  
 275, 299, 301  
   treatments, 299  
 N,N-dimethyl methanesulfonamide, 315  
 Non-opioid mechanism, 231  
 Non-steroidal anti-inflammatory drug  
 (NSAIDs), 57  
 Non-volatile residue, 222  
 Normalize appetite, 28  
 North  
   India (NI), 109, 215, 341  
   temperate zone, 99  
 Nuclear, 90, 130, 235, 274, 361, 375  
   factor erythroid 2 (NFE2), 274  
 Nurns, 337  
 Nutraceuticals, 153  
 Nutrient management, 37, 109, 216, 298

## O

Obesity, 62, 132, 177, 268, 270  
 Oblique, 204  
 Oblong, 22, 201, 202, 292, 343  
 Obscure, 212  
 Obtrusive, 3  
*Ocimum*, 89–91, 99, 101–104, 107,  
 109–111, 114–116, 118, 130, 132, 137,  
 145, 147, 153  
   *sanctum*, 107, 109–112, 114, 115, 147,  
 153  
 Odor, 23, 28, 93, 100, 105, 115, 248, 268,  
 324, 358–361, 363–367  
 Ogon, 36  
 Oil  
   distillation facilities, 321  
   extraction techniques, 350  
   qualitative, 345  
 Oleo-gum resin, 261–263, 275  
 Oleoresin, 23, 295, 298, 299, 304  
 Operator, 61  
 Operculum lying, 204  
 Opportunities, 373  
 Optimum soil moisture tension, 216

- Oral  
   health, 97, 153  
   hygiene, 27  
   practice, 10  
 Orange essential oils, 366  
 Oregano, 119, 322  
 Organic  
   fertilizers, 108  
   matter content (OMC), 345  
 Ornamental, 7, 8, 91, 96, 106, 107, 214, 320, 327, 343  
 Osmoprotectants, 9  
 Osmosis, 224  
 Osteoarthritis, 176, 177, 246  
 Osteoporosis, 181, 246  
 Ovate rhombic, 342  
 Ovules, 168, 208  
 Oxalic acid, 27  
 Oxidative stress, 12, 232, 273
- P**
- Pacific region, 190  
 Paprika, 119  
 Parched, 3  
 Parsley, 119  
 Patent, 74, 136, 180, 305, 370  
 Pathogens, 57, 120, 124, 175, 176, 197, 288, 300, 344, 368  
 Pedicel, 199, 205–207, 213, 350  
 Pennveined, 203, 204  
 Pentacyclic terpene, 40  
 Pentadecanoic acid, 315  
 Pentose, 171  
 Pepper, 97, 119  
 Peppermint, 201  
 Perceptive medication, 10  
 Perennial, 6, 21, 34, 35, 74, 90, 98, 101, 102, 168, 291, 315, 317  
   herbaceous vine, 21  
 Perillyl alcohol (POH), 359  
 Peroxisome proliferative-activated  
   gamma receptor (PPAR $\gamma$ ), 178  
   receptor (PPAR), 272  
 Perpetual species, 3  
 Persian literature, 10  
 Persistent bark, 200  
 Pesticidal activities, 369  
 Pests, 112, 220  
 Petroleum ether, 62, 179, 237, 288, 354  
 Phagocytic action, 127  
 Pharmaceutical, 62, 129, 181, 242, 250, 320, 337  
   products, 91, 93, 192  
 Pharmacological, 5, 9, 22, 23, 40, 136, 172, 185, 195, 250, 268, 276, 284, 285, 288, 291, 369  
   activity, 5, 40, 173, 268, 276, 284, 288  
   agents, 172  
   effects, 230  
   properties, 121  
 Phellandrene and piperitone, 197  
 Phenolic, 108, 128, 170, 227  
   acids, 1, 91, 93  
 Phenols, 24, 40, 116, 119, 171  
 Phenotypically, 24  
 Phenylalanine, 39, 245  
   ammonia-lyase (PAL), 21, 245  
 Phenylpropanoids, 39, 40, 120, 130, 131  
 Phosphofructokinase (PFK), 122  
 Phyllotaxy, 99, 100, 199, 212, 342  
 Phylum, 35, 101, 167  
 Physiological side effects, 4  
 Phyto- constituents, 39  
 Phytochemical, 4, 5, 58, 61, 91, 93, 118, 136, 166, 170, 195, 356, 376  
   analysis, 5, 116  
   groups, 5  
   studies, 1, 39  
 Phytochemistry, 3, 8, 12, 170, 261, 263  
 Phytoconstituent, 4, 55, 116, 133, 225, 303  
 Phytomolecules, 89, 130, 153  
 Phytoremediation, 8, 22  
 Pierre green, 36  
 Pigment content, 108  
 Pinching, 112  
   operation, 112  
 Pinkish tinge, 23  
 Pittsburgh sleep quality index (PSQI), 365  
 Plaguing, 136  
 Plant  
   animal, 5  
   microbe interactions, 5  
   taxa, 5  
   tissues, 171, 215, 224  
   variety protection and farmers right (PVPFR), 186

- Plantae*, 35, 101, 167, 208  
Plantation, 7, 23, 37, 187, 189, 198,  
213–216, 222, 298, 321, 346  
  areas, 190  
  management, 214  
Planting, 37, 109, 215, 298, 346  
  date, 346  
  density, 346  
  time, 109  
Plaque  
  accumulation (PLA), 241  
  index (PI), 133, 134  
Plasma, 56, 175, 177, 232  
Plumajillo, 10  
*Pneumococcus*, 338  
Pneumonia, 3, 10, 175, 176, 238, 240  
Pneumonic conditions, 4  
Pollens, 9, 188  
Pollinated buds, 336  
Polyacetylenes, 4  
Polymerase chain reaction (PCR), 234, 242,  
245  
Polymorphic evaluation, 243  
*Pongamia pinnata*, 36  
Portable nature, 224  
Portrayed, 10, 40, 58, 62  
Post-harvest handling, 38, 302, 354  
Pot marigold, 3  
Potent biologically active molecules, 266  
Potential biomolecules, 131, 246  
Powdery mildews, 221  
Power-operated equipment, 39  
Preadipocytes, 59  
Pre-clinical studies, 131  
Predominant chronic musculoskeletal  
  disorder, 246  
Pregnanol, 170  
Preliminary phase, 37  
Pressure fluctuations, 224  
Principal component analysis (PCA), 118  
Prior, 37, 110, 198, 204, 215, 224, 247, 262  
Probing depth (PD), 241  
Processing techniques, 115, 129, 222, 242  
Profound scope, 24  
Profusion, 4  
Progenitors, 243, 246  
Progesterone, 263  
Pro-inflammatory, 174, 269  
Propagation, 36, 108, 170, 186, 187, 214,  
215, 275, 295, 296, 300, 324, 327, 348,  
351, 352  
Propane chemicals, 315  
Propanoic acid, 118  
Prostaglandin E2 (PGE2), 180, 231  
Prostate cancer (PC), 175, 271  
Protein kinase A (PKA), 176, 234  
Protozoa, 175  
Protrusions, 217  
Pruning, 216–220, 299, 347, 348, 352, 353  
*Pseudococcus*, 38  
*Pseudomonas*, 237, 300  
  *aeruginosa*, 57, 145, 237, 240, 288  
Psycho-somatic ailments, 24  
Pulmonary, 3, 5  
  aid, 5  
  illnesses, 3  
  species, 5  
  symptoms, 4  
  treatments, 5  
P-vinylguaiaicol, 315, 330
- ## Q
- Quantitative trait locus (QTL), 245, 246  
  mapping, 244  
Quaternary ammonium moiety, 9  
Quench, 91, 93  
Quercetin, 178, 185, 227, 267  
Quinalphos, 38  
Quinic acid, 9  
Quinones, 170
- ## R
- Radiation, 118, 348  
Rahmrose, 171  
Rainfall, 345  
Rationale, 3, 350  
Reactive oxygen species (ROS), 119, 286,  
361  
Recalcitrant, 214  
Receptor, 5, 123, 177, 269, 361  
  activator of NF- $\kappa$ B ligand (RANKL), 270  
Recombination techniques, 244  
Red  
  blood cells (RBC), 129  
  imported fire ant (RIFA), 62

- Redox, 91, 93  
 Reestablishment, 202, 351  
 Reinforcement, 2  
 Rejuvenating, 23, 166, 262  
     brain, 23  
 Relative humidity (RH), 107  
 Repellent, 8, 62, 125, 189, 195, 196, 237, 248, 289  
     effects, 235  
 Rescue, 37  
 Reserpine, 122  
 Respiratory diseases, 3  
 Resurrection, 136, 284, 321  
 Reunion basil, 100  
 Reversion shoots, 201, 202  
 Rheumatic  
     complaints, 11  
     pain, 10, 28, 94  
 Rheumatoid arthritis, 177  
 Rhizome, 21–23, 27, 34–38, 40, 56–62, 171, 179, 284–288, 290, 292–306  
     formation, 34, 295  
     planting materials, 298, 299, 301  
     powder, 27  
 Rhytidome, 200  
 River edges, 28  
 Root collar, 218  
 Rootstock, 295  
 Rosemary, 119, 336, 337, 343, 359, 363, 364, 366  
 Rosmarinic acid, 118, 145  
 Rotarod activity, 361  
 Rough stream, 6
- S**
- Safer alternative therapeutics, 22  
 Safety, 135, 367  
 Sage, 119, 366  
 Saline, 107, 111, 134, 213, 226  
     soils, 111, 213  
*Salmonella typhi*, 57, 145, 176, 238, 240, 288  
 Sandy, 213, 275, 345  
 Saponins, 24, 58, 59, 116, 118, 166, 170–172, 179, 226, 304  
 Sapwood, 221  
 Savory flavors, 336  
 Scab, 113  
 Scalds, 337  
 Scanning electron microscope (SEM), 235, 240  
 Scape, 22  
 Schistosoma worm's typography, 235  
 Scots language, 6  
 Secondary  
     plant metabolites, 39  
     veins, 34  
 Sedative, 11, 23, 27, 189, 283, 288, 318, 323, 335, 359, 360, 365  
 Seed  
     propagated plantations, 214  
     propagation entails, 214  
 Seedling leaves, 201  
 Segregate, 243, 244  
 Semiarid  
     locales, 3  
     regions, 186  
 Semi-perennials, 168  
 Sequenced characterized amplified region (SCAR), 246  
 Sequence-related amplified polymorphism (SRAP), 316, 374–376  
 Serotonin, 122  
 Sesquiterpene, 1, 9, 39, 40, 94, 120, 185, 195, 225, 226  
     lactones, 4, 9, 40  
 Sesquiterpenoids, 39, 40, 263, 315  
 Sharp bypass-style secateurs, 217  
 Sheep red blood cells (SRBCs), 127  
 Shikimate-phenylpropanoid pathway, 9  
 Shrubs, 102, 218  
 Siddha medicine, 24  
 Simple sequence repeat (SSR), 130, 186, 244, 245, 250, 373–375  
 Sinusitis, 21, 28, 196, 222, 247  
 Skin  
     eruptions, 28  
     health, 134  
 Slovenia, 24  
 Slug damage, 37  
 Snakebite, 11  
 Soil  
     analysis, 345  
     condition, 107  
     nutrient applications, 299  
     preparation, 345

- requirements, 345
  - texture, 345
  - Solitary
    - polygonal crystals, 23
    - prominent mid vein, 34
  - Solvent extraction, 354
  - Spasmodic diseases, 1
  - Specimen tree, 217
  - Spermatophyta, 35, 208
  - Spice, 10, 27, 105, 106, 285, 286, 336
  - Spicy flavor, 23, 27, 105
  - Sprouted rhizomes, 36, 37
  - Stamens, 205
  - Staminal ring, 206
  - Staphylococcus aureus*, 57, 145, 175, 237–240, 288, 369
  - Starch grains, 23
  - Statistics, 92, 193, 194, 242, 284, 319, 325
  - Steam distillation, 223, 224
    - method, 223
  - Stellar area, 23
  - Steroid, 40, 165, 166, 171, 172, 176, 177, 180, 196, 263, 271
  - Steroidal, 57, 170, 171, 174, 179, 261, 263
    - compound cancer therapy, 173
    - hormones, 171
  - Sterols, 1, 39, 170, 222, 263, 304
  - Stigmastanol, 170
  - Stimulant, 27, 58, 89, 95, 96, 189, 286
    - activity, 122
  - Stomachic, 27, 287, 335
  - Storage, 38, 302, 355
  - Stout, 168
  - Strategies, 323, 349
  - Streptococcus*, 134, 288, 289, 338, 357, 369
  - Streptozotocin, 56, 121, 177, 272
  - Sub-chronic toxicity, 129
  - Subcritical-water extraction (SWE), 225
  - Subero-phellodermal layer, 200
  - Subgenus fabrica*, 340
  - Subphylum, 35
  - Subtropical, 3, 28, 36, 168, 186, 187, 284, 288
    - areas, 101
  - Supercritical fluid extraction (SFE), 223, 225, 233
  - Superior eucalypt genotypes, 214
  - Superoxide, 128, 176, 179
  - Supplemental merits, 224
  - Sweet
    - cane, 34
    - flag, 22, 23, 34, 36, 37, 40, 57–60, 62, 74
    - leaves, 34
    - rhizomes, 40, 59
  - Symphyomyrtus, 204–206
  - Sympodial, 34, 292
  - Synovial inflammation, 176, 177
  - Syphilis, 166, 176
  - Systolic blood pressure (SBP), 232, 358
- T**
- Tannins, 24, 116, 118, 123, 170, 171, 225, 226, 228, 315
  - Taraxacum officinale*, 3
  - Taxonomic status, 339
  - Taxonomically laminas, 90
  - Taxonomy, 102, 104, 118, 181, 292
  - Technology transfer, 74, 305
  - Tender, 27, 98, 113, 336, 343, 344
    - inflorescence, 27
    - lavenders, 343
  - Terminal raceme, 99
  - Termites, 221
  - Terpene, 40, 124, 374
  - Terpenoidal constituents, 263
  - Terpenoids, 1, 8, 91, 93, 123, 131, 185, 189, 198, 225, 226, 263
  - Tertiary veins, 34
  - Testicular toxicity, 128
  - Tetra locular fruits, 212
  - Tetraploid, 9, 28, 39
  - Texture glaucous, 211
  - Thai lemon basil, 105
  - Thaumastocoris peregrines*, 221
  - The Australian Lavender Growers Association (TALGA), 326
  - T-helper cells, 133
  - Therapeutic, 3, 4, 6, 9, 21, 22, 56, 58, 89, 95, 96, 130, 131, 153, 165, 166, 171, 173, 185, 189, 193, 231, 262, 268, 274, 276, 315, 338, 358, 359, 369, 376
    - applications, 153
    - efficacy, 21
    - properties, 136
    - uses, 337
  - Three
    - flowered axillary cyme, 204

petal corolla, 168  
 sepal calyx, 168  
 Tidal volume, 4  
 Tissue culture, 352  
 Toothache, 11, 27, 28, 287  
 Total  
   calories intake (TCI), 132  
   cholesterol, 122  
   flavonoids, 108, 227  
   knee replacement (TKR), 246, 247  
   phenolics, 108, 233  
 Toxicity, 303  
 Trade, 7, 23, 92, 192, 284, 322  
 Traditional medicine, 2, 3, 5, 12, 23, 74,  
   166, 248, 286, 318  
 Transplantation, 108, 110, 216, 351  
 Tricyclic, 40  
 Triglycerides level, 122  
 Triploid, 24, 39  
 Triterpene, 1, 24, 265  
   glycoside, 39, 40  
 Triterpenoid, 265  
   saponins, 39, 40  
 Tropics, 190  
 Trunk, 187, 189, 200, 202, 211, 213,  
   217–219  
*Trychosanthes diocia*, 97  
 Tuberculosis, 11, 125, 239  
 Tulsi lace wing, 112

## U

Uniform biomass production, 187  
 Unique  
   habit, 217  
   role, 2  
 Unsaturated, 8, 9, 40  
   fats, 8  
 Unusual feminine dying, 10  
 Unweighted pair group method with arith-  
   metic mean (UPGMA), 243, 244  
 Urceolate, 206, 207  
 Uterine discharge, 11

## V

Vacuum distillation, 225  
 Vaginal discharge, 337  
 Value additions, 119, 304, 306

Vanilla pods, 27  
 Vanomycin-resistant *Enterococcus faecalis*  
   (VRE), 367  
 Varicose veins, 11  
 Variegatus, 35, 36  
 Vascular  
   cell adhesive molecules (VCAM-1), 176  
   smooth muscle cells (VSMC), 176  
 Vegetative reproduction, 170  
 Venation, 203  
 Ventral surface, 91, 99, 112, 113, 342  
 Vermifuge, 27, 95, 189  
 Vinegars, 119, 319  
 Visual analog scale (VAS), 247  
 Volatile  
   compounds, 94, 130, 323, 358  
   fraction, 222  
   medicinal, 24  
   oil, 39, 99, 118, 119, 195, 224, 230, 237,  
   263, 293, 303

## W

Water distillation, 224  
 Weed control, 216, 347  
 Western  
   cultures, 10  
   ghats, 165, 341  
   medicine experts, 24  
 Wetland, 28  
   monocot, 21, 74  
 White blood cell (WBC), 127, 247  
 Wide assortment, 3  
 Wilt, 113  
 Winter bronzing bug, 221  
 World  
   eucalyptus, 192  
   Health Organization (WHO), 2, 3, 136,  
   166, 369  
   lavandula oil markets, 324  
   renowned medicinal plant species, 2  
   Trade Organization (WTO), 136

## X

Xanthone glycoside, 40  
 Xenobiotics, 126  
 Xenotransplanted mice, 2334



**Y**

Yarrow, 1, 3, 4, 6, 8–11  
Yield, 9, 22, 38, 93, 94, 106, 110–112, 114,  
115, 130, 131, 187, 188, 213, 215, 216,  
218, 222, 224, 226, 248, 275, 293–295,  
297–302, 319, 321, 323–326, 329, 344,  
346, 348–350, 352–356

**Z**

Zebrafish, 291  
Zero side-effects, 192  
Z-guggulsterone, 263  
Zimbabwe, 230  
Zinc (Zn), 107, 111, 294, 295  
*Zingiberaceae*, 283, 284, 286, 292, 295, 306  
*Zinnias*, 3

# Advances in Medicinal and Aromatic Plants

Production, Processing,  
and Pharmaceuticals

VOLUME 2



Amritesh C. Shukla | Sunita Facknath  
Debashis Mandal | Bernadette Montanari  
Editors



CRC Press  
Taylor & Francis Group

APPLE ACADEMIC PRESS

**ADVANCES IN MEDICINAL AND  
AROMATIC PLANTS**

**Volume 2**

**Production, Processing, and Pharmaceutics**

Advances in Medicinal and Aromatic Plants: Production, Processing, and Pharmaceutics,  
2-volume set

Hardback ISBN: 978-1-77491-488-5

Paperback ISBN: 978-1-77491-489-2

Ebook ISBN: 978-1-03268-690-5

**Volume 1:**

Hardback ISBN: 978-1-77491-790-9

Paperback ISBN: 978-1-77491-791-6

**Volume 2:**

Hardback ISBN: 978-1-77491-792-3

Paperback ISBN: 978-1-77491-793-0

# **ADVANCES IN MEDICINAL AND AROMATIC PLANTS**

**Volume 2**

**Production, Processing, and Pharmaceutics**

*Edited by*

**Amritesh C. Shukla, PhD**

**Sunita Facknath, PhD**

**Debashis Mandal, PhD**

**Bernadette Montanari, PhD**

**AAP** | APPLE  
ACADEMIC  
PRESS

First edition published 2025

**Apple Academic Press Inc.**

1265 Goldenrod Circle, NE,  
Palm Bay, FL 32905 USA

760 Laurentian Drive, Unit 19,  
Burlington, ON L7N 0A4, CANADA

**CRC Press**

2385 NW Executive Center Drive,  
Suite 320, Boca Raton FL 33431

4 Park Square, Milton Park,  
Abingdon, Oxon, OX14 4RN UK

© 2025 by Apple Academic Press, Inc.

*Apple Academic Press exclusively co-publishes with CRC Press, an imprint of Taylor & Francis Group, LLC*

Reasonable efforts have been made to publish reliable data and information, but the authors, editors, and publisher cannot assume responsibility for the validity of all materials or the consequences of their use. The authors, editors, and publishers have attempted to trace the copyright holders of all material reproduced in this publication and apologize to copyright holders if permission to publish in this form has not been obtained. If any copyright material has not been acknowledged, please write and let us know so we may rectify in any future reprint.

Except as permitted under U.S. Copyright Law, no part of this book may be reprinted, reproduced, transmitted, or utilized in any form by any electronic, mechanical, or other means, now known or hereafter invented, including photocopying, microfilming, and recording, or in any information storage or retrieval system, without written permission from the publishers.

For permission to photocopy or use material electronically from this work, access [www.copyright.com](http://www.copyright.com) or contact the Copyright Clearance Center, Inc. (CCC), 222 Rosewood Drive, Danvers, MA 01923, 978-750-8400. For works that are not available on CCC please contact [mpkbookspermissions@tandf.co.uk](mailto:mpkbookspermissions@tandf.co.uk)

Trademark notice: Product or corporate names may be trademarks or registered trademarks and are used only for identification and explanation without intent to infringe.

---

**Library and Archives Canada Cataloguing in Publication**

Title: Advances in medicinal and aromatic plants : production, processing, and pharmaceuticals / edited by

Amrithesh C. Shukla, PhD, Sunita Facknath, PhD, Debashis Mandal, PhD, Bernadette Montanari, PhD.

Names: Shukla, Amrithesh C., editor. | Facknath, Sunita, editor. | Mandal, Debashis, editor. | Montanari, Bernadette, editor.

Description: First edition. | Includes bibliographical references and indexes.

Identifiers: C anadiana ( print) 2 0230593216 | C anadiana ( ebook) 2 0230593275 | I SBN 9 781774914885 ( set) |

ISBN 9781774917923 (v. 2 ; hardcover) | ISBN 9781774917930 (v. 2 ; softcover) | ISBN 9781032686905 (ebook)

Subjects: LCSH: Medicinal plants. | LCSH: Aromatic plants. | LCSH: Materia medica, Vegetable. | LCSH: Botany, Medical. | LCSH: Pharmacognosy.

Classification: LCC QK99.A1 A38 2024 | DDC 581.6/34—dc23

---

ISBN: 978-1-77491-792-3 (hbk)

ISBN: 978-1-77491-793-0 (pbk)

## About the Editors

---



**Amrithesh C. Shukla, PhD**

*Professor, Department of Botany,  
University of Lucknow, Lucknow, India*

Amrithesh C. Shukla, PhD, is currently working as a Professor in the Department of Botany at the University of Lucknow, India. Dr. Shukla did his DPhil and DSc in Botany at the University of Allahabad, India. He served as a Reader/Professor and Head of the Department of Horticulture, Aromatic and Medicinal Plants at Mizoram University, Aizawl, India (2007–16). He has been working on medicinal and aromatic plants, cultivation, conservation, bioprospection, natural products, drug development, and patenting since 1995. He has standardized various scientific methods, such as MSGIT, MDKT MS-97, NCCLS (2002–03), and successfully handled six major research projects and is currently supervising one European Union project (No. 8944160). He has developed commercial herbal formulations and has US, UK, Japanese, and Indian patents. In addition to this, he has supervised 21 master's theses and 10 PhD dissertations. He has published over 115 research papers/articles in nationally and internationally reputed journals as well as 10 books (authored four and edited six), published by AAP-CRC Press (2019), Springer (2020), etc.

Dr. Shukla works as an editor, associate editor, and editorial board member of many internationally reputed journals, such as the *American Journal of Food Technology*, *Journal of Pharmacology and Toxicology*, *Research Journal of Medicinal Plants*, and as reviewer for *Scientific Reports*, *International Journal of Dermatology*, *European Journal of Medicinal Plants*, *African Journal of Agricultural Research*, *International Journal of Agricultural Chemistry*, and *Journal of Herbs, Spices, and Medicinal Plants*.

Prof. Shukla has vast overseas experience in R&D for medicinal and aromatic plants in India and several countries in Asia and the Pacific regions. He has been an invited speaker at the Indo-Brazilian Symposium (2020); and delivered lecture and chaired session at the ISHS-IV Asia Symposium on Quality Management in Postharvest Systems, Jeonju, Korea (2017).

He is a member of the International Society for Horticultural Science, Belgium (2016). He was an invited scientist at the International Conferences on Controlled Atmosphere and Fumigation in Stored Products (CAF), Gold Coast, Australia (2004); CAF, Fresno, USA (2000); 7th International Working Conference on Stored-Product Protection, Beijing, China (1998); and 4th European Foundation for Plant Pathology, Berlin, Germany. He has also been a Visiting Professor at the University of Mauritius (2014) and at the University of British Columbia, Canada (2013–14), as well as a member of an expert panel for promotion to Professor in the Department of Botany and Microbiology, College of Science, King Saud University, Saudi Arabia (2018), and in the Research Degrees and Scholarships Committee, Murdoch University, Perth, Australia (2019–21).

For his outstanding scientific contribution, Prof. Shukla has been honored with a Y.S. Murty Memorial Gold Medal; Prof. R.C. Pant Memorial Award; NESAS-Scientist of the Year Award; ISC-Member of the Sectional Committee, Plant Sciences Section of the 101st Indian Science Congress; and IPS Medal-98. He has been the executive councilor of the Indian Botanical Society; chairman of the International Symposium on Sustainable Horticulture (ISSH-2016); member of the State-Level Steering Committee for the National Mission on Medicinal Plants, Government of Mizoram; program coordinator of the Indian Academy of Sciences, Bangalore; program coordinator – CSIR-CIMAP Training; convener at the ASSOCHAM Conference; course director of RAMAPS; and convener – NCNRM, India. In addition, he is a fellow of the Ethnobotanical Society, the Society of Life Sciences, the Indian Botanical Society, the International Young Scientist Association, and the Linnean Society of London (2021).



**Sunita Facknath, PhD**

*Professor, Faculty of Agriculture,  
University of Mauritius, Mauritius*

Sunita Facknath, PhD, is a Professor engaged in teaching and research in agricultural technology for the past 25 years at the University of Mauritius. She has published more than 100 research papers and articles in reputed journals and conference proceedings. In addition, she dealt with 20 research projects externally funded by important internally renowned institutes/agencies, such



as the World Bank, European Union, International Atomic Energy Agency, ACU, African Union, Development Finance International, Climate and Development Knowledge Network (CDKN), etc. Further, she is a consultant agriculturist for many public-private sectors and NGOs based in Mauritius (FAO, EUCDP, UNDP, UNEP-Mauritius, FANRPAN, Mauritius Research Council, Government of Mauritius; SGS Co Ltd., DDS, MACOSS, etc.). She has guided 15 MPhil and PhD students and also has profound administrative experience at the University of Mauritius and also at multiple national and international bodies like the African Network of Research on Bruchids, Mauritius Council for Social Services (MACOSS), African Regional Program in Insect Science (ARPIS) Academic Board, Fishermen Investment Trust, Ministry of Fisheries and Rodrigues, National Biosecurity Technical Advisory Committee, Mauritius Standards Bureau Committee, National Marine Biotechnology Advisory Council, National Ocean Knowledge Cluster Advisory Council, UoM Senate, etc.



**Debashis Mandal, PhD**

*Assistant Professor, Department of Horticulture,  
Aromatic and Medicinal Plants,  
Mizoram University, Aizawl, Mizoram, India*

Debashis Mandal, PhD, is an Assistant Professor in the Department of Horticulture, Aromatic and Medicinal Plants at Mizoram University, Aizawl, Mizoram, India. He is a young academician and research fellow who has been working in sustainable hill farming for the past 11 years. He did his PhD at BCKV, India, and was a post-doctoral project scientist at IIT, Kharagpur, India. He previously worked as an Assistant Professor at Sikkim University, India, and has published 48 research papers and book chapters in reputed journals and books. He has also published nine books from Apple Academic Press, American Academic Press, and Lambert Academic Publishing. He is also working as a member of the Working Group Lychee and Other Sapindaceae Crops, ISHS, Belgium, and is also a member in the ISHS section on tropical and subtropical fruits, organic horticulture, and the commission on quality and postharvest horticulture. Currently, he is working as an Editor-in-Lead (Horticulture) for the *International Journal of Bio-Resources and Stress Management (IJBSM)* and editorial board member of *Bulletin Agrotechnology, Research on Crops, Crop Research, Journal of*

*Postharvest Technology, Senhri Journal of Multidisciplinary Studies*, etc. Dr. Mandal is also an editorial advisor in Horticulture Science for Cambridge Scholar Publishing, United Kingdom, and a regular reviewer of journals that include *Fruits, HortScience, Acta Physiologica Plantarum, and African Journal of Agricultural Research, Journal of Food Quality*, etc. Further, he is a consultant horticulturist in the Department of Horticulture and Agriculture (Research and Extension), Government of Mizoram, India, and Himadri Specialty Chemicals Ltd., and is also handling externally funded research projects. He was a convener for the International Symposium on Sustainable Horticulture, 2016, India, and a co-convener for the International Conference of Bio-Resource and Stress Management, 2017, Jaipur, India. In addition, he was a session moderator and keynote speaker at the ISHS Symposium on Litchi, India, in 2016, on postharvest technology in Vietnam, 2014, and at South Korea, 2017, and AFSA Conference in 2018, Cambodia. He is the recipient of the Best Editor Award (2017) by IJBSM, the Young Achiever Award (2019) by SADHNA, the Best Researcher Award (2020) by Scifax, and the Young Scientist Award (2020) by the Society of Tropical Agriculture. He has visited countries like Thailand, China, Nepal, Bhutan, Vietnam, South Korea, South Africa, and Cambodia for professional meetings, seminars, and symposia. His thrust areas of research are organic horticulture, pomology, postharvest technology, plant nutrition, and micro-irrigation.



**Bernadette Montanari, PhD**

*Interdisciplinary Institute of Social Studies,  
University Sidi Mohamed Ben Abdellah,  
Fez, Morocco*

Bernadette Montanari, PhD, is a proactive Research Scholar with degrees (PhD Ethnobiology and MSc Ethnobotany) from the School of Anthropology and Conservation, University of Kent, UK. Her work is at the intersection of medicinal plants, natural resources and natural products as well as in the development for women and community enterprises, women's traditional ecological knowledge, social policies, and social justice. She has consistent research activities through multiple interdisciplinary research projects on the social-economic impact of international and national policies on community development. Her latest two Marie-Curie Fellowships of the European Union reflect her engagement. The first related to policies for the recognition of women's traditional knowledge in natural product

development in the Green Morocco Plan, Morocco; the latter on the factors that determined the attribution of Access to Benefit Sharing (ABS) of the Nagoya Protocol for mint farmers in India and for women working in argan oil cooperatives in Morocco. She has published several significant research papers and book chapters in reputed international journals and books. She is currently a research member of the Interdisciplinary Institute of Social Studies at the University Sidi Mohamed Ben Abdallah, Fes, Morocco, where she is pursuing her work on community development. She is an affiliated member of the Centre for Biocultural Diversity, University of Kent, UK, and a collaborating researcher at the Centre for Research in Anthropology at the University Institute of Lisbon, Portugal. Moreover, she is a member of several organizations: Société Française d'ethno-pharmacologie, France; Conservatoire des Plantes à Parfum, Médicinales et Aromatiques (CNPMAI), France; IUCN Sustainable Use and Livelihoods Specialist Group (SULi); Species Survival Commission (SSC) and Commission on Environmental, Economic, and Social Policy (CEESP); IPACC, North Africa. Previously she held professional affiliations with the Laboratoire Population, Environnement & Développement (LPED), University Aix-Marseille, France; Women and Global Perspectives Program (WGPP), University of Illinois, USA, among others.



**Taylor & Francis**

Taylor & Francis Group

<http://taylorandfrancis.com>

# Contents

---

<i>Contributors</i> .....	<i>xiii</i>
<i>Abbreviations</i> .....	<i>xv</i>
<i>Preface</i> .....	<i>xxi</i>
<b>1. <i>Mentha</i> spp.: A Miraculous Plant with Pharmaceutical Uses.....</b>	<b>1</b>
Ankita Maurya, Richa Sharma, Himanshu Yadav, Debashis Mandal, and Amritesh C. Shukla	
<b>2. <i>Neem</i>: The Drug Cabinet of Mother Nature .....</b>	<b>55</b>
Moumita Malakar and Debashis Mandal	
<b>3. <i>Patchouli (Pogostemon cablin Benth.)</i>: A Comprehensive Review on the Medicinal Aromatic Plant with its Industrial Utilization.....</b>	<b>131</b>
Sonia Singh, Shilpi Pathak, Nidhi Sharma, and Nitin Agrawal	
<b>4. <i>Pippali (Piper longum L.)</i>: A Plant with Versatile Pharmaceutical Uses.....</b>	<b>163</b>
Richa Sharma, Ankita Maurya, Himanshu Yadav, Amritesh C. Shukla, and Sumpam Tangjang	
<b>5. <i>Pomegranate (Punica granatum)</i>: A Medicinal and Commercial Perspective.....</b>	<b>219</b>
Shilpa Vakshasya and Gopal Dixit	
<b>6. <i>Rhubarb (Rheum sp.)</i>: A Rare and Endangered Medicinal Plant of the Himalayas .....</b>	<b>241</b>
Meenakshi Thakur	
<b>7. <i>Rose (Rosa sp.)</i>, More Than Just Beautiful: Exploring the Therapeutic Properties of the Rose Species .....</b>	<b>263</b>
Naoko Takahashi	
<b>8. <i>Safed Musli</i>: A Critical Review on its Bioactive Compounds, Medicinal Properties, and Biological Activity.....</b>	<b>299</b>
Sabyasachi Banerjee, Utsab Chakraborty, and Sankhadip Bose	

<b>9. Bishop's Weed or Ajwain (<i>Trachyspermum ammi</i> Linn.): A Traditional Medicinal Plant with Pharmacological Importance, Ethno-Botanical Uses, and Nutritional Benefits for Quality Life Improvement .....</b>	<b>355</b>
Somenath Das	
<b>10. <i>Tinospora cordifolia</i> (Willd.) Miers: A Review on the Medicinal Aromatic Plant with Industrial and Therapeutical Utilization.....</b>	<b>381</b>
Sonia Singh, Nitin Agrawal, and Yogesh Murti	
<b>11. White Tea: An Emerging Gift of Nature and Bioprospection Towards the Development of Novel Herbal Formulations, Nutraceuticals, and Cosmetics.....</b>	<b>403</b>
Dhrubojyoti Mukherjee, Partha Palit, Shubhadeep Roychoudhury, Shubhajit Halder, and Subhash C. Mandal	
<b><i>Index</i>.....</b>	<b>419</b>

# Contributors

---

## **Nitin Agrawal**

Faculty of Pharmacy, Raja Balwant Singh Engineering Technical Campus, Bichpuri, Agra, Uttar Pradesh, India

## **Sabyasachi Banerjee**

Department of Phytochemistry, Gupta College of Technological Sciences, Asansol, West Bengal, India

## **Sankhadip Bose**

School of Pharmacy, The Neotia University, Sarisa, West Bengal, India

## **Utsab Chakraborty**

School Pharmacy, YBN University, Rajaulatu, Namkum, Ranchi, Jharkhand, India

## **Somenath Das**

Department of Botany, Burdwan Raj College, Burdwan, West Bengal, India

## **Gopal Dixit**

Upadhi PG College, (MJP Rohilkhand University), Pilibhit, Uttar Pradesh, India

## **Shubhajit Halder**

Department of Chemistry, Hislop College, Nagpur, Maharashtra, India

## **Moumita Malakar**

Department of Horticulture, Central University of Tamil Nadu, Neelakudy, Thiruvavur, Tamil Nadu, India

## **Debashis Mandal**

Department of Horticulture, Aromatic and Medicinal Plants, Mizoram University, Aizawl, Mizoram, India

## **Subhash C. Mandal**

Pharmacognosy and Phytotherapy Research Laboratory, Division of Pharmacognosy, Department of Pharmaceutical Technology, Jadavpur University, Kolkata, West Bengal, India

## **Ankita Maurya**

Department of Botany, University of Lucknow, Lucknow, Uttar Pradesh, India

## **Dhrubojoyoti Mukherjee**

Pharmacognosy and Phytotherapy Research Laboratory, Division of Pharmacognosy, Department of Pharmaceutical Technology, Jadavpur University, Kolkata, West Bengal, India

## **Yogesh Murti**

Institute of Pharmaceutical Research, GLA University, Mathura, Uttar Pradesh, India

## **Partha Palit**

Department of Pharmaceutical Sciences, Drug Discovery Research Laboratory, Division of Pharmacognosy, Assam University (A Central University), Silchar, Assam, India

## **Shilpi Pathak**

Institute of Pharmaceutical Research, GLA University, Mathura, Uttar Pradesh, India

## **Shubhadeep Roychoudhury**

Department of Life Science and Bioinformatics, Assam University (A Central University), Silchar, Assam, India

**Nidhi Sharma**

Noida Institute of Engineering and Technology, Greater Noida, Uttar Pradesh, India

**Richa Sharma**

Department of Botany, University of Lucknow, Lucknow, Uttar Pradesh, India;  
Rajiv Gandhi University, Rono Hills, Doimukh, Arunachal Pradesh, India

**Amritesh C. Shukla**

Department of Botany, University of Lucknow, Lucknow, Uttar Pradesh, India

**Sonia Singh**

Institute of Pharmaceutical Research, GLA University, Mathura, Uttar Pradesh, India

**Naoko Takahashi**

United Nations Staff, Rome, Italy

**Sumpam Tangjang**

Rajiv Gandhi University, Rono Hills, Doimukh, Arunachal Pradesh, India

**Meenakshi Thakur**

College of Horticulture and Forestry (Dr. Y.S. Parmar University of Horticulture and Forestry),  
Neri, Hamirpur, Himachal Pradesh, India

**Shilpa Vakshasya**

St. Alloysius College, Pilibhit, Uttar Pradesh, India

**Himanshu Yadav**

Department of Botany, University of Lucknow, Lucknow, Uttar Pradesh, India



# Abbreviations

---

$^{13}\text{C}$ -NMR	carbon-13 nuclear magnetic resonance
$^1\text{H}$ -NMR	proton nuclear magnetic resonance
5-HIAA	5-hydroxyindoleacetic acid
5-FU	5-fluorouracil
AAILE	aqueous <i>A. indica</i> leaf extract
ABTS	2,20-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid)
ACF	aberrant crypt foci
ADR	Adriamycin
AFLP	amplified fragment length polymorphism
AFRI	Arid Forest Research Institute
ai	active ingredient
AI	azadirachtin
AJC	ajmodadichurna
ALP	alkaline phosphatase
ALT	alanine transaminase
APC	antigen-presenting cells
ApMV	apple mosaic virus
ArMV	Arabis mosaic virus
AST	aspartate aminotransferase
ATP	adenosine Triphosphate
AZ	azadirachtin
BHA	butylated hydroxyl anisole
CAF	Chinese Academy of Forestry
CAM	chick chorioallantoic membrane
CAT	catalase
CC	column chromatography
$\text{CCL}_4$	carbon tetrachloride
CEA	carcinoembryonic antigen
CFB	corrugated fiberboard
CH	cholesterol
CMV	cucumber mosaic virus
COX-2	cyclooxygenase
CTL	cytotoxic T lymphocyte
DA	dopamine
DAA	days after anthesis
DAD	diode array detection
DDW	double distilled water

DES	deep eutectic solvent
DIPAS	Defense Institute of Physiology and Allied Sciences
DLA	Dalton's Lymphoma Ascites
DMBA	7,12-dimethylbenz-(a)-anthracene
DOPAC	3,4-dihydroxyphenylacetic acid
DPPH	1,1-diphenyl-2-picrylhydrazyl
DTH	delayed-type hypersensitivity response
EAC	Ehrlich ascites carcinoma
EC	epicatechin
ECG	epicatechin gallate
ED	erectile dysfunctions
ED <sub>50</sub>	median effective dose
EGC	epigallocatechin
EGCG	epigallocatechin-3-gallate
EHPEA	Ethiopian Horticulture Producer and Exporters Association
ELISA	enzyme-linked immunosorbent assay
EOs	essential oils
EPA	Environmental Protection Act
ER	enhancement ratio
ESI-MS <sup>n</sup>	electrospray ionization multistage mass spectrometry
ETI	ethical trading initiative
FID	flame-ionization detection
FMA	fermented <i>M. arvensis</i>
FOS	fructooligosaccharides
FYM	farmyard manure
GC	gas chromatography
GC-MS	gas chromatography-mass spectrometry
GCSF	granulocyte colony-stimulating factor
GM-CSF	granulocyte-macrophage colony-stimulating factor
GSH	glutathione
GSHP <sub>x</sub>	glutathione peroxidase
H <sub>2</sub> N <sub>2</sub>	influenza A virus subtype
H <sub>2</sub> O <sub>2</sub>	hydrogen peroxide
HBP	hamster buccal pouch
HCl	hydrochloric acid
HDHC	heavy-duty hand cleanser
HDL	high-density lipoproteins
HIV	human immunodeficiency virus
HPLC	high-performance liquid chromatography
HPTLC	high-performance thin layer chromatography
HSCCC	high-speed counter-current chromatography
HSV-1	herpes simplex type-1
HVA	homo-vanillic acid

IC <sub>50</sub>	half maximal inhibitory concentration
ICFRE	Indian Council for Forest Research and Education
ICM	integrated crop management
IFN	Interferons
IGRs	insect growth regulators
IL-1 $\beta$	interleukin-1 $\beta$
IL-2	interleukin-2
IL-6	interleukin-6
IMC	indomethacin
INN	international neem network
iNO	inducible NO
IPC	international patent classification
IPM	integrated pest management
IPNM	integrated plant nutrient management
IR	infrared
I $\beta$	inhibitor protein
K <sup>+</sup>	potassium ion
KFC	Kenya Flower Council
KVIC	Khadi and Village Industries Commission
LC-MS	liquid chromatography-mass spectrometry
LDH	lactate dehydrogenase
LDL	low-density lipoproteins
LER	land equivalent ratio
LPO	lipid peroxidation
LPS	lipopolysaccharide
LT50	median lethal time
MA	<i>M. arvensis</i>
MAPs	medicinal and aromatic plants
MBC	minimum bactericidal concentration
MCX	multi-commodity exchange
MDA	methylenedioxyamphetamine
MIC	minimum inhibition concentration
MMP	matrix metalloproteinase
MNNG	N-methyl-N-nitro-N-nitroso-guanidine
MPTP	1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine
MS	mass spectroscopy
MTT	methyl thiazolyldiphenyl-tetrazolium bromide
NADPH	nicotinamide adenine dinucleotide phosphate
NDEX	National Commodity and Derivatives Exchange
NFEs	neem fruit extracts
Nf-k $\beta$	nuclear factor kappa enhancer of B cells.
NK	natural killer
NLE	neem leaf extract

NLGP	neem leaf glycoprotein
NMCEIL	National Multi Commodity Exchange of India
NMR	nuclear magnetic resonance
NO	nitric oxide/nitrous oxide
NOS	3,4-nitric oxide synthases
NSE	neem seed extracts
OHM	Orchard Health Management
OVA	ovalbumin
PA	patchouli alcohol
PAR	photosynthetically active radiation
PARP <sub>s</sub>	poly(ADP-ribose) polymerases
PBMC	peripheral blood mononuclear cells
PCA	principal component analysis
PCNA	proliferating cell nuclear antigen
PGE2	prostaglandin E2
PGPRs	plant growth promoting rhizobacteria
PI-PLC $\gamma$ 1	phosphoinositide-specific phospholipase C
PMS	premenstrual syndrome
PNN	polymorpho nuclear neutrophil
PNRS	prunus necrotic ring spot virus
PPP	public-private partnership
PSQI	Pittsburg sleep quality index
PTTH	prothoracicotropic hormone
PTZ	pentylenetetrazol
RCV-1	rose cryptic virus-1
RI	retention index
ROS	reactive oxygen species
RP-HPAE	reverse-phase high-pressure anion exchange
SCF	supercritical fluid
SGOT	serum glutamic oxaloacetic transaminase
SGPT	serum glutamic-pyruvic transaminase
SLRS	strawberry latent ring spot
SOD	superoxide dismutase
SOS	global response to DNA damage
SRB	sulforhodamine blue
SRBC	sheep red blood cell
STPLC	sitopaladichurna
TAA	tumor-associated antigen
TCM	<i>Traditional Chinese Medicine</i>
TG	triglyceride
TH	tyrosine hydroxylase
TIMP-1	tissue inhibitor of metalloproteinases
TLC	thin-layer chromatography

TNF	tumor necrosis factor
TNF- $\alpha$	tumor necrosis factor-alpha
TomRSV	tomato ring spot virus
TPC	total protein content
TRSV	tobacco ring spot virus
TSM	tobacco streak virus
UAE	ultrasound-assisted extraction
UV	ultraviolet
VEGF	vascular endothelial growth factor
VMA	vanillylmandelic acid
VSV	vesicular stomatitis
WHO	World Health Organization
WPH	white pH
YGND	Yunan Guangming Neem Development Company



# Taylor & Francis

Taylor & Francis Group

<http://taylorandfrancis.com>

# Preface

---

The progression of human civilization has brought about enormous changes in society and livelihood. However, these changes have also yielded different health problems in the process of making the earth more hospitable. We witness critical health issues today but medical evolution has also brought about a range of solutions to these. Herbal medicine and the therapeutic properties of natural products have gained immense importance simultaneously as well. Besides their dietary and cosmetic uses, new dimensions in the use of medicinal and therapeutic herbs are being explored. Extensive research has led to the discovery of medicinal uses of various plants and herbs, their bioactive compounds, and their therapeutic role in human and livestock health. Compared to plant variability, diversity, and human needs, this is still a needle in the ocean. A lot of more work needs to be done in this field.

Bioactive compounds isolated from different plants have been researched and used for various needs. Their use in entomo-pathological formulations, has paved the way for eco-friendly control of disease and pests in crops. It has thus provided a healthier means of food grain production, free from pesticide contamination. Shelf-life management of fresh-cut, unprocessed, and processed food has success stories of using herbal products, essential oils, and formulations. Enormous industrial and cosmetic have also been reported for essential oils extracted from plants. It is as if Mother Nature is facilitating an on-going in-depth search for potent life in the realm of natural biodiversity and coming up with gems for nurturing life in a healthier way, with the process continuing indefinitely.

This volume, *Advances in Medicinal and Aromatic Plants: Production, Processing, and Pharmaceuticals (Vol. 2)* is an effort to compile profuse research information and scientific reports available for making comprehensive editions for catering to the needs of researchers, academician, scholars, farmers, industrialist, entrepreneurs, and extension workers. The current volume has covered information on mentha, neem, patchouli, pippali, pomegranate, rhubarb, rose, safed musli, ajwain, tinospora, and tea for its cultivation, marketing, processing, bio prospection, and therapeutic uses.

—*Editors*



**Taylor & Francis**

Taylor & Francis Group

<http://taylorandfrancis.com>



## CHAPTER 1

---

# *Mentha* spp.: A Miraculous Plant with Pharmaceutical Uses

ANKITA MAURYA,<sup>1</sup> RICHA SHARMA,<sup>1</sup> HIMANSHU YADAV,<sup>1</sup>  
DEBASHIS MANDAL,<sup>2</sup> and AMRITESH C. SHUKLA<sup>1</sup>

<sup>1</sup>*Department of Botany, University of Lucknow, Lucknow, Uttar Pradesh, India*

<sup>2</sup>*Department of Horticulture, Aromatic and Medicinal Plants, Mizoram University, Aizawl, Mizoram, India*

---

### ABSTRACT

Menthol mint, named as *Mentha arvensis* L., which is an aromatic and medicinal oil-yielding herb with minty flavor belongs to the mint family, distributed, and grown all throughout the world mainly in tropical/subtropics and temperate zones. The genus *Mentha* traditionally used in numerous systems of treatment including the Ayurvedic, Chinese, and Unani system. *Mentha* spp. are used for remedy of various illnesses of diseases/disorders; as an antiseptic, analgesic, carminative, nervous disorders, nose and throat diseases, gastric problem, stomach ache, chest pains, insomnia, and snake and insect bites. The herb is propagated for its essential oil (EOs), mostly utilized in food, cosmetics, herbal medicines, and pharmaceutical industries. The oil contains menthol, considered as major components. Extract of *M. arvensis* plant part (leaves, stem, root, and inflorescence) has shown to possess various activity such as antioxidant, antifungal, antibacterial, anti-inflammatory, insecticidal, hepatoprotective, anti-asthmatic effect, and anti-allergic activity; as well as show effect against cardiovascular disease, anti-angiogenic effect, and antiulcerogenic activity, etc. The demand of *Mentha* oil has been raised

extremely in pharmaceutical industry. Although, *Mentha* species are having great economic, but there are number of ‘pests and diseases’ viz., fungi, virus, bacteria, nematode, and insects, which deteriorate the quantitative and qualitative yield of *Mentha*. These ‘pest and disease’ sometimes decrease the essential oil production, up to 60–80%. An integrated disease management approach implementation is required to control this disease effectively. Host resistance, inter-cropping, time of planting and careful use of fungicides and pesticides are important components in management package of pest and diseases.

In the present chapter, we are focusing on the different aspects of *M. arvensis* such as phytochemistry, pharmacological aspects, and future opportunities to investigate this plant. The information, shared in this review will provide an exhaustive knowledge in exploring the usefulness of main active compounds of *Mentha* in various medical and related fields.

## 1.1 INTRODUCTION

According to World Health Organization, nearly 80% of population in developing nations are exploitation botanical medicine systems (extracts of natural origin as medicines or health-promoting agents) and around 3.3 billion populaces are utilizing medicinal flora for therapeutic purposes. Among them, approximately, 25% of active substances in medicines are obtained from plants/plant extracts. Over the last 150 years, pharmacists, as well as researchers, have isolated and purified “active” components from medicinal plants in an effort to produce authentic pharmaceutical medicines (Thawkar, Jawarkar, Kalamkar, Pawar, & Kale, 2016).

Mint is an aromatic plant that belongs to the Lamiaceae family (known as mint family) and is a common medicinal oil yielding herb cultivated extensively in the temperate and tropical region of the world. *Mentha* species has long been known as a kitchen herb for humans. *M. arvensis* introduced in India by Regional Research laboratory, Jammu, in 1952, and now cultivated throughout India. At the present time it’s considered to be the most popular essential oil crops in Uttar Pradesh (Chand, Patra, Anwar, & Patra, 2004). Currently, In the international market, India is the leading producer and exporter, followed by China, Brazil, and the United States. The economic sustainability of *Mentha* cultivation depends on its profitability among smallholders. Hence, mint growers consider *Mentha* as a

cash crop in Indo-Gangetic plains because it does not disturb or replace the cultivation of any major Rabi (winter) or Kharif (rainy) crop (Choudhary, Badal, Singh, & Osti, 2017; Singh et al., 2020). *Mentha* herb is susceptible to weeds and many ‘pests and diseases’ namely fungi, viruses, bacteria, and nematode and insects. These pathogens impose different constraints and deteriorate the quantitative and qualitative losses of production (Pandey et al., 2019).

*Mentha* genus is well known for its traditional uses and its medicinal properties in Ayurvedic, Unani, and Chinese system. According to the classical literature, it has been called *Misni* by Unani scholars. Its three types, Pahari, Jangal, and Bustani, have been described (Saleem & Idris, 2016). The use of *M. arvensis* is mentioned in the traditional medicinal system and available literature has suggested that tea made from its leaves can be used to cure fever, headache, digestive problems and other mild ailments. While the essential oil is widely used to treat low-intensity fungal and bacterial infections of the human skin, it is also used to treat a number of other conditions (Salehi et al., 2018). *M. arvensis* are known to contain monoterpene alcohol which is found as main component in essential oil is referred as menthol, which gives cooling minty flavor and smell to this herb (Farco & Grundmann, 2013). The menthol is well-known cooling characteristics and remaining minty odor of the oil and used in a various product and revealed diverse biological properties like anti-microbial, anti-inflammatory, anti-cancer activities and also as insect repellents or fumigants (Kamatou, Vermaak, Viljoen, & Lawrence, 2013). The pharmacological properties of this plant also include radioprotective, anti-fungal, antibacterial, antioxidant activity, hepatoprotective, insecticidal activity, anti-asthmatic effect, anti-allergic activity, cardioprotective, anti-angiogenic effect, and antiulcerogenic activity (Thawkar, Jawarkar, Kalamkar, Pawar, & Kale, 2016; Aihetasham, Umer, Akhtar, Din, & Rasib, 2015; Chetia & Saikia, 2020; Dar, Masoodi, Wali, Mir, & Shapoo, 2014; Malik et al., 2012; Naseem, Zahid, Hanif, & Shahid, 2020; Sagadevan, Suresh, Kumar, & Revathy, 2014; Sevindik, 2018; Sharma, Rasal, Patil, & Joshi, 2018). Therefore, all these characteristics features of *M. arvensis* are considered as a commercial and pharmaceutical based crop with great significance in their applications worldwide.

We believe that the present chapter will provide a better understanding of *M. arvensis* and its properties. This data may be precious in planning future observations, particularly clinical preliminaries, and in growing new pharmaceuticals containing *M. arvensis* or its bioactive components.

## 1.2 BOTANY, PRODUCTION, AND CROP PROTECTION

### 1.2.1 BOTANICAL TAXONOMIC CLASSIFICATION

The genus *Mentha* is a member of Lamiaceae family. The taxonomic classification of the plant is as described as below:

- **Kingdom:** *Planta*.
- **Division:** *Magnoliophyta*.
- **Class:** *Magnoliopsida*.
- **Order:** *Lamiales*.
- **Family:** *Lamiaceae (Labiatae)*.
- **Genus:** *Mentha*.

### 1.2.2 SYNONYMS AND VERNACULAR NAMES

More than 3,000 names have been recorded for the *Mentha* plant since 1753. Mint plants probably originated in Europe and the Mediterranean, from where it extended to other parts of the Earth and now occurred in all five continents (Salehi et al., 2018; Peter, 2006). *Mentha arvensis* has more than 142 synonyms. The plant, *Mentha* is to be called by vernacular names like Pudina (Sanskrit), ban pudina (Hindi), chetamargugu (Kannada), iyeccakkirai (Tamil) and so on detailed in Table 1.1 (Brahmi, Khodir, Mohamed, & Pierre, 2017).

**TABLE 1.1** Vernacular Names of *Mentha arvensis* L.

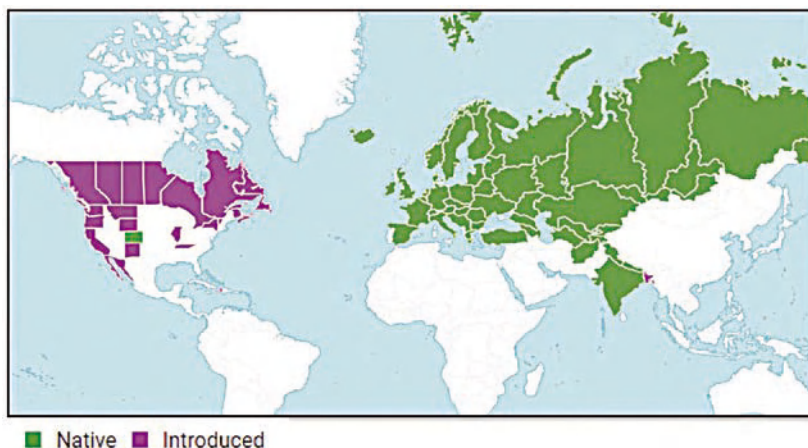
Region	Vernacular Names
India	Sanskrit: Pudina, Putiha; Hindi: Ban pudina, Paudina, Podina, Pudina, Pudinah; Kannada: Chetamargugu, Chetni-marugu; Tamil: Iyeccakkirai, Iyeccirkirai, Kumarakamuli, Potina; Malayalam: Putina, Puttina, Puttityana; Telugu: Igaenglikoora, Igaenglikura; Marathi: Pudina; Mizo: Pudina; Urdu: Ab-i-podina, Arq nana, Nana (pudina), Podina, Podina khushk, Podina taza, Pudina, Pudinah
English	Japanese mint, Corn mint, Menthol mint, Field mint, Wild mint

**TABLE 1.1** (Continued)

Region	Vernacular Names
Arabic	Fodanaje-hindi, Fotanaje-hindi, Habaqulhind, Naanaaul-hind, Nana, Nana hindi, Nana yabani
Persian	Pudinah
China	Bo He
Spain	Menta
French	Menthe anglaise, Menthe poivrée, Sentebon
Georgian	P'it'na, Pitna
German	Pfefferminze, Minze, Edelminze, Englische Minze
Thai	Bai saranai, Peppeo-mint, Saranae, Saranae yipun
Turkish	Nane
Vietnam	Rau thom, Húng nhũ, Húng dũi, Bạc h Húng giũ
Portugal	Hortelã

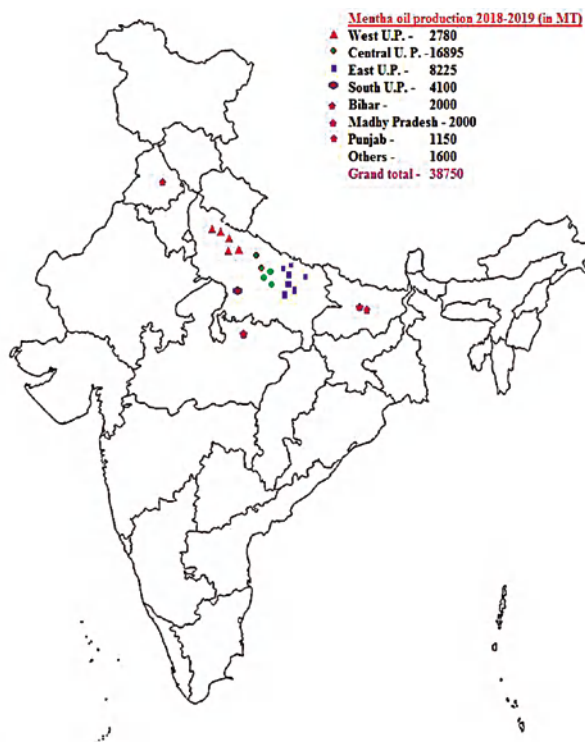
### 1.2.3 GEOGRAPHICAL SOURCE

*Mentha* genus has around 30 species that are found mostly in temperate and tropical/subtropical climates across the world (Figure 1.1) (Lawrence, 2007; Padalia, Verma, Chauhan, Sundaresan, & Chanotiya, 2013; Štefanidesová et al., 2019). The genus name *Mentha* comes from the Greek word *Menthe*, which refers to a mythological nymph who transformed into this plant. It is mainly cultivated on a vast scale in India, China, Japan, Thailand, Paraguay, Brazil, and Angola (Salehi et al., 2018; Singh, Singh, Singh, Singh, & Kumar, 2014). *M. arvensis* was first brought into India in 1952 by Col. R.N. Chopra and I.C. Chopra from Japan through the courtesy of UNESCO, and cultivated in 1954 by the Regional Research Laboratory, Jammu (Chand, Patra, Anwar, & Patra, 2004; Munsii, 1992; Vivek et al., 2009). *Mentha* is cultivated annually in the sub-tropical agro-climate region of Indo-Gangetic plains in the states of Uttar Pradesh, Uttarakhand, Himachal Pradesh, Punjab, and Bihar with maximum area in Uttar Pradesh. The cultivation of *Mentha* in Uttar Pradesh is done in central region namely Barabanki, Sitapur, Ambedkar Nagar and Lucknow districts and in tarai belt namely Moradabad, Badaun, Rampur, and Bareilly districts (Figure 1.2). The occurrence and distribution of *Mentha* with its species is summarized in Table 1.2 and Figure 1.3 (Peter, 2006; Lawrence, 2007; Ghosh & Chatterjee, 1978; Gobert, Moja, Colson, & Taberlet, 2002).



**FIGURE 1.1** Occurrence and geographical distribution of *M. arvensis* (Mentha, 2020).

Source: Reprinted [or adapted] from Mentha L., by Royal Botanic Gardens, Kew.



**FIGURE 1.2** Indian *M. arvensis* growing areas (PRAKASH Chemicals, 2018).

Source: Adapted from Prakash Chemicals, 2018.

**TABLE 1.2** Occurrence and Distribution of *Mentha* with its Species

Plants with Species	Synonyms	Common Name	Distribution and Occurrence	Habitat
<i>M. arvensis</i> L.	<i>M. lapponica</i> Wahlenb. <i>M. parieterifolia</i> J. Beck.	Corn mint, Field mint, Wild mint	Western Europe, the Himalayas, India, China, Siberia, North America.	Moist fields and roadsides
<i>M. suaveolens</i> Ehrh.	<i>M. rotundifolia</i> , <i>M. macrostachya</i> , <i>M. insularis</i>	Apple mint	Southern and western Europe, and Mediterranean region.	Damp and wet locations.
<i>M. longifolia</i> (L.) Huds.	<i>M. incana</i> Wield. <i>M. spicata</i> L. var. <i>longifolia</i> L. <i>M. sylvestris</i> L.	Biblical mint, silver mint, Horse mint.	North west Africa, Siberia, western Asia, India, West south Europe.	Wet alpine meadows and stream banks.
<i>M. spicata</i> L.	<i>M. viridis</i> <i>M. romana</i> <i>M. glabra</i> <i>M. candicans</i> <i>M. rubra</i> <i>M. sylvestris</i> var. <i>glabra</i>	Native spearmint	Europe and southern temperate Asia, Ireland, China.	Stream banks, lake shores, moist farms and road sides, often cultivated.
<i>M. aquatica</i> L.	<i>M. hirsute</i> <i>M. palustris</i> <i>M. capitata</i> <i>M. dubia</i> <i>M. aquatic</i> <i>M. ortmanniana</i> <i>M. purpurea</i> <i>M. pyrifolia</i> <i>M. dumetorum</i> <i>M. perhirsuta</i>	Horse mint, marsh mint, water mint.	Europe, Turkey, Asia, Africa, North America	Lakes, Wet edges of ponds, and canals.
<i>M. piperita</i> L.	<i>M. balsamea</i> Wild	Peppermint	Europe, India, China	–

TABLE 1.2 (Continued)

Plants with Species	Synonyms	Common Name	Distribution and Occurrence	Habitat
<i>Mentha citrata</i> Ehrh	<i>M. citrate</i> <i>M. adspersa</i> <i>M. aquatic</i> <i>M. piperita</i>	Bergamot mint, Lemon mint	India, North America and Central Europe, Italy	Lakes, Wet edges of ponds, and canals.
<i>Mentha gracilis</i> Sole	<i>Mentha cardiaca</i> (S.F. Gray) Bak.)	Scotch mint, ginger mint	China, east Asia, Russian, Canada, USA	–
<i>M. canadensis</i> L.	<i>M. arvensis</i> var. <i>piperascens</i> Malinv	Chinese mint	China, east Asia, Russian, Canada, USA	Lake shores, streambanks, moist areas and roads.
<i>M. haplo-calyx</i> Briq.	–	Japanese peppermint	Asia, New Zealand, Cuba, Mexico, Brazil, USA, India, Europe	–
<i>M. requienii</i> Bentham	<i>Thymus parvifloru</i> <i>Thymus corsicus</i> <i>Audibertia pusilla</i> <i>Menthella requienii</i> <i>Thymus micranthus</i> <i>Audibertia parviflora</i>	Corsican mint	Tyrrhenian Isles (Corsica, Sardinia, Montecristo, Caprera)	–
<i>M. pulegium</i> L.	<i>Pulegium vulgare</i> <i>P. erectum</i> <i>M. aromatic</i> <i>P. aromaticum</i> <i>P. pubescen</i> <i>P. heterophyllum</i> <i>P. omentellum</i> <i>P. daghestanicum</i>	Squaw mint, Mosquito plant.	Europe, northwards to Ireland, Poland, and extending to southern and western Ukraine.	Wetland areas, pool banks and waysides.

Note: –: not known.

Source: Peter (2006); Lawrence (2007); Ghosh & Chatterjee (1978); Gobert, Moja, Colson, & Taberlet (2002)

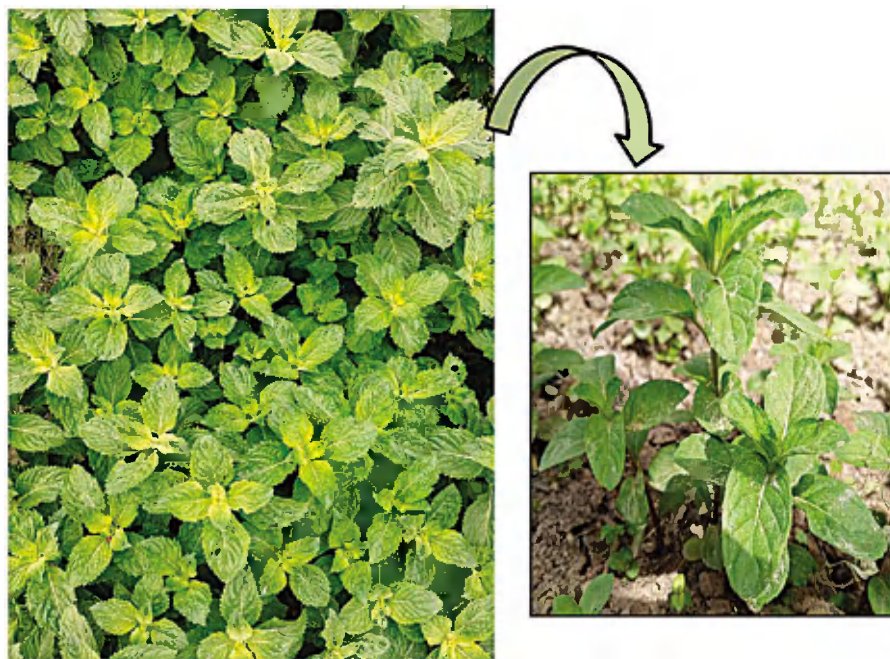




**FIGURE 1.3** Pie chart representing various species of genus *Mentha* (Peter, 2006; Lawrence, 2007; Ghosh & Chatterjee, 1978; Gobert, Moja, Colson, & Taberlet, 2002).

#### 1.2.4 MORPHOLOGY

The genus *Mentha* belongs to Lamiaceae family, and classified within the tribe Mentheae. There are over 260 genera and about 7,000 species in the Lamiaceae family. Tribe Mentheae also includes the some economically important genera viz., *Origanum*, *Rosmarinus*, *Salvia*, *Thymus*, *Cedronella*, *Hedeoma*, *Agastache*, *Monarda*, *Hyssopus*, *Nepeta*, *Satureja*, and *Calamintha* (Lawrence, 2007). *Mentha* is an aromatic oil-yielding plant, perennial, and herbaceous in nature that grows 10–120 cm on erect, square, branched stems and characterized by its wide-spreading stolons that grow both below and on top of ground. Plants having big leaves arranged in opposite, oblong (relatively narrow) to lanceolate or ovate in shape, serrated at the edges and are often downy with variety of colors, including purple–blue, gray–green, dark green and occasionally pale yellow. The flowers are bisexual, zygomorphic bilaterally symmetrical and small in size, white or purple color, Campaulate/ bell-shaped, have longer stamens than petals, located in the leaf axils which produced in false whorls known as verticillasters. Fruits are nutlets, brown in color containing a single seed. The plant calyx has tubular, lobe shape, often purplish, and corolla has two lips and four sub-equal lobes. The chromosome number in the genus *Mentha* is  $x = 12$ , but other species differ widely. Due to the existences of volatile EOs in the leaves and other parts of plant, the mint has pleasant minty aroma (Figure 1.4) (Peter, 2006; Brahmi, Khodir, Mohamed, & Pierre, 2017).



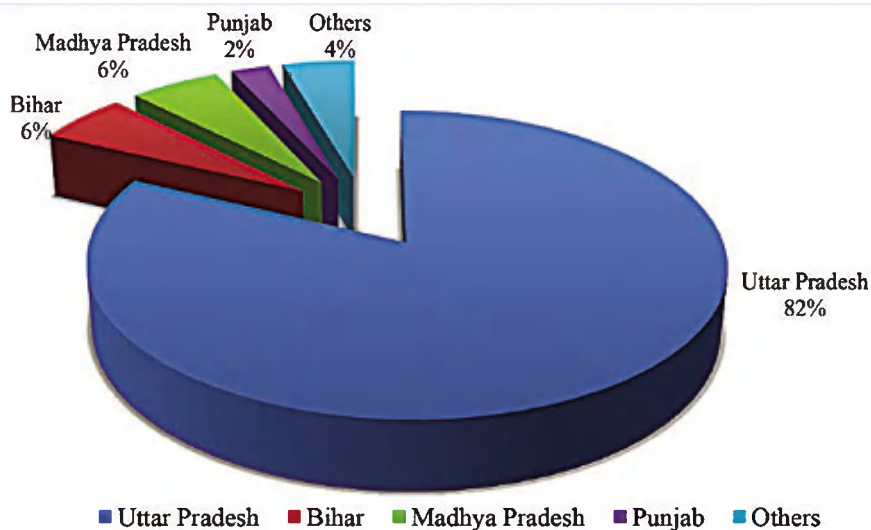
**FIGURE 1.4** Morphological diagram of *Mentha arvensis* L.

### 1.2.5 CULTIVATION

In the global market of the *Mentha* production; India is the world's largest consumer, producer, and exporter of *Mentha* (Bajeli, Tripathi, Kumar, Tripathi, & Upadhyay, 2016). India's contribution in global market is 75%–80% of the total global production of *Mentha* spp. Export of mint products from India has been increasing rapidly in the last few years. For the maximum share, *M. arvensis* is cultivated annually in the sub-tropical agro-climate region of Indo-Gangetic plains; Uttar Pradesh with maximum cultivated area is followed by Uttarakhand, Himachal Pradesh, Punjab, and Bihar (Figure 1.5). In India, with a total production of 344.73000 MT (metric tons) and productivity of 1.74 MT/ha (metric tons/hectare), Uttar Pradesh is the largest *Mentha* oil producing state producing an area of about 198,000 hectares. *Mentha* usually cultivated in central region of Uttar Pradesh viz., Barabanki, Sitapur, Ambedkar Nagar and Lucknow districts, and in tarai belt viz., Moradabad, Badaun, Rampur, and Bareilly districts. Uttar Pradesh is known as export basket for *Mentha* oil (Pal, Mohanty, & Devarani, 2015). Some websites reported that southern, eastern, and central parts of Uttar

Pradesh produce 4100 MT, 8225 MT, and 16895 MT of mint oil respectively which is represented in Figure 1.6. Because of this, the economic condition of the farmers in this region is mostly depending on *Mentha* cultivation. The major commercially cultivated spp. in India is *M. arvensis* L. var. *piperascens* (Japanese mint), *M. spicata* L. (spearmint), *M. piperita* L. (peppermint.), *M. cardiaca* Baker (Scotch spearmint), *M. viridis* L. (garden mint) and *M. citrata* Ehrh (bergamot mint), which cultivated on more than 2,50,000 hectare of land in India (Figure 1.7) (Pandey et al., 2019). Common varieties of *M. arvensis* is commercially cultivated in India, viz. *Koshi*, *Himalaya*, *MAS-l*, *Saksham*, *Shivalik*, *Gomti*, and *Kalka*. These are early-maturing, high yield, higher menthol content and pest and disease resistant than traditional varieties.

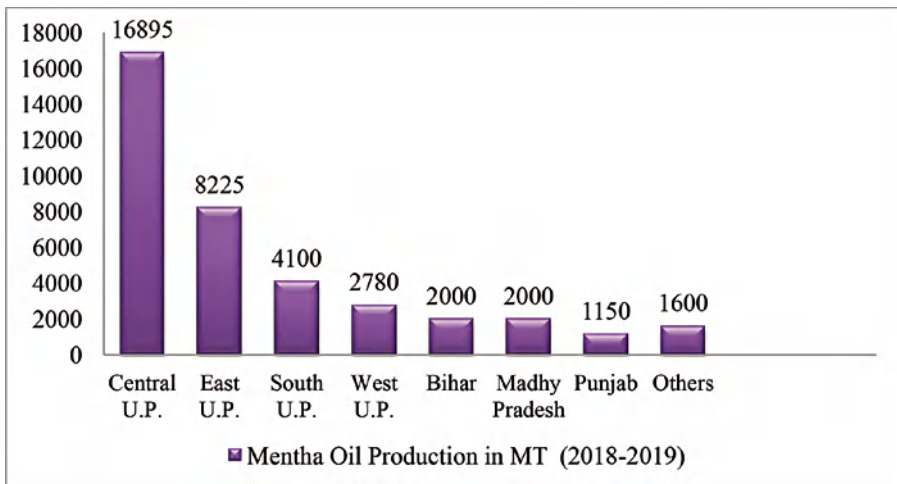
In India, *Mentha* have been widely cultivated for over 60 years. However, the geographical areas of India are suitable for mint cultivation, with the largest area occupied by Indus-Ganga plains, located in the north-central part of the Indian subcontinent; extend westward from the combined delta of the Brahmaputra River basin and the Ganges River in the Indus River basin. The area is characterized by various soils and agro-climates conditions. Well drained loamy soil high in organic matter content with pH 6.5 to 7.0 is suitable for vegetative growth of *Mentha* cultivation. *Mentha* is propagated mainly through



**FIGURE 1.5** The pie chart represents the mint growing area in India in hectares (2018–2019).

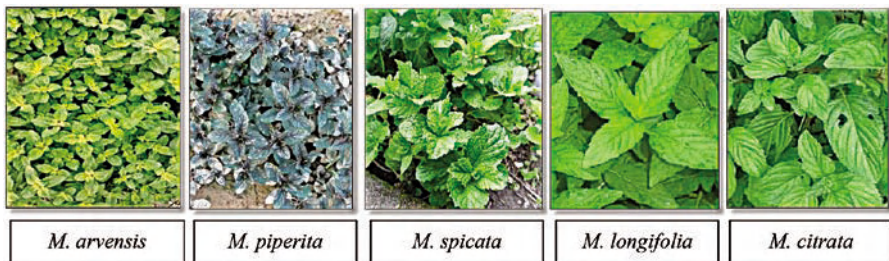
Source: Data retrieved from: PRAKASH Chemicals, “Mentha Oil,” 2018; <http://www.prk-chemicals.com/2018.html>.

the creeping stolons and terminal cuttings during the months of December–January and for *M. arvensis*, last week of January–early February, delayed planting leads to a significant reduction in yield. *Mentha* plant is generally planted in during the months of June–July (Tiwari, 2016). The water requirement is very high; hence frequently irrigation is required for the crop. About 15 times irrigations is required for maximum yield of crop. *Mentha* cultivation requires heavy nutrient in the soil. Therefore, for optimum growth and yield of *Mentha* requires tolerant application of fertilizers. The use of micronutrients like iron, phosphorus, nitrogen increases its yield by 20–55%.



**FIGURE 1.6** Mint oil production in India in MT (2018–2019).

Source: Adapted from Prakash Chemicals, 2018



**FIGURE 1.7** Five major cultivated species of the *Mentha* in India.

### **1.2.6 CROP PROTECTION**

*Mentha* crop is sensitive to many biotic and abiotic stresses and affected by many pests and diseases (viz., fungi, viruses, bacteria, and nematode and insects), Mint does not compete well with weeds and susceptible to a range of diseases. Therefore, weed infestation and these ailments impose significant constraints on mint oil production affecting its quality and quantity. Management of pest and diseases of mint is very important both from an economical and environmental perspectives as well. A number of mint disease management techniques have been developed and used. There is a need to implement an integrated disease management approach for effective control of the disease. Host resistance, inter-cropping, time of planting and careful use of fungicides and pesticides are important components in management package of pest and diseases.

#### **1.2.6.1 WEED**

The presence of weeds is a major reason of deterioration in the quality of the mint oil production, and the crop is infested with varieties of seasonal weeds. Annual weeds have become a major factor of weed management compared to perennial weeds, which is a minor problem for most mint fields. Therefore, weeds must be controlled to reduce the potential loss of mint production and economic yield which causes lower profitability. Use of herbicides is partially successful due to the wide varieties of weeds. Herbicides such as Oxyfluorfen (0.5 kg/ha), Pedimenthalin (1.0 kg/ha), Dalapon (4 kg/ha), Diuron (0.4 kg/ha) and Gramaxone (2.5 kg/ha) have been found to be quite effective against weeds, but the use of herbicides should be avoided due to adverse effects (Chand, Patra, Anwar, & Patra, 2004; Peter, 2006; Lawrence, 2007; Singh, Singh, Singh, Singh, & Kumar, 2014; Kothari & Singh, 1994; Yadav et al., 2019). However, the best management of weeds is the unified use of mulching, manual or mechanical, and chemical method; in which manual weeding method is most common in India. Some of the important weeds of *Mentha* are summarized in Table 1.3 (Kaur, Singh, Bhullar, Shergill, & Kaur, 2013; Singh & Saini, 2008).

**TABLE 1.3** Some Important Weeds of *Mentha arvensis* (Kaur, Singh, Bhullar, Shergill, & Kaur, 2013; Singh & Saini, 2008)

Weed spp.	Common Name	Family Name	Life Cycle
<i>Arenaria serpyllifolia</i> L.	Sandwort	Caryophyllaceae	Annual
<i>Poa annua</i> L.	Annual bluegrass	Poaceae	Perennial
<i>Melilotus indicus</i> (L.) All.	Indian sweet clover	Fabaceae	Annual
<i>Phalaris minor</i> Retz.	Littleseed canarygrass	Poaceae	Annual
<i>Digitaria ischaemum</i> (Schreb.) Muhl.	Smooth crabgrass	Poaceae	Annual
<i>Eleusine indica</i> (L.) Gaertn.	Goosegrass	Poaceae	Annual
<i>Cyperus rotundus</i> L.	Purple nutsedge	Cyperaceae	Perennial
<i>C. compressus</i> L.	Annual sedge	Cyperaceae	Perennial
<i>Echinochloa colona</i> L. Link	Jungle rice	Poaceae	Annual
<i>Eclipta alba</i> (L.) Hassk.	False daisy/Bhringraj	Asteraceae	Annual
<i>Caesulia axillaris</i> Roxb.	Pink node flower	Asteraceae	Annual
<i>Ammannia baccifera</i> L.	Monarch redstem	Lythraceae	Annual
<i>Trianthema portulacastrum</i> L.	Black pigweed	Aizoaceae	Annual
<i>Acrachne racemose</i> (B. Heyne ex Roth) Ohwi	Chinkhe	Poaceae	Annual
<i>Digera arvensis</i> Forsk.	False amaranth	Amaranthaceae	Annual
<i>Cleome viscosa</i> L.	Asian spider flower	Cleomaceae	Annual
<i>Phyllanthus niruri</i> L.	Stonebreaker	Phyllanthaceae	Perennial
<i>Physalis minima</i> L.	Wild cape gooseberry	Solanaceae	Annual
<i>Chenopodium album</i> L.	Wild spinach/Bathua	Amaranthaceae	Annual
<i>Asphodelus tenuifolius</i> Cav.	Wield onion/Pyazi	Asphodelaceae	Annual
<i>Trigonella polycerata</i> L.	Fenugreek	Fabaceae	Annual

### 1.2.6.2 PATHOGENS

Mints are associated with huge numbers of microbial pathogens and pests and are susceptible to a range of diseases that cause considerable damage to crop and influence both quantity and overall quality of oil content. Among the more than 30 pests and diseases of mint crop have already been reported, around a dozen are of major economic significance.

#### 1.2.6.2.1 Fungi

The mainly economically threatening fungal ailments of *Mentha* are caused by fungi with *Puccinia menthae* (rust), *Verticillium dahliae* (wilt), *Alternaria*

*alternata* (leaf spot), *Helminthosporium spiciferum* (leaf blight), *Erysiphe cichoracearum* (powdery mildew), *Phoma stasseri* (stem rot) and *Rhizoctonia solani/bataticola* (stolon and root rot) being the most important fungal pathogens.

### 1. Mint Rust Disease:

- i. **Symptoms:** These of mint rust disease is small (ellipsoidal or obovoidal), powdery, bright orange, brown or yellow, pustules (uredospores) on the underside of the leaves and young shoots during rainy season. Later on, leaves turn yellow and fall off, when teliospores (overwintering spores) produces; and spreads rapidly from one plant to another, and gradually devastate the entire crop within few days (Kalra et al., 2005; Mekonnen, Manahile, & Mengesha, 2015).
- ii. **Casual Organism:** Rust disease is caused by fungal pathogen *Puccinia menthae*. It is widely deteriorating pathogen in Uttar Pradesh, which is a prime area of mint cultivation and causes heavy losses to the crop (Mekonnen, Manahile, & Mengesha, 2015; Bhat, Maheshwari, Kumar, & Kumar, 2002).
- iii. **Disease Management:** Use of disease-free planting materials and the eradication of old rust infected mint plants is the major preventive method of rust disease, and also helps to prevent disease from spreading and reduce the rust inoculum. Treatment of runners with hot water to obtain rust-free planting material and use of resistant variety is common method of disease management. Application of fungicides like mancozeb propiconazole, Diclobutazol, nickel chloride (Pandey et al., 2019; Kalra et al., 2005), Folicur plus, Baycor (Margina & Zheljzkov, 1994, 1996), tebuconazole, belixasol, and plantovax (Kalra et al., 2005), offer reliable protection against mint rust. Authors in (Mekonnen, Manahile, & Mengesha, 2015) reported that application of crude extracts of *Datura stramonium* L., *Mesal anceolata* L. and *Milletia ferruginea* L. were effective against mint rust.

### 2. Leaf Spot:

- i. **Symptoms:** Infection appears in the form of asymmetrical dark brown spots. These spots occur on the surface of the leaves which are encircled by pale yellow margin; leading to serious

defoliation during summer season that is commonly widespread and to a marked reduction in EOs content. The ailment can be also allied with uredia of *P. menthae* (mint rust) on menthol mint with the uredia on the under surface and the *Alternaria* spots occurring on the upper surface of leaves.

- ii. **Causal Organism:** The disease is caused by mainly *Alternaria alternata* and other fungal pathogens viz. *Corynespora cassiicola*, *Curvularia lunata*. It causes economic losses by causing serious defoliation of the mint plant (Bhat, Maheshwari, Kumar, & Kumar, 2002).
- iii. **Disease Management:** Spraying mint plants with chlorothalonil (Kalra, Singh, Patra, & Kumar, 2003), copper fungicides (Kalra et al., 2005) are effective against the disease. Application of *Pseudomonas fluorescens* (Karnwal, 2011), and plant extracts of Lantana provides effective control of the disease (Bisht, Kumar, Purohit, & Srinivasanraghvan, 2013).

### 3. Leaf Blight of Mint:

- i. **Symptoms:** These of leaf blight disease of *M. arvensis* was reported in India in the year 2011. The symptoms of diseased plant show dark brown color from margins or tip towards the leaf lamina; later on, the entire leaf turned brown and curled upwards, and gives blighted look.
- ii. **Causal Organism:** Leaf blight disease of mint is caused by pathogen *Helminthosporium spiciferum*. *H. Spiciferum* (Kumar, Gupta, & Verma, 2013).

### 4. Wilt Disease:

- i. **Symptoms:** The major signs of the wilt disease are dwarfing the plant, one-sided development of branches, etiolating, and wilting. The pathogen infects the roots, thus affecting the regular growth and development of the affected plants; and the leaves turn yellow, curled, and in the end dry. The disease mainly spreads throughout contaminated stolons when used as propagating material.
- ii. **Causal Organism:** Wilt disease is caused by pathogen *Verticillium albo-atrum*, *V. dahliae* and *Fusarium oxysporum* (Mekonnen, Manahile, & Mengesha, 2015).



iii. **Disease Management:** Use of healthy planting material, heat treatment of rhizomes at 48°C for 35 minute or 47°C for 55-minute, ethyl bromide application for soil fumigation and crop rotation are very useful method of the wilt severity reduction (Pandey et al., 2019; Kalra et al., 2005). Authors in (Gupta, Sharma, & Naik, 2011) reported that plant-derived essential oils of clove and ajwain are effective against the wilt disease.

## 5. Rhizome/Stem Rot:

i. **Symptoms:** The major symptoms of the rot disease are black to dark brown lesions, cankers on stems and rhizomes. On aboveground part, infection occurs near the soil-surface part of stems, and sunken cankers formation, subsequently girdle the stem which causes the plant to collapse. In case of underground infection occurred on the rhizomes plants develop black lesions that subsequently coalesce, leading to normal necrosis of the rhizomes.

ii. **Causal Organism:** The fungal pathogens *Phoma strasseri*, and *Sclerotinia sclerotioru* are responsible for the rot disease. Rhizome rot is the major serious disease which causes heavy economic losses. Stem rot can be especially severe in the green house and losses as high as sometimes 90% have occurred in the greenhouse (Perveen, Haseeb, & Shukla, 2007).

iii. **Disease Management:** Use of healthy planting material, heat treatment of plant material, and application of combined formulation of bio agents *Trichoderma harzianum* and *Pseudomonas fluorescens* provides effective control of the rot disease.

## 6. Stolon Rot and Root Rot:

i. **Symptoms:** During rainy season, it occurs on the underground parts of the *Mentha* plant and infected stolon. The major symptoms of stolon rot consist of reddish brown to black discoloration on stolon region of the stem, drying of leaves of infected plants followed by leaves wilt and turn yellow and finally rotting of entire plant (Muthukumar & Venkatesh, 2012).

ii. **Causal Organism:** The disease is caused by multiple pathogens viz., *Macrophomina phaseoli*, *Pythium aphanidermatum*, *Theilavia basicola*, *Rhizoctonia bataticolala*; out of which *T. basicola* is widely deteriorating pathogen in Uttar Pradesh, and causes heavy losses to the crop (Bhat, Maheshwari, Kumar, & Kumar, 2002).

- iii. **Disease Management:** Usage of disease-free planting material; treatment of stolon with 0.5% Dithane Z-78 or Dithane M-45 before planting, application of bio agent *Pseudomonas fluorescens* more effective in lysing the cell wall of fungal pathogens and reducing the rot severity (Pandey et al., 2019; Karnwal, 2011).

## 7. Powdery Mildew:

- i. **Symptoms:** These of powdery mildew diseased plant shows powdery circular white patches on both surfaces (upper and lower) of the leaves; later on, it spreads to the stem and other parts of the plant.
- ii. **Causal Organism:** The fungal pathogen *Erysiphe cichoracearum* are responsible for the powdery mildew disease; and reported from Argentina, Russia, and India. It reduces the yield of essential oil up to 20%–50% (Bhat, Maheshwari, Kumar, & Kumar, 2002).
- iii. **Disease Management:** Application of ground sulfur or dusting with wettable sulfur @ 0.2%. Spraying of Hexasul or Karathane WD 0.05% at 15 days interval effectively controls the disease.

### 1.2.6.2.2 Bacterial Disease

Several bacterial diseases have been observed to infect the *Mentha* crop:

#### 1. White Spot-on Mint:

- i. **Symptoms:** White spot diseased plant shows small water-soaked yellow patches on the edges of leaf, later on, at advanced stages, the spots caused leaf abscission (Maia et al., 1996).
- ii. **Causal organism:** White spot-on mint disease is caused by bacterial pathogen *Pseudomonas cichorii*.

### 1.2.6.2.3 Viral Disease

Viruses are obligate parasites and mint crop are also affected by viruses. Several viruses belonging more than 12 genera which cause diseases to have been reported worldwide but there are only few reports of viral diseases on mints from India.

### 1. Mosaic Disease:

- i. **Symptoms:** Thees of mosaic diseased plant shows high incidence of leaf mosaic, showing necrotic spots on leaves, deformity, and affect apical plant growth severely and the leaves of the newly developed apex are small with very distinctive symptoms (Sevik, 2012).
- ii. **Causal Organism:** Mosaic disease of mint is caused by viral pathogen Cucumber mosaic virus (CMV).

### 2. Begomovirus Disease:

- i. **Symptoms:** These of Begomovirus disease plant shows high incidence of drastic reduction in the crop yield up to range of 50 to 60%; and plant show foliar rugosity, light yellow mosaic on leaves, upward curling and crinkling of plant.
- ii. **Causal Organism:** Bagomovirus disease is caused by viral pathogen Tomato leaf curl Pakistan virus (Samad, Gupta, Shasany, Ajayakumar, & Alam, 2009).

#### 1.2.6.2.4 Nematodes

The commercial cultivation of mint crop endures a great yield loss due to root-lesion and root knot nematodes in the region of Indo-Gangetic plains because the heavy nature of the soils in this region also remediates nematode infestation.

### 1. Root Knot Nematode:

- i. **Symptoms:** These of the root knot disease are characterized by smaller and chlorotic leaves; uprooted plant; the rootlets and root-hairs are fewer and shorter than those of uninfected plants; and the roots have small knots/galls.
- ii. **Causal Organism:** *Meloidogyne incognita* (Kofoid and White) Chitwood and other nematodes viz. *M. javanica* are responsible for the root knot disease. It is an important deteriorating pathogen that causes an economical loss of more than US \$100 bn per year globally; it reduces crop yields up to 73%; and *M. javanica* reduces oil yield up to 25–30% (Pandey et al., 2019; Pandey, 2005a, b; Pandey, Mishra, Tiwari, Singh, & Kalra, 2011; Sultan et al., 2017).

## 2. Root Lesion Nematode:

- i. **Symptoms:** Infected plants show stunted plant development, leaf burning, and lesions on the root system. It is considered to be the most deteriorating nematode pest of *Mentha*, which reduces crop production; by foliage 46%, by root mass 86%, and by oil yields 95% (Lawrence, 2006). Root-lesion nematodes can interact with the soil pathogen *Verticillium dahlia*; which reduces crop yields up to 40% more than by nematodes alone (Pandey et al., 2019; Sultan et al., 2017).
- ii. **Causal Organism:** Root lesion disease caused by *Pratylenchus* spp.
- iii. **Disease Management:** Use of disease-free sucker, nematode free soil for sucker's multiplication, and eliminating important weed and alternate hosts of phytonematodes. Application of Carbofuran, combination of carbofuran and neem seed powder, combined use of oil seed cakes of neem and bio-agent *Trichoderma harzianum*, dual application of plant growth promoting Rhizobacteria (PGPRs) and mutualistic fungal endophytes effectively controls the nematode disease (Perveen, Haseeb, & Shukla, 2007; Pandey, Mishra, Tiwari, Singh, & Kalra, 2011; Pandey, 2005).

### 1.2.6.3 INSECT PESTS

A large number of insect pests are found in India associated with *Mentha* crops, which cause substantial damage to crop yield. Some major relatively insect pests of *Mentha* and insecticides frequently used to control them in India are shown in Table 1.4 (Lawrence, 2007; Bhat, Maheshwari, Kumar, & Kumar, 2002; Weller, Green, Janssen, & Whitford, 2000; Ricupero, Desneux, Zappalà, & Biondi, 2020).

## 1.3 PHYTOCHEMISTRY

### 1.3.1 ESSENTIAL OIL CONSTITUENTS

The genus *Mentha* contains highly important volatile oils, and presence of different bioactive secondary metabolites in the different solvent extracts of mint. Plant metabolites of mints are extracted using various solvent

**TABLE 1.4** Major Insect Pest of *Mentha* spp.

Pest	Zoological Name	Affected Part of Plant	Chemical Used	References
Termites	<i>Microtermis shasi</i> , <i>Odontotermis obesus</i>	Attacks underground parts of plant which damages the root system and main stem. Plants get cut at the base.	Use of Gondal mixtures (asafetida, rosin, <i>Gardenia gummifera</i> and aloe, in the ratio of 2:2:1:2 diluted in water); and insecticides like dieldrin, chlordane, toxaphene, and heptachlor.	Lawrence (2007); Bhat, Maheshwari, Kumar, & Kumar (2002)
Cutworms	<i>Agrotos flammatra</i>	After being sprouted, young shoots get damaged, Scission of plant in Collar region.	Spraying with metasystox, malathion or thiometan; Soil treatment with Chloropyrophos.	Lawrence (2007); Weller, Green, Janssen, & Whitford (2000)
Polyphagous caterpillars	Larval stage of members of the order lepidoptera.	Defoliating the crop within a few days.	Spraying 2% folidol or 5% diptrex (for early stage) with endrin or thiodon (for advanced stage).	Bhat, Maheshwari, Kumar, & Kumar (2002)
Polyphagous semiloopers	<i>Achaea janata</i>	Voraciously devour the tender foliage.	Spraying with Endosulfan or carbayl mixed in water.	Bhat, Maheshwari, Kumar, & Kumar (2002)
Hairy caterpillar	<i>Diacrisia oblique</i>	Leaves are damaged	Quinolphos sprays	Lawrence (2007)
White flies	<i>Bemesia tabaci</i>	Lay eggs on the ventral surface of the leaves and leaves badly infested; Sucks the juice and Spread's viruses.	Sprayed with rosin compounds to destroy the insects; phosphomidon sprays	Lawrence (2007); Bhat, Maheshwari, Kumar, & Kumar (2002)
White grub	<i>Leucophalis coneophora</i>	Roots and leaves are eaten away.	Savidol or Chloropyrophos treatment of soil.	Lawrence (2007)
Macho	<i>Macrosiphum pisi</i> and <i>Aphis species</i>	Sucks plant juice and transmits viruses.	Phosphomidon sprays	Lawrence (2007)
Mint leaf roller	<i>Syngamia abruptalis</i>	Rolling of leaves	Monocrotophos sprays.	Lawrence (2007)
Red pumpkin beetle	<i>Aulocophora favicollis</i>	Buds and leaves are eaten away.	Monocrotophos, pyrethrin sprays	Lawrence (2007)

**TABLE 1.4** (Continued)

<b>Pest</b>	<b>Zoological Name</b>	<b>Affected Part of Plant</b>	<b>Chemical Used</b>	<b>References</b>
Pod borer	<i>Heliothes armigera</i>	Leaves and buds are eaten away.	Cipermetheline and malathion sprays.	Lawrence (2007)
Mint flea beetle	<i>Longitarsus waterhousei</i>	Affected plants are stunted, usually red in color, occur in spots in the field; stunted plants may die.	Malathion and methomyl sprays.	Weller, Green, Janssen, & Whitford (2000)
Mint bud mite	<i>Florido tarsonemus</i> sp.	Stunting and distortion of the upper part of plant	Planting stock from mite-free areas, crop rotations, use of miticide propargite.	Weller, Green, Janssen, & Whitford (2000)
Aphids	<i>Myzus persicae</i>	Leaves get distorted and/or turn yellow, leaves may have necrotic spots and/or stunted shoots; aphids encourage sooty mold's growth by secreting honeydew.	Insecticidal soaps or use of canola or neem oil.	Ricupero, Desneux, Zappalà, & Biondi (2020)

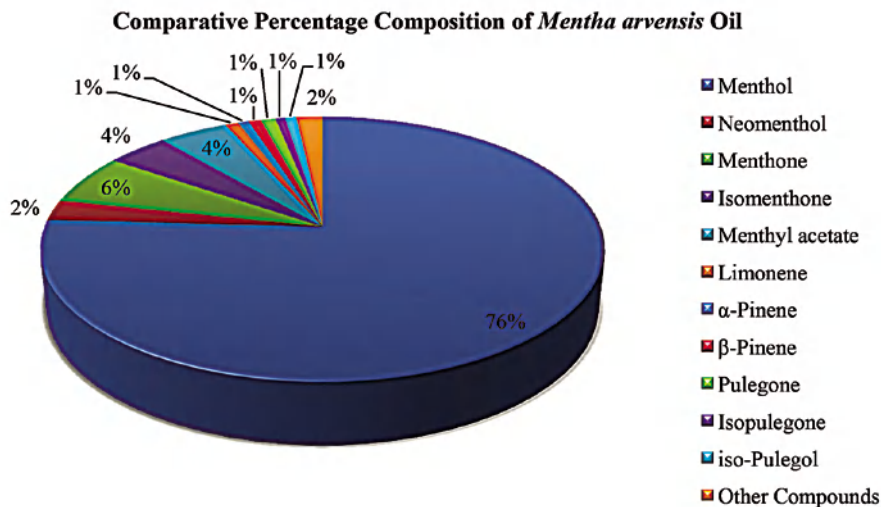
*Source:* Lawrence (2007); Bhat, Maheshwari, Kumar, & Kumar (2002); Weller, Green, Janssen, & Whitford (2000); Ricupero, Desneux, Zappalà, & Biondi (2020).

extraction systems viz., water, methanol, ethanol, acetone, and petroleum ether extracts, which are selected based on polarity level and their ability of extraction. However, the volatile constituents/essential oil is extracted using the hydro-distillation process. The volatile oil of *M. arvensis* collected from various cultivation areas and harvesting period were generally different. Mint essential oil comprises more than 200 constituents, which influenced by interaction between the season, cultivar, crop age, genotype, climatic conditions, environment, geographic location, technique of extraction, harvest time and kind of storage. However, the most abundant components of the volatile oil are a complex mixture of monoterpenoids represented by oxygenated monoterpenes followed by mono-terpene hydrocarbons and sesquiterpene hydrocarbons (Chetia & Saikia, 2020; Brahmi, Khodir, Mohamed, & Pierre, 2017; Padalia et al., 2013; Kasrati et al., 2017; Pandey, Rai, & Acharya, 2003). The phytochemical study revealed that, several flavonoids, tannins, steroids, terpenoids, alkaloids, polyphenols, saponins, cardiac glycosides, anthraquinone, free anthraquinone, carotenoids, coumarins, and phenolic have been detected from various plant parts of *M. arvensis* (Chetia & Saikia, 2020; Sagadevan, Suresh, Kumar, & Revathy, 2014; Kumar, Khajuria, & Aggarwal, 2012; Patil et al., 2015; Roy & Mallick, 2017).

The EOs is collected from the fresh aerial parts (leaves, stem, and flower) of the mint plant using Clevenger apparatus. Variations in the amount of phytoconstituents present in relation to different regions and variant varieties are summarized in Table 1.5 (Zachariah & Leela, 2006). Using GC-MS techniques (Gas Chromatography-Mass Spectrometry) some of chemical compounds have been isolated as EOs and identified on the basis of RT (retention time), RI (retention index), coinjection with standards, mass spectra library search and by comparing mass spectral data and RI with various literatures (Padalia et al., 2013). GC-MS identified various compounds in the EOs of mint, the most important compounds of which are menthol, menthone, limonene, menthyl acetate, iso-menthone, neomenthol, pulegone, Camphor, (Z)-3-Hexenol, 3-Octanal, borneol,  $\alpha$ -pinene,  $\beta$ -pinene,  $\beta$ -Myrcene, iso-Pulegol,  $\beta$ -Caryophyllene, (E)- $\beta$ -Farnesene, terpinen-4-ol,  $\alpha$ -terpineol, piperitone, carvone, germacrene-D, Piperitone, Germacrene D-4-ol, Spathulenol, and 1,8-Cineole (Figure 1.8) (Padalia et al., 2013; Pandey, Rai, & Acharya, 2003; Kumar, Khajuria, & Aggarwal, 2012; Makkar, Sharma, & Kaur, 2018; Nilo et al., 2017; Pandey, Dubey, & Saini, 2010; Pino, Rosado, & Fuentes, 1996; Singh et al., 2005; Verma et al., 2010). Around twenty-seven compounds have been identified using GC-MS analysis, including oxygenated monoterpenes, monoterpene hydrocarbons, sesquiterpene hydrocarbon,

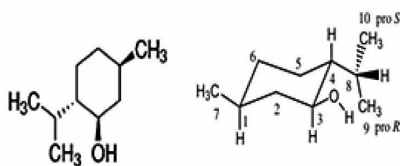
oxygenated sesquiterpenes and aliphatic compounds. Among which, menthol were considered as a major component (Padalia et al., 2013; Kasrati et al., 2017). Using GC-MS analysis, various compounds isolated and identified in the EOs of *Mentha*, the major compounds of which are limonene (0.02%), 1,8-cineole (0.16%), sabinene (0.18%), myrcene (0.21%),  $\alpha$ -pinene (0.43%),  $\beta$ -pinene (0.46%),  $\beta$ -caryophyllene (0.52%), cis-3-hexenol (0.62%), neomenthol (1.05%), menthyl acetate (1.49%), isomenthone (2.72%), menthone (4.10%) and L-menthol (78.87%) (Ahmad, Darokar, & Tandon, 2011). Menthol [5-methyl-2-(1-methylethyl) cyclohexanol; 2-isopropyl-5-methylcyclohexanol or p-menthan-3-ol] is a cyclic monoterpene alcohol with three asymmetric carbon atoms. Molecular formula of Menthol is  $C_{10}H_{20}O$  and molecular weight is 156.27. It occurs as four pairs of optical isomers namely (+) and (-)-menthol, (+) and (-)-isomenthol, (+) and (-)-neomenthol, (+) and (-)-neoisomenthol as in Figure 1.9 (Farco & Grundmann, 2013; Kamatou, Vermaak, Viljoen, & Lawrence, 2013; Klumpp et al., 2020; Vishwakarma et al., 2019). Another study done on the essential oil obtained by the variant cultivars of *M. arvensis* viz., 'Himalaya,' 'Kosi,' 'Kalka' and 'Saksham' have found to differ from 0.38%–1.0%, 0.35%–1.2%, 0.26%–1.2% and 0.42%–1.1% respectively, and has identified twenty-six components including major biomolecules menthol, menthyl acetate, menthone, neomenthol, isomenthone, and limonene (Verma et al., 2010). Another investigation revealed that, around six compounds have been identified using GC analysis, including Menthol, Menthone, (+) Limonene, Transmethone, Menthol Acetate and Pinediol compounds (Pandey, Dubey, & Saini, 2010). Makkar et al. examined the essential oil of *M. arvensis* and stated 34 chemical components including piperitone (1.32%), menthone (5.00%), neomenthyl acetate (5.18%), isomenthone (5.24%) and menthol (77.94%) using GC-MS techniques (Makkar, Sharma, & Kaur, 2018). Another study found around 26 components in the oil of *M. arvensis* constituting 99.5% of the identified components, including sesquiterpene hydrocarbons (0.8%), monoterpene hydrocarbons (4.7%) and oxygenated monoterpenoids (93.6%). Among which, menthol (75.8%) were considered as a major component followed by menthone (6.3%), isomenthone (4.1%), menthyl acetate (3.0%) and neomenthol (2.7%) (Prakash et al., 2018). Using GS technique, identified about 300 constituents in the essential oil of *M. arvensis*, the major compounds of which are menthol (30–50%) followed by menthone (17–35%), iso-menthone (5.0–13.0%), methyl acetate (1.5–7.0%), 1,8-cineole (maximum 1.5%), limonene (1.5–7.0%), iso-pulegol (1–3%), pulegone (maximum 2.0%), and carvone (maximum 2.0%) (Kalemba & Synowiec, 2019).



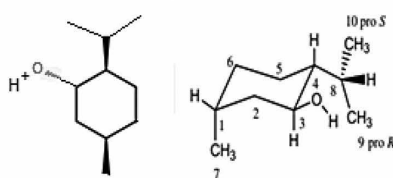


**FIGURE 1.8** Comparative percentage composition of *Mentha arvensis* oil yield (Padalia et al., 2013; Pandey, Rai, & Acharya, 2003; Kumar, Khajuria, & Aggarwal, 2012; Zachariah & Leela, 2006; Makkar, Sharma, & Kaur, 2018; Nilo et al., 2017; Prakash et al., 2018).

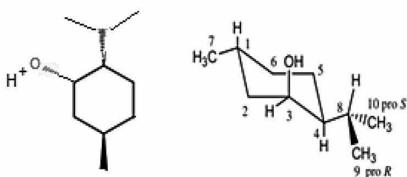
**A. (+) Menthol**



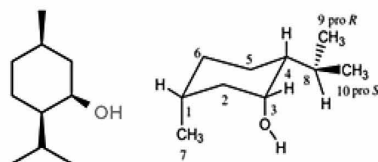
**B. (+) Isomenthol**



**C. (+) Neomenthol**



**D. (+) Neoisomenthol**



**FIGURE 1.9** Menthol and its isomers (A–D).

Source: Adapted from PubChem., n.d.

**TABLE 1.5** Chemical Structures of the Major Phytochemicals of *M. arvensis* (PubChem., n.d.)

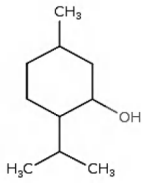
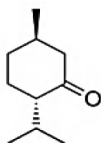
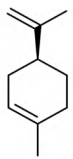
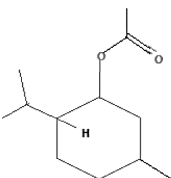
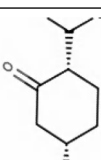
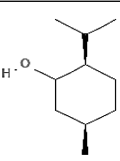
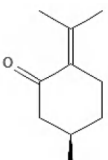
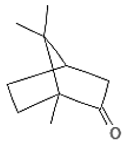
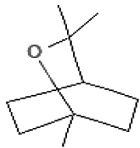
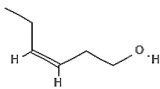
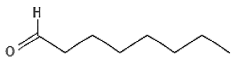
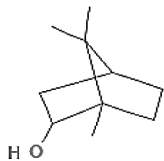
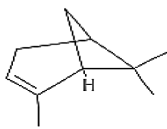
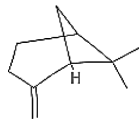
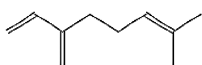
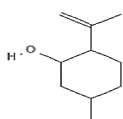
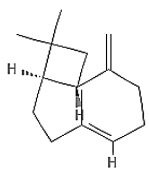
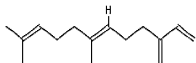
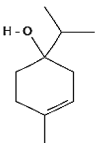
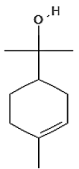
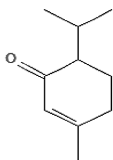
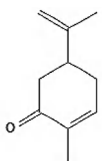
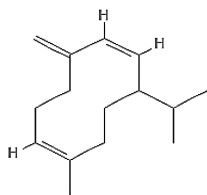
Sl. No.	Phytochemical Compound	Chemical Formula	Chemical Structure	IUPAC Name
1.	Menthol	$C_{10}H_{20}O$		(1R,2S,5R)-2-isopropyl-5-methylcyclohexanol
2.	Menthone	$C_{10}H_{18}O$		(2S,5R)-2-Isopropyl-5-methylcyclohexanone
3.	Limonene	$C_{10}H_{16}$		1-methyl-4-prop-1-en-2-ylcyclohexene
4.	Menthyl Acetate	$C_{12}H_{22}O_2$		(5-methyl-2-propan-2-ylcyclohexyl) acetate
5.	Iso-Menthone	$C_{10}H_{18}O$		(2S,5S)-5-methyl-2-propan-2-ylcyclohexan-1-one
6.	Neomenthol	$C_{10}H_{20}O$		(2R,5R)-5-methyl-2-propan-2-ylcyclohexan-1-ol
7.	Pulegone	$C_{10}H_{16}O$		(5R)-5-methyl-2-propan-2-ylidenecyclohexan-1-one

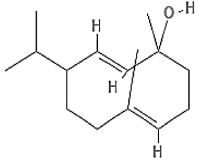
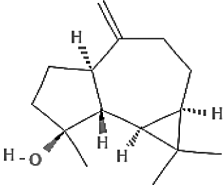
TABLE 1.5 (Continued)

Sl. No.	Phytochemical Compound	Chemical Formula	Chemical Structure	IUPAC Name
8.	Camphor	$C_{10}H_{16}O$		1,7,7-trimethylbicyclo [2.2.1] heptan-2-one
9.	1,8-Cineole	$C_{10}H_{18}O$		1,3,3-trimethyl-2-oxabicyclo [2.2.2] octane
10.	(Z)-3-Hexenol	$C_6H_{12}O$		(Z)-hex-3-en-1-ol
11.	3-Octanal	$C_8H_{16}O$		Octanal
12.	Borneol	$C_{10}H_{18}O$		1,7,7-trimethylbicyclo [2.2.1] heptan-2-ol
13.	$\alpha$ -Pinene	$C_{10}H_{16}$		2,6,6-trimethylbicyclo [3.1.1] hept-2-ene
14.	$\beta$ -Pinene	$C_{10}H_{16}$		6,6-dimethyl-2-methylidenebicyclo [3.1.1] heptane
15.	$\beta$ -Myrcene	$C_{10}H_{16}$		7-methyl-3-methylidene-octa-1,6-diene
16.	Iso-Pulegol	$C_{10}H_{18}O$		5-methyl-2-prop-1-en-2-ylcyclohexan-1-ol

**TABLE 1.5** (Continued)

Sl. No.	Phytochemical Compound	Chemical Formula	Chemical Structure	IUPAC Name
17.	$\beta$ -Caryophyllene	$C_{15}H_{24}$		(1R,4E,9S)-4,11,11-trimethyl-8-methylidenebicyclo[7.2.0]undec-4-ene
18.	(E)- $\beta$ -Farnesene	$C_{15}H_{24}$		(6E)-7,11-dimethyl-3-methylidenedodeca-1,6,10-triene
19.	Terpinen-4-ol	$C_{10}H_{18}O$		4-methyl-1-propan-2-ylcyclohex-3-en-1-ol
20.	$\alpha$ -Terpineol	$C_{10}H_{18}O$		2-(4-methylcyclohex-3-en-1-yl)propan-2-ol
21.	Piperitone	$C_{10}H_{16}O$		3-methyl-6-propan-2-ylcyclohex-2-en-1-one
22.	Carvone	$C_{10}H_{14}O$		2-methyl-5-prop-1-en-2-ylcyclohex-2-en-1-one
23.	Germacrene-D	$C_{15}H_{24}$		(1Z,6Z)-1-methyl-5-methylidene-8-propan-2-ylcyclodeca-1,6-diene

**TABLE 1.5** (Continued)

Sl. No.	Phytochemical Compound	Chemical Formula	Chemical Structure	IUPAC Name
24.	Germacrene D-4-Ol	$C_{15}H_{26}O$		(2E,7E)-1,7-dimethyl-4-propan-2-ylcyclodeca-2,7-dien-1-ol
25.	Spathulenol	$C_{15}H_{24}O$		(1aR,4aR,7S,7aR,7bR)-1,1,7-trimethyl-4-methylidene-1a,2,3,4a,5,6,7a,7b-octahydrocyclopropa[h]azulen-7-ol

Source: Chemical structure, Chemical formula, and IUPAC Name. Retrieved from: <https://pubchem.ncbi.nlm.nih.gov/>.

### 1.3.2 NON-VOLATILE CHEMICAL CONSTITUENTS

Investigators isolated some bioactive compounds of *M. arvensis* from deep eutectic solvent (DES) and aqueous methanol using ultrasound-assisted extraction (UAE). With the application of Liquid chromatography–mass spectrometry (LC-MS), nine new compounds were isolated and identified as p-coumaric and caffeic acid which are hydroxycinnamic acid derivatives and some flavonoids such as chrysin, naringenin, phenylpyruvic acid, pino-cembrin, and hesperidin (Naseem, Zahid, Hanif, & Shahid, 2020). Another study revealed that, presence of six bioactive secondary metabolites viz., cardiac glycosides, flavonoids, saponins, alkaloids, tannins, and terpenoids in the acetonic and methanolic solvent extracts of leaves of *Mentha*. Among which, maximum secondary metabolites were observed in acetonic and methanolic extracts, and saponin and alkaloids compounds were observed only in acetonic extract (Patil et al., 2015). Using high-performance liquid chromatography coupled with PDA detection, nine different phytochemical components were isolated and identified from the genus *Mentha* as caffeic acid, apigenin, luteolin-7-O-glucoside, eriocitrin, luteolin, rosmarinic acid, naringenin-7-O-glucoside, isorhoifolin, and eriodictyol (Dorman, Koşar, Kahlos, Holm, & Hiltunen, 2003).

With the application of GC-MS, 11 different phytochemical components were extracted and identified from the mint as N-ethyl-hexahydro-1H-azepine,

2-Methyl-E-E-3,13-octadecadien-1-ol, Tricyclo [4.2.1.1(2,5)] deca-3,7-dien-9-one,10-hydroxy-10-methyl-, 7-Oxabicyclo [4.1.0] heptan-2-one, 6-methyl-3-(1-methylethyl), Phenol, 2-methyl-5-(1-methylethyl), stereoisomer, 5,5,6-Trimethyl-2 phenylethynylbicyclo [2.2.1] heptan-2-ol, 2-Cyclopenten-1-one,2-(2-butenyl)-4-hydroxy-3-methyl, 3-Cyclopenten-1-one, 2-hydroxy-3-(3-methyl-2-butenyl), 5,8,11,14-Eicosatetraenoic acid, methyl ester, 1-(1-chloro-2,3 dimethylcyclopropyl)-3, 3-dimethyl-1-butyne and Isoborneol (Aihetasham, Umer, Akhtar, Din, & Rasib, 2015). *Mentha* phytochemical compounds obtained from different source treatments such as either in fresh, and dried form of plant material were subjected to quantitative analysis, revealed the detection of around 100 individual terpenoids and aromatic compounds of which 1,8-cineole,  $\beta$ - and  $\alpha$ -pinene, *trans*-, and *cis*- $\beta$ -ocimene, sabinene,  $\beta$ -caryophyllene and germacrene D were the main ones (Shelepova et al., 2014). Using (LC-ESI-MS) and HPLC-DAD technique, chemical constituents ursolic acid, rosmarinic acid, luteolin, oleanolic acid and isoorientin, were identified from the aerial part of menthol mint ethanolic extract (Zhang et al., 2015).

Four secondary metabolites-tannins, cardiac glycosides, steroids, and flavonoids were obtained from the methanolic extract of Japanese mint leaf. Using GC-MS analysis, 19 biochemical compounds were extracted and identified from the *M. arvensis* plant parts (leaves and roots) in which 2,4 Dioxaspiro[5.5] undec-8-ene, 3,7,9-trimethyl, gamma sitosterol, 4H-Pyran-4-one,2,3-dihydro-3,5-dihydroxy-6-methyl-, alpha.-Tocopherol.beta.-D-mannoside, neophytadiene, phytol, linolenic acid, n-hexadecanoic acid and ethyl linolenate were the maximum in percentage (Sagadevan, Suresh, Kumar, & Revathy, 2014). Apart from this, some study revealed that distilled biomass (free from terpenoids) obtained from *M. arvensis* contained different major biopolymers such as cellulose (38–42%), hemicellulose (27–30%), lignin (12–15%), lipids (0.5–0.8%), followed by chlorophyll and waxes (Prakash et al., 2018).

## 1.4 PHARMACOLOGICAL ACTIVITIES

The past investigation have revealed that *Mentha* and its phytochemicals compounds possess various biological activities including mainly antibacterial, antiviral, antifungal, anti-inflammatory, antioxidant, insecticidal, and acaricidal properties as in Figure 1.10 (Sevindik, 2018).

### 1.4.1 ANTIOXIDANT ACTIVITY

The phytochemicals obtained from various extracts of *M. arvensis* showed ABTS radical scavenging and DPPH activity (Chetia & Saikia, 2020). Some

study revealed that, antioxidant activity of *M. arvensis* plant extract protects against hydrogen peroxide-induced DNA damage in human lymphocytes. The study were found the presence of flavonols mainly morin in the plant extract, which are important for preventing per-oxidation and oxidative damage to DNA (Lin et al., 2013). Methanolic leaf extract of *M. arvensis* were tested with enzymatic and non-enzymatic methods. Among them, enzymatic antioxidants catalyzed and glutathione S transferase was analyzed in the enzymatic method and ascorbic acid in the non-enzymatic method. The study showed that extracts proved to be a good source of having strong antimicrobial effects. Such activities were evidenced by the nitrous oxide scavenging, free radical scavenging property, reducing power property, iron chelating and H<sub>2</sub>O<sub>2</sub> scavenging (Dar, Masoodi, Wali, Mir, & Shapoo, 2014). Additionally, ethanolic extract of *M. arvensis* using DPPH assay with IC<sub>50</sub> value ~41 µg/mL showed, free radical scavenging properties compared to the standard antioxidant ascorbic acid with IC<sub>50</sub> value ~19 µg/mL (Biswas, Saha, & Ali, 2014). Investigator investigated that antioxidant efficacy of *M. arvensis* using ABTS (2,2'-azino-bis 3-ethylbenzothiazoline-6-sulfuric acid) assay. Another study found that, the essential oil of menthol mint is a free radical scavenger with highest antioxidant activity at 4.0 mg mL<sup>-1</sup> concentration (Kumar, Dubey, Tiwari, Tripathi, & Sinha, 2007). Pandian et al. investigated that antioxidant efficacy of *M. arvensis* EOs using FRAP (ferric ion reducing antioxidant power), and DPPH (2,2-diphenyl-1-picrylhydrazyl) assay. The study showed that, the EOs of *Mentha* is a free radical scavenger showing highest antioxidant activity with EC<sub>50</sub> values of 0.55 mg/100 g (Pandian et al., 2017).

#### **1.4.2 ANTIBACTERIAL ACTIVITY**

Methanolic extract of *Mentha* leaves were screened to possess inhibitory action against five human pathogenic bacteria. Out of these bacteria *Escherichia coli*, *Proteus vulgaris*, *Klebsiella pneumoniae* were gram negative and *Staphylococcus aureus* and *Bacillus subtilis* were gram positive (Sagadevan, Suresh, Kumar, & Revathy, 2014; Suresh et al., 2012). Another study also showed that, photochemical derived from ethanol extract of *M. arvensis* namely tannin, phenols, flavonoids, steroids, and volatile oils show antimicrobial efficacy under *in vitro* condition, against strains of *Pseudomonas aeruginosa*, *Escherichia coli*, *Shigella flexneri*, *Staphylococcus aureus* and *Klebsiella pneumoniae* (Sugandhi & Bai, 2011). Methanolic extracts of the plant showed maximum zone of inhibition against *S. aureus* using agar well diffusion assay (Patil et al., 2015). The *Mentha* plant possessed antibacterial

action against three bacterial strains namely, *Escherichia coli*, *Bacillus cereus*, *B. subtilis*, *Staphylococcus aureus*, *S. epidermis*, and *Enterococcus faecalis* by agar well diffusion method (Chetia & Saikia, 2020). Though, the ethanolic extract obtained from *M. arvensis* inhibited the growth of the *Staphylococcus aureus* a gram positive (+) bacterial strains (Do Nascimento, Campos, & Da Costa, 2009). Another study also showed that, inter-nodal callus and leaves extracts from *Mentha arvensis* possess *in vitro* antimicrobial efficacy by disc diffusion method against four bacterial strains namely, *Streptococcus pyogenes*, *Bacillus subtilis*, *Proteus vulgaris*, and *Salmonella typhi* (Johnson, Wesely, Kavitha, & Uma, 2011). Another investigation found that antimicrobial activity of menthol compounds derived from *M. arvensis* against four bacterial strain *Candida albicans*, *Proteus mirabilis*, *Staphylococcus aureus* and *Escherichia coli* using broth dilution assay (Mickienė, Ragažinskienė, & Bakutis, 2011). Naseem et al. explained the DES extract of *M. arvensis*, showed that larger zone of inhibition with MIC against on *Staphylococcus aureus* and *Escherichia coli* using broth micro-dilution method (Naseem, Zahid, Hanif, & Shahid, 2020). Zhang et al. investigate the ethanol extract of different parts of *M. arvensis* showed the antibacterial effect against *Acinetobacter baumannii* a multi-drug resistant, using liquid chromatography–mass spectrometry (LC-ESI-MS). The study revealed that, extract exhibited dose-dependent growth inhibitory effects against *A. baumannii* with Minimum inhibitory concentration (MIC) and Minimum bactericidal concentration (MBC), and induced protein leakage and potent ROS generation in bacterial cells (Zhang et al., 2015).

### **1.4.3 ANTIFUNGAL ACTIVITY**

The bioactive compounds, mainly menthol (69.2%) present in the mint essential oil exhibited suppression action on the conidia germination and mycelial growth of *Alternaria alternata* (Fries) Keissler under *in vitro* and *in vivo* condition (Perveen & Bokhari, 2020). Another investigation showed that, acetone extract of *M. arvensis* leaves possess antifungal activity against mycelial growth of the *Penicillium chrysogenum* (Chetia & Saikia, 2020). DES extract of *M. arvensis*, showed that larger zone of inhibition with MIC against two fungal strain *Fusarium solani* and *Aspergillus niger* using broth micro-dilution method (Naseem, Zahid, Hanif, & Shahid, 2020). Additionally, essential oil component, menthol showed anti-fungal activity against two human pathogens *Fusarium oxysporum* and *Trichophyton mentagrophytes*



using disc diffusion test (Pandey, Rai, & Acharya, 2003). The essential oil component, menthol, and menthone possessed anti-fungal activity against *Fusarium moniliforme* and *Rhizoctonia solani* in a dose-dependent manner with ED<sub>50</sub> value 495 µg/ml and 331 µg/ml respectively (Makkar, Sharma, & Kaur, 2018). Apart from this, EOs of menthol mint showed absolute toxicity against Navjot 4NSt and Saktiman 3NSt, two toxigenic strains of *Aspergillus flavus* at MIC 0.05 mg mL<sup>-1</sup>. The study revealed that, the oil was highly sensitive against *Sclerotium rolfsii*, *A. fumigatus*, and *Helminthosporium oryzae* at 0.10 mg mL<sup>-1</sup> (Kumar, Dubey, Tiwari, Tripathi, & Sinha, 2007). Furthermore, antifungal activity has been seen in EOs of *M. arvensis* against *A. flavus* LHP5 and completely inhibited fungal growth at 1,000 µL L<sup>-1</sup> (Kumar, Shukla, Singh, Singh, & Dubey, 2009).

#### **1.4.4 ANTIVIRAL ACTIVITY**

Ethanollic leaf extract of *M. arvensis* were screened to possess antiviral activity against the herpes simplex type-1 (HSV-1) and vesicular stomatitis (VSV) viruses using simplified plaque reduction assay. The study revealed that, extract showed a minimum inhibitory concentration (MIC) value of 0.002–0.1 mg/ml against both viruses (Ali et al., 1996). Another study reported that direct virucidal activity of peppermint oil against Herpes simplex virus type 1 (HSV-1) and type 2 (HSV-2) and reduced plaque formation effectively with IC<sub>50</sub> value at 0.002% and 0.0008% for HSV-1 and HSV-2, respectively (Schuhmacher, Reichling, & Schnitzler, 2003).

#### **1.4.5 ANTI-INFLAMMATORY ACTIVITY**

Chemical compound that obtained from aqueous and ethanolic extracts of various parts (leaves, stem, and root) of *Mentha*, exhibited that inhibiting histamine release from mast cells and/or block histamine receptors using histamine-induced paw edema test (Malik et al., 2012). Rosmarinic acid, ursolic acid, and oleanolic acid isolated from *M. arvensis* by using LC/MS/MS technique showed anti-inflammatory activity; and use as an anti-inflammatory agent (Shen et al., 2011). Another study showed that, synergetic effects of *M. arvensis* leaf oil with acting phyto-active materials, non-psychoactive phytocannabinoids from the *Cannabis sativa* plant, extract of *Olive europaea* fruit oil, and *Silica colloidalanhydrous* against in reducing deep tissue pain and inflammation of joints and skeletal muscles induced by osteoarthritis/arthritis or/and caused by trauma (Siurkus, 2019).

### **1.4.6 CYTOTOXICITY ACTIVITY**

A number of studies have shown that the chemical constituents of *Mentha* plants contain cytotoxic properties that can be used to develop anticancer agents. Aqueous and methanolic extracts of *M. arvensis* plant showed anti-proliferative effect against various cancer cell lines namely MCF-7, COLO-205, THP-1, and NCI-H322 from 6 different origins (colon, breast, leukemia, lung, glioblastoma, and prostate) at concentration of 100 µg/mL using sulforhodamine blue (SRB) under *in-vitro* (Sharma, Hussain, Gupta, & Saxena, 2014). Using microtitration cytotoxicity assay, ethanolic leaf extract of *M. arvensis* showed cytotoxicity activity against HeLa cells with  $CD_{50}$  value 0.1 mg/ml (Ali et al., 1996). Another study showed that, EOs of *M. arvensis* leaves possess cytotoxicity activity against the breast cancer (MCF-7) and prostate cancer (LNCaP) cell lines with the (3-[4,5-dimethylthiazole-2-yl]-2,5-diphenyltetrazolium bromide) MTT assay. However, it has resulted that the inhibitory effect of *M. arvensis* EOs on cell viability ranged from 91% to 97% at 0.5 mg mL<sup>-1</sup> (Hussain, Anwar, Nigam, Ashraf, & Gilani, 2010).

### **1.4.7 HEPATOPROTECTIVE ACTIVITY**

Investigator investigated in rats that aqueous, ethanol, and chloroform leaves extracts of *Mentha* showed hepatoprotective activity against Carbon tetrachloride (CCL<sub>4</sub>) induced liver damage. Study revealed that, extract found the presence of alkaloids, glycosides, flavonoids, triterpenoids, steroids, carbohydrates, tannins, and phenolic compounds. Among them, mainly flavonoids have a protective effect against CCL<sub>4</sub> induced hepatotoxicity in rats (Patil & Mall, 2012).

### **1.4.8 ANTI-ASTHMATIC EFFECT**

The herb, *Mentha arvensis*, is well known as traditional medicine in curing bronchial asthma. Sharma et al. investigated that EOs of *M. arvensis* contains oxygenated monoterpenes and more than 70% menthol along with other chemicals compound. Among them menthol showed anti-asthmatic effect and suppressed immunological response to ovalbumin (OVA) and relaxes bronchial smooth muscles in mice (Sharma, Rasal, Patil, & Joshi, 2018).

### **1.4.9 ANTI-ALLERGIC ACTIVITY**

The ethanolic extract of different parts of *M. arvensis* plant (leaf, stem, and root) exhibits a high inhibitory effect against histamine release from mast cells with the histamine release inhibition assay; mast cell being well known for their important role in anaphylomic and allergic reactions (Malik et al., 2012). Another study has shown, flavonoids possess an antiallergic potential and have an inherent ability to modify the body's response to allergies and use them as nature's biological response modifier (Aiyelaagbe & Osamudiamen, 2009).

### **1.4.10 CARDIOVASCULAR DISEASE**

Crude extract of *M. arvensis* were screened to their effects on arachidonic acid metabolism. Though, it is resulted that inhibition of arachidonic acid metabolite thromboxane B<sub>2</sub>-a stable analog of thromboxane-A<sub>2</sub>, produced via cyclooxygenase pathway and lipoxygenase product 1 and 12-hydroxyeicosatetraenoic acid produced via lipoxygenase pathway and also showed antiplatelet activity in the form of thromboxane-B<sub>2</sub> which is one of the strongest proponents of platelet aggregation. The study also revealed that MA inhibited of platelet aggregation which may be significant mechanism for observed beneficial effects of *Mentha* plant in patients with ischemic heart disease (Thawkar, Jawarkar, Kalamkar, Pawar, & Kale, 2016).

### **1.4.11 ANTI-ANGIOGENIC EFFECT**

Anti-angiogenic properties of mint oil was evaluated using chick chorioallantoic membrane assay under *in vivo* condition. However, it is resulted that methanol and ethanol leaves extracts of *Mentha* plant showed a major reduction in total number of blood vessels, ethyl acetate extracts affected for new blood vessel formation; this would play a crucial role as an anti-angiogenic effect and prevent CAM angiogenesis (Sonawane, Shinde, & Jadhav, 2016).

### **1.4.12 ANTIULCEROGENIC ACTIVITY**

With the three experimental models viz., ethanol induced ulceration, 0.6 mol/L HCl induced ulceration and 90% ibuprofen induced gastric ulceration,

tannins, and flavonoids compounds were isolated and identified from the *M. arvensis* plant extract showed a significant reduce in the pH value of gastric juice, total acidity and ulcer number in the ibuprofen induced pyloric ligation ulcer model in rats. Hence, this study indicates the mint has antisecretory, cytoprotective, and antiulcerogenic actions (Londonkar & Poddar, 2009).

#### **1.4.13 ANTI-STRESS EFFECT**

Investigators investigated that phytochemical compound rosmarinic acid isolated from *M. arvensis* (MA) extract and fermented *M. arvensis* (FMA) using HPLC analysis showed potent anti-stress effect in immobilized rats. The study concluded that MA and FMA treatment-controlled stress-related hormone in rats by decreasing  $\beta$ -endorphin and corticosterone and increasing serotonin level. This treatment also improved the duodenum histology, daily food intake and body weight in rats (Tian et al., 2018).

#### **1.4.14 ANTIAFLATOXIGENIC ACTIVITY**

EOs of menthol mint were screened to their effects on aflatoxin B1 production by the toxigenic *Aspergillus flavus* strain namely Saktiman 3NSt of in SMKY medium. Though, it has resulted that menthol oil inhibits aflatoxin B1 production at 0.05 mg mL<sup>-1</sup> and mycelial growth at 0.10 mg mL<sup>-1</sup>, and reduces the possibility of aflatoxin contamination in food products (Kumar, Dubey, Tiwari, Tripathi, & Sinha, 2007). Another study showed that, EOs of *Mentha* spp. reduced the production of Aflatoxin B1 at approximately 200  $\mu$ L L<sup>-1</sup> and onwards (Kumar, Shukla, Singh, Singh, & Dubey, 2009).

#### **1.4.15 INSECTICIDAL ACTIVITY**

Chemical compound obtained from ethanolic seed extracts of *M. arvensis* possessed antitermitic activity against *Heterotermes indicola* (Wasmann). Investigation revealed that, extract exhibit antitermitic activity in a dose dependent manner and exhibited percent mortality at 10%, 5% and 3% conc. was 100%, 72% and 60%, respectively after 96 hours with LT<sub>50</sub> value 38.48, 67.54, and 83.19 hour respectively (Aihetasham, Umer, Akhtar, Din, & Rasib, 2015). Apart from this, EOs of *Mentha* spp. showed insecticidal activity against *Callosobruchus chinensis* using a direct-contact method. This investigation indicated that, the insecticidal activity of essential oil was found to be directly proportional to concentration and exposure period. The

100% mortality rate of insects was recorded in oil at 200  $\mu\text{L L}^{-1}$  for 2 hours, while absolute mortality was recorded at 1  $\mu\text{L L}^{-1}$  over the 10 h exposure period (Kumar, Shukla, Singh, Singh, & Dubey, 2009).

#### **1.4.16 ACARICIDAL ACTIVITY**

Using filter paper bioassays and fumigant, the essential oil of *Mentha* sp. showed acaricidal activity against *Tyrophagus putrescentiae* a stored food mite, in comparison to activity of benzyl benzoate a synthetic acaricide. However, it has resulted that all isomer of menthol, except (+)-isomenthol, indicates acaricidal activities against *T. putrescentiae*. This study indicates that the  $\text{LD}_{50}$  for menthol against *T. putrescentiae* was equal to 0.55 and 0.96  $\text{mg/cm}^2$  for the filter paper bioassays and fumigant, respectively. The result showed the values of fumigant and filter paper bioassays were about 12.18 times and about 15.18 times more effective against stored food mite, respectively as compared to benzyl benzoate (Park, Yang, & Lee, 2014). Another study indicates the, essential oil of *M. arvensis* leaves caused total mortality of the house dust mites, *Dermatophagoides farinae* and *D. pteronyssinus*, and stored food mite, *Tyrophagus putrescentiae* at doses of 5  $\mu\text{g/cm}^2$ , with an  $\text{LD}_{50}$  value of 1.46, 1.83, and 3.41  $\mu\text{g/cm}^2$ , respectively. The relative toxicity of essential oil, calculated as a proportion of  $\text{LD}_{50}$  of benzyl benzoate versus the  $\text{LD}_{50}$  of essential oil, was 6.74, 5.01, and 3.52 times more active than that of the acaricide, respectively (Jeon & Lee, 2016).

#### **1.4.17 DENTAL HEALTH**

*Mentha* herb is also used for oral dentifrice as it can provide freshness in the breath and also removes foul breath due to menthol component and also create an un-favorable environment for bacteria (Balakrishnan, 2015).

### **1.5 TRADITIONAL USES**

#### **1.5.1 AS HERBAL TEAS**

The upper part of *Mentha* spp. viz., leaves, stems, and flowers traditionally used as condiments and herbal teas both in fresh as well as dried form because of their distinct aroma. And due to its antibacterial, antiviral, and anti-inflammatory properties tea can fight clogged sinuses due to infections, the common cold, and allergies. The phytochemical constituent rosmarinic acid present in *Mentha* plant, herbal tea reduce symptoms of allergic



**FIGURE 1.10** Schematic representation of pharmacological activities of *Mentha* spp.

reactions, such as itchy eyes, runny nose and asthma (Baser, Kürkçüoğlu, Tarımcılar, & Kaynak, 1999; Hajlaoui et al., 2009; Oh, Park, Ahn, Park, & Kim, 2011; Asghari et al., 2018).

### 1.5.2 AS FOOD

The young stem tips of the mint plant commonly used as food (Tian et al., 2018). The mint plant is also used in sprinkling over fruits, salads, combining with cilantro or basil to make mint pesto, and fresh chopped mint to carrots, green beans, peas, zucchini, or cauliflower to prepare minted vegetables.

### 1.5.3 AS MEDICINE

In ancient time, *Mentha* species has been known for its medicinal uses for treatment of bronchitis, nausea, flatulence, ulcerative colitis, anorexia, and

liver ailments. It is used as folk remedy because of its antimicrobial, carminative, spasmolytic, anti-inflammatory, choleric, antiemetic, diaphoretic, analgesic, antispasmodic, anticatarrhal, stimulant, and emmenagogue activities (Tian et al., 2018; Hajlaoui et al., 2009; Asghari et al., 2018).

## **1.6 PATENT RELATED TO MENTHA SPP.**

### **1.6.1 PATENT NUMBER: US 20190167749A1**

The invention relates to the delivery system and oleo gel composition with active phytochemical components extracted from *Mentha arvensis* and *Cannabis sativa* for deep tissues pain reduction and inflammation of joints and skeletal muscles induced by osteoarthritis/arthritis or/and caused by trauma (Siurkus, 2019).

### **1.6.2 PATENT NUMBER: US 20190112547A1**

The invention is related to a cultivation method of hybrid mint plant denominated 'Teton Mint' which is a new *Mentha* sp. cultivar designated 14-27-89 for production of essential oil composition (Roberts, 2019).

### **1.6.3 PATENT NUMBER: US 20180352767A1**

The invention relates to a method for cultivation of hybrid mint plant identified as 'Blue Mountain Mint' designated 14-27-71 for production of essential oil composition (Roberts, 2018).

### **1.6.4 PATENT NUMBER: US007410937B2**

The invention relates to a new heavy duty hand cleanser (HDHC) which can be used with/without a solvent. It is highly biodegradable, non-ecotoxic, highly efficient with maximum skin tolerance and has no systemic toxicity. The cleansing compositions include the combination of natural essential oils (*Mentha piperita*, *M. arvensis* and *Eucalyptus globules*), provides a pleasant odor, fresh, and flowery Smell without using any perfume (Grascha & Joyce, 2008).

**1.6.5 PATENT NUMBER: US 20050150027A1**

The invention is related to a novel different *Mentha* plant of *Mentha piperita* 'Cim Indus,' which has a high quantity of menthofuran (most important constituent for aroma of the EOs) ranging between 22 and 30%, pulegone between 9.0 and 18% of total oil content, with EOs content ranging between 0.32 and 0.40% of the total oil content (Khanuja et al., 2005).

**1.6.6 PATENT NUMBER: US00PP12791P2**

The invention relates to a novel *M. arvensis* high yielding stable variety 'Damroo' which is capable of producing viable seeds and phenotypically homogeneous seed-derived plant population with high mint oil yield capability (Patra et al., 2002).

**1.6.7 PATENT NUMBER: US005871988A**

The invention relates to cDNA encoding (-)-4S-limonene synthase from Spearmint (*M. spicata*) (Croteau & Colby, 1999).

**1.6.8 PATENT NUMBER: US00PP10935P**

The invention relates to a different hybrid plant 'Himalaya' (*M. arvensis*) which can be characterized by its high oil yield with menthol-rich, vigorous growth, tolerance to rust and improved regeneration potentials such as corynespora leaf spot, Alternaria leaf blight and powdery mildew (Kumar et al., 1999).

**1.6.9 PATENT NUMBER: US00PP08645P**

The invention is related to a distinct variety of mint plant known as *Mentha spicata* botanically which is resistant to mint rust and verticillium wilt. EOs extracted from this plant has high menthone and low l-menthol content relatively (Sturtz, 1994).

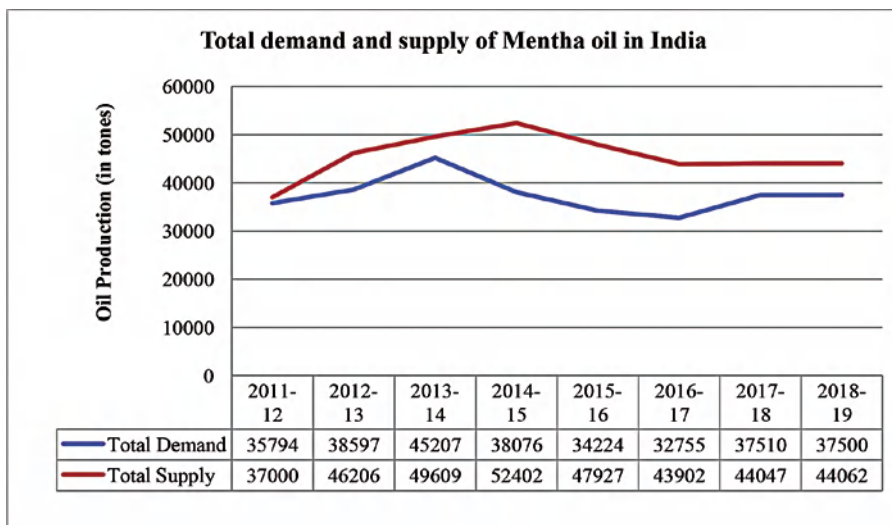
**1.6.10 PATENT NUMBER: US005182194A**

The invention relates to method for preparing thiol compounds P-MENTHA-8-THOL-3-ONE (Kerkenaar, Schmedding, & Nieuwegein, 1993).



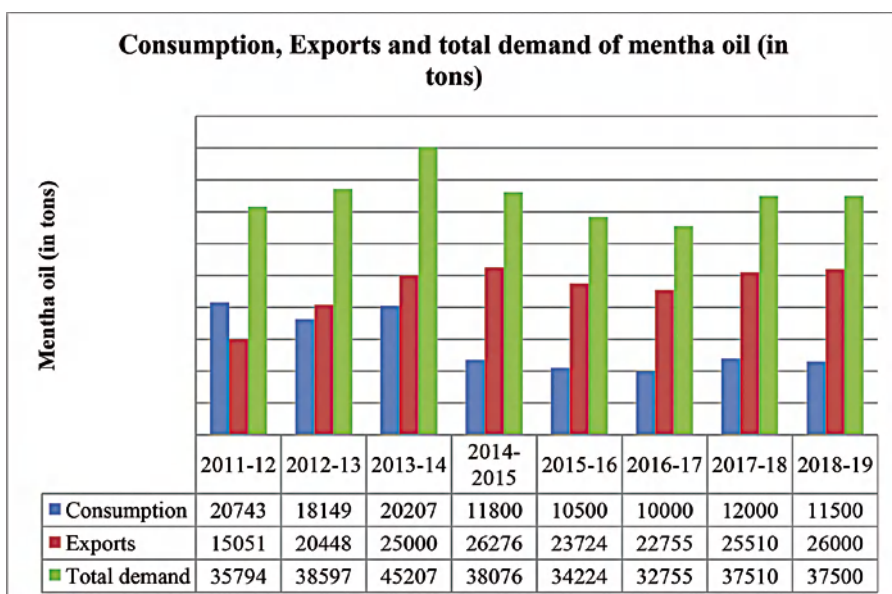
## 1.7 MARKET TRADE AND ITS APPLICATION

Mentha genus is well known for its EOs and chemical constituents mainly menthol extensively used in herbal medicines; pharmaceutical industry; food industries; cosmetic industries; used in organic chemistry; used as raw material in toothpowder, toothpaste, antiseptic mouth rinses, mouth fresheners, cough drops, chewing tobacco, perfumes, desserts, mint chocolates, chewing gums and candies that has increased its market demand. India is world's largest producer which produces 75–80% of global production and annually produces 48,500–50,000 tone an area under 3,00,000 hectares, and exporting nearly 22,500 tons in various countries including Brazil, Argentina, France, Japan, Germany, USA, UK, etc. Uttar Pradesh contributes nearly 90% of India's total production and ranked first in Mentha production. Total demand of Mentha oil was highest in 2013–2014, total supply along with difference in demand and supply was highest in 2014–2015 which are represented in Figure 1.11. Figure 1.12 represents that export of Mentha oil exceeds its consumption from 2012–2013 onwards and highest export was observed in 2014–2015. In India, there are 3 national commodity exchanges namely National Multi Commodity Exchange of India (NMCEIL), National Commodity and Derivatives Exchange (NDEX) and Multi Commodity Exchange (MCX) that offer future price. However, the average price of Mentha oil is 1,023/Kg, with fluctuations ranging from Rs 1,012 to Rs. 1,320 or more per kg, depending on harvest season and off-season (Kumar, Suresh, Singh, & Singh, 2011). Some of the companies that sell Mentha oil in India also export are Malik Polychem Ltd (Delhi), Essential Oils Manufacturers India AOS Product (Uttar Pradesh), Indian Aroma Exports Essential Oil Manufacturer (Uttar Pradesh), Herbochem Industries (Uttar Pradesh), Hariom Industries and Chemicals (Uttar Pradesh), JD Chem India (Delhi), India Essential Oils (Delhi), Mentha And Allied Products Limited (Delhi), Natures Natural India (Delhi), Pioneer Aromatics and Agri Solutions (Uttar Pradesh), Quality Mint and Allied Chemicals (Uttar Pradesh), Micro Lifesafe HealthCare (Punjab), Bhandari Hosiery Exports Limited (Punjab), Samde Aromatic Pvt. Ltd. (Rajasthan), Silverline Chemicals Ltd (Haryana), Akhil Healthcare Pvt Ltd (Gujarat), Alpha Menthol (Gujarat), Essential Natural Oils Manufacturers (Maharashtra), Maya Aromatics (Madhya Pradesh), and Green Essence Extraction Pvt. Ltd. (Odisha), etc. These companies purchase raw material of Mentha or Mentha oil from the cultivators, filtered, and distilled in their dispensation unit and packed in bottles or drums for export.



**FIGURE 1.11** Total demand and supply of Mentha oil in India during 2011–2019.

Source: Adapted from KEDIA Advisory – Mentha oil Outlook – May 2019.



**FIGURE 1.12** Data of consumption, exports, and total demand of Mentha oil in India during 2011–2019.

Source: Adapted from KEDIA Advisory – Mentha oil Outlook – May 2019.

### **1.7.1 INDUSTRIAL USE**

Menthol is a major component obtained from *M. arvensis* which are used in various pharmaceutical products and in cosmetics as stimulant, inhibitor, and antiseptic. Menthol have unique minty flavor which is used in various food products, oral products such as tooth paste and mouth fresheners, fragrance constituent used in detergents, cosmetics, and perfumes, soaps, and industrial fragrances because of its physiological cooling effect (Akram et al., 2011).

### **1.7.2 COSMETIC INDUSTRY**

MAPs plant extracts, oils, and waxes are widely used in cosmetic industries and have become a famous trend. Nowadays, herbal based cosmetic products are more in demand than chemical-based products. As per reports of the International Patent Classification (IPC), the genus *Mentha* has 25 patents under IPC number A61K-036/534 in the application for skin care. It has been applied mainly in formulations for the treatment of acne, firming, and slimming skin, and skin surgeries to increase the fatty tissue of the skin. Monoterpenes mainly menthol and menthone derived from the essential oil of *Mentha* have pleasing odor and skin conditioning properties which helps to soothe dry, itchy irritated skin due to contact dermatitis or allergies (César, Carnevale, Porto, & Campos, 2017). Some investigators have studied the effect of anti-microbial efficacy of mint essential oil in cosmetic formulations containing collagen hydrolysate and are generally used in Dentifrices and toothpastes products (Carvalho, Estevinho, & Santos, 2016).

### **1.7.3 AS BIO-ADSORBENT**

Dyes which are significant components of discharged waste by industries, especially the textile sector, and can significantly affect the photosynthetic activity of aquatic life and may even be toxic to some aquatic life. Ahmed & Kumar investigated that probable use of agricultural waste of *Mentha* to eliminate acidic dyes Patent Blue VF and Alizarin Red S which are most hazardous dyes responsible for skin and eyes irritation, from aqueous solutions using the Langmuir and Freundlich models (Ahmad & Kumar, 2008).

#### **1.7.4 ALTERNATIVE RENEWABLE BIOFUEL**

Genus *Mentha* is well known for its valuable EOs, and after extraction of EOs the distilled biomass is normally considered as waste product. Some investigators investigate that; the efficient utilization of distilled biomass can synthesize high value chemicals or produce alternative renewable biofuel. The study revealed that the physicochemical characterizations of biomass showed that distilled biomass had a higher percentage of cellulose. So distilled lignocellulosic biomass can be a potential candidate for biochemical production and biofuel (Prakash et al., 2018).

#### **1.7.5 POSTHARVEST DECAY CONTROL**

Fruits and vegetables are enriched with high moisture content, which is likely to be susceptible to various pathogens, bacteria, and fungi, and then cause diseases, which lead to high production losses during pre-harvest and post-harvest stage. Some study revealed that, vegetables, and fruits are effective against the treatment of essential oils to control post-harvest decay and reduce their loss and improve their quality, shelf life, and safety (Kalemba & Synowiec, 2019). The EOs *M. arvensis* have potential to be used as botanical fungi toxicants. The volatile oils from mint plants have revealed fungicidal activity against post-harvest diseases such as blue mold rot of citrus fruits caused by *Penicillium italicum* (Tripathi, Dubey, Banerji, & Chansouria, 2004). Another study revealed that, Essential oil of *Mentha* showed strong postharvest fungicidal and insecticidal activity against *Aspergillus flavus* (stored product fungi) and *Tribolium castaneum* and, *Sitophilus oryzae* (insect pests), at 600 ppm (Varma & Dubey, 2001).

### **1.8 CONCLUSION**

The oil-yielding herb, *Mentha* genus is known for its pharmaceutical properties from ancient time. *Mentha* and their extracts and essential oil are being used for various purposes; and well known for their mankind's medicinal uses, in particular for the treatment of cold, fever, and digestive and cardiovascular disorders. *Mentha* plant that contain a mixture of phytochemicals such as phenols, flavonoids, volatile oil, and tannins, exhibit several biological activities viz., antioxidant, antibacterial, antifungal, antitumor, anticancer, antiallergic, and anti-inflammatory activities as well as have various uses in industrial and other fields (Figure 1.13). As it is very well evident from literature that major phytochemicals of *Mentha* have possess

advanced therapeutic potential, therefore the plant metabolites of mint can be explored and provide significant potential for development of natural drugs. This chapter summarizes all the latest updated experimental and research work with respect to the pharmacological efficiency of the plant.

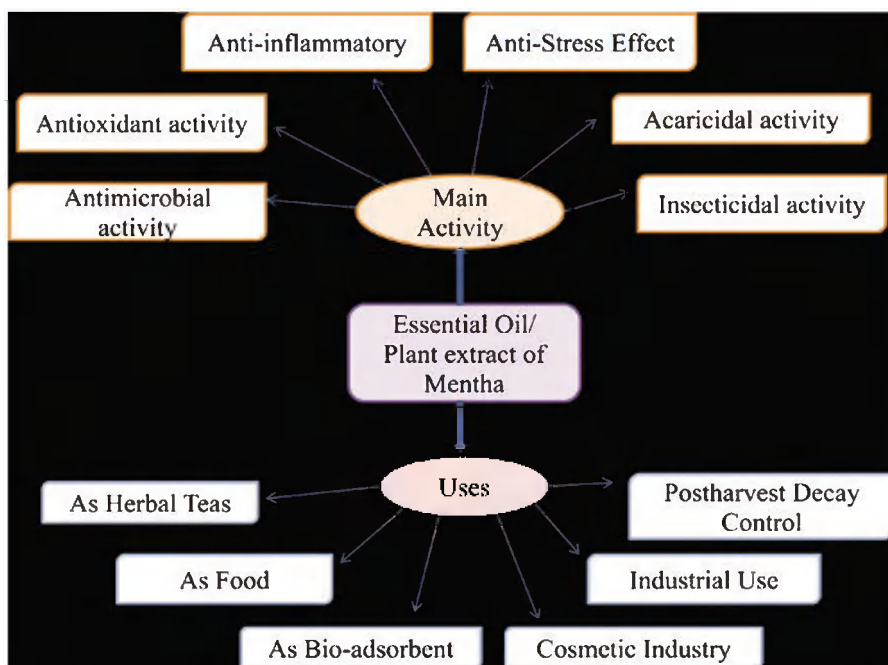


FIGURE 1.13 Various activities and uses of essential oils/plant extract of *Mentha*.

## KEYWORDS

- acaricidal activity
- anti-asthmatic effect
- essential oil
- *Mentha arvensis*
- menthol
- pest and disease
- pharmacology
- phytochemistry

## REFERENCES

- Ahmad, A., Darokar, M. P., & Tandon, S., (2011). Antimicrobial activity of isolates and derivatives ex Indian *Mentha arvensis* essential oil. *J. Essent. Oil Bear. Plants*, 14(6), 796–804. doi: 10.1080/0972060X.2011.10644007.
- Ahmad, R., & Kumar, R., (2008). Comparative adsorption study for the removal of alizarin RED S and patent blue VF by using *Mentha* waste. *Curr. World Environ.*, 3(2), 261–268. doi: 10.12944/CWE.3.2.09.
- Aihetasham, A., Umer, M., Akhtar, M. S., Din, M. I., & Rasib, K. Z., (2015). Bioactivity of medicinal plants *Mentha arvensis* and *Peganum harmala* extracts against *Heterotermes indicola* (Wasmann) (Isoptera). *Int. J. Biosci. IJB*, 7(5), 116–126. doi: 10.12692/ijb/7.5.116-126.
- Aiyelaagbe, O. O., & Osamudiamen, P. M., (2009). Phytochemical screening for active compounds in *Mangifera indica* leaves from Ibadan, Oyo State. *Asian J. Inf. Technol.*, 2(1), 11–13.
- Akram, M., et al., (2011). *Mentha arvensis* Linn.: A review article. *J. Med. Plants Res.*, 5(18), 4499–4503.
- Ali, A. M., Mackeen, I. M. M., El-SHARKAWY, S. H., Hamidi, J. A., Ahmadi, F. B. H., & Lajisi, N. H., (1996). *Antiviral and Cytotoxic Activities of Some Plants Used in Malaysian Indigenous Medicine*, 19(2), 8.
- Asghari, B., Zengin, G., Bahadori, M. B., Abbas-Mohammadi, M., & Dinparast, L., (2018). Amylase, glucosidase, tyrosinase, and cholinesterases inhibitory, antioxidant effects, and GC-MS analysis of wild mint (*Mentha longifolia* var. *calliantha*) essential oil: A natural remedy. *Eur. J. Integr. Med.*, 22, 44–49. doi: 10.1016/j.eujim.2018.08.004.
- Bajeli, J., Tripathi, S., Kumar, A., Tripathi, A., & Upadhyay, R. K., (2016). Organic manures a convincing source for quality production of Japanese mint (*Mentha arvensis* L.). *Ind. Crops Prod.*, 83, 603–606. doi: 10.1016/j.indcrop.2015.12.064.
- Balakrishnan, A., (2015). Therapeutic uses of peppermint: A review. *J. Pharm. Sci. Res.*, 7(7), 474–476.
- Baser, K. H. C., Kürkçüoğlu, M., Tarımcılar, G., & Kaynak, G., (1999). Essential oils of *Mentha* SPECIES from Northern Turkey. *J. Essent. Oil Res.*, 11(5), 579–588. doi: 10.1080/10412905.1999.9701218.
- Bhat, S., Maheshwari, P., Kumar, S., & Kumar, A., (2002). *Mentha* species: *In vitro* regeneration and genetic transformation. *Mol. Biol. Today*, 3(1), 11–23.
- Bisht, S., Kumar, P., Purohit, J., & Srinivasanraghvan, A., (2013). *In vitro* management of curvularia leaf spot of maize using botanicals, essential oils and bio-control agents. *The Bioscan*, 8(3), 731–733.
- Biswas, N. N., Saha, S., & Ali, M. K., (2014). Antioxidant, antimicrobial, cytotoxic and analgesic activities of ethanolic extract of *Mentha arvensis* L. *Asian Pac. J. Trop. Biomed.*, 4(10), 792–797. doi: 10.12980/APJTB.4.2014C1298.
- Brahmi, F., Khodir, M., Mohamed, C., & Pierre, D., (2017). Chemical composition and biological activities of *Mentha* species. In: El-Shemy, H. A., (ed.), *Aromatic and Medicinal Plants – Back to Nature*. InTech.
- Carvalho, I. T., Estevinho, B. N., & Santos, L., (2016). Application of microencapsulated essential oils in cosmetic and personal healthcare products: A review. *Int. J. Cosmet. Sci.*, 38(2), 109–119. doi: 10.1111/ics.12232.

- César, F. C. S., Carnevale, N. F., Porto, G. S., & Campos, P. M., (2017). Patent analysis: A look at the innovative nature of plant-based cosmetics. *Quím. Nova*, *40*(7), 840–847. doi: 10.21577/0100-4042.20170022.
- Chand, S., Patra, N. K., Anwar, M., & Patra, D. D., (2004). Agronomy and uses of menthol mint (*Mentha arvensis*)-Indian perspective. *Proc Indian Natl. Sci. Acad.*, *B70*(3), 269–297.
- Chetia, J., & Saikia, L. R., (2020). Antimicrobial activity assay and phytochemical study of different aerial parts of *Mentha arvensis* L. collected from Dibrugarh, Assam. *J. Sci. Res.*, *64*(1), 103–112. doi: 10.37398/JSR.2020.640115.
- Choudhary, H., Badal, P. S., Singh, V., & Osti, R., (2017). Economics of menthol mint cultivation in India: Shifting from traditional farming to income-based farming. *Indian J. Econ. Dev.*, *13*(2a), 232. doi: 10.5958/2322-0430.2017.00071.3.
- Croteau, R. B., & Colby, S. M., (1999). *DNA Encoding Limonene Synthase from Mentha Spicata*. 5,871,988.
- Dar, M. A., Masoodi, M. H., Wali, A. F., Mir, M. A., & Shapoo, N. S., (2014). Antioxidant potential of methanol root extract of *Mentha arvensis* L. from Kashmir region. *J. Appl. Pharm. Sci.*, *4*(3), 50–57. doi: 10.7324/JAPS.2014.40311.
- Do Nascimento, E. M., Campos, A., & Da Costa, J. G., (2009). Phytochemical prospection, toxicity, and antimicrobial activity of *Mentha arvensis* (Labiatae) from Northeast of Brazil. *J. Young Pharm.*, *1*(3), 210. doi: 10.4103/0975-1483.57066.
- Dorman, H. J. D., Kosar, M., Kahlos, K., Holm, Y., & Hiltunen, R., (2003). Antioxidant properties and composition of aqueous extracts from *Mentha* species, hybrids, varieties, and cultivars. *J. Agric. Food Chem.*, *51*(16), 4563–4569. doi: 10.1021/jf034108k.
- Farco, J. A., & Grundmann, O., (2013). Menthol – pharmacology of an important naturally medicinal ‘cool.’ *Mini-Rev. Med. Chem.*, *13*(1), 124–131.
- Ghosh, M. L., & Chatterjee, S. K., (1978). Cultivation of *Mentha citrata* Ehrh in Burdwan District, West Bengal. *Proc. Indian Acad. Sci.-Sect. B*, *87B*(5), 157–160.
- Gobert, V., Moja, S., Colson, M., & Taberlet, P., (2002). Hybridization in the section *Mentha* (*Lamiaceae*) inferred from AFLP markers. *Am. J. Bot.*, *89*(12), 2017–2023. doi: 10.3732/ajb.89.12.2017.
- Grascha, P. B., & Joyce, N. P., (2008). *Hand Cleansing Formulation*. US 7,410,937 B2.
- Gupta, A., Sharma, S., & Naik, S. N., (2011). Biopesticidal value of selected essential oils against pathogenic fungus, termites, and nematodes. *Int. Biodeterior. Biodegrad.*, *65*(5), 703–707. doi: 10.1016/j.ibiod.2010.11.018.
- Hajlaoui, H., et al., (2009). Biological activities of the essential oils and methanol extract of two cultivated mint species (*Mentha longifolia* and *Mentha pulegium*) used in the Tunisian folkloric medicine. *World J. Microbiol. Biotechnol.*, *25*(12), 2227–2238. doi: 10.1007/s11274-009-0130-3.
- Hussain, A. I., Anwar, F., Nigam, P. S., Ashraf, M., & Gilani, A. H., (2010). Seasonal variation in content, chemical composition and antimicrobial and cytotoxic activities of essential oils from four *Mentha* species: Biological activities of *Mentha* essential oils. *J. Sci. Food Agric.*, *90*(11), 1827–1836. doi: 10.1002/jfsa.4021.
- Jeon, Y. J., & Lee, H. S., (2016). Chemical composition and acaricidal activities of essential oils of *Litsea cubeba* fruits and *Mentha arvensis* leaves against house dust and stored food mites. *J. Essent. Oil Bear. Plants*, *19*(7), 1721–1728. doi: 10.1080/0972060X.2016.1211964.
- Johnson, M., Wesely, E., Kavitha, M., & Uma, V., (2011). Antibacterial activity of leaves and inter-nodal callus extracts of *Mentha arvensis* L. *Asian Pac. J. Trop. Med.*, *4*(3), 196–200. doi: 10.1016/S1995-7645(11)60068-0.

- Kalemba, D., & Synowiec, A., (2019). Agrobiological interactions of essential oils of two menthol mints: *Mentha piperita* and *Mentha arvensis*. *Molecules*, 25(1), 59. doi: 10.3390/molecules25010059.
- Kalra, A., Singh, H. B., Pandey, R., Samad, A., Patra, N. K., & Kumar, S., (2005). Diseases in mint: Causal organisms, distribution, and control measures. *J. Herbs Spices Med. Plants*, 11(1, 2), 71–91. doi: 10.1300/J044v11n01\_03.
- Kalra, A., Singh, H. B., Patra, N. K., & Kumar, S., (2003). Integrated host plant resistance and fungicide application on leaf blight control in menthol mint (*Mentha arvensis* L.). *J. Herbs Spices Med. Plants*, 10(2), 83–87. doi: 10.1300/J044v10n02\_09.
- Kamatou, G. P. P., Vermaak, I., Viljoen, A. M., & Lawrence, B. M., (2013). Menthol: A simple monoterpene with remarkable biological properties. *Phytochemistry*, 96, 15–25. doi: 10.1016/j.phytochem.2013.08.005.
- Karnwal, A., (2011). Mycolytic effect of fluorescent *Pseudomonas* in biocontrolling of fungal phytopathogenic *Curvularia lunata*, *Fusarium oxysporum*, *Alternaria padwickii* and *Rhizoctonia solani*. *Arch. Phytopathol. Plant Prot.*, 44(12), 1128–1134. doi: 10.1080/03235408.2010.482419.
- Kasrati, A., Alaoui, J. C., Spooner-Hart, R., Legendre, L., Leach, D., & Abbad, A., (2017). Chemical characterization and biological activities of essential oil obtained from mint timija cultivated under mineral and biological fertilizers. *J. Anal. Methods Chem.*, 2017, 1–7. doi: 10.1155/2017/6354532.
- Kaur, T., Singh, S., Bhullar, M. S., Shergill, L. S., & Kaur, R., (2013). Effect of planting methods and weed control on productivity of Japanese Mint (*Mentha Arvensis* L.). *Indian J. Agric. Res.*, 47(3), 243–247.
- KEDIA Advisory – *Mentha Oil Outlook*, (2019). Kedia Stocks & Commodities Research Pvt Ltd.
- Kerkenaar, A., Schmedding, D. J. M., & Nieuwegein, J. B., (1993). *Method for Preparing P-Mentha-8-Thol-3-One*. 5,182,194.
- Khanuja, S. P. S., et al., (2005). *Mint Plant 'INDUS.'* US 2005/0150.027 P1.
- Klumpp, D. A., et al., (2020). Synthesis of menthol glycinates and their potential as cooling agents. *ACS Omega*, 5(8), 4043–4049. doi: 10.1021/acsomega.9b03624.
- Kothari, S. K., & Singh, K., (1994). Chemical weed control in Japanese mint (*Mentha arvensis* L.). *J. Essent. Oil Res.*, 6(1), 47–55. doi: 10.1080/10412905.1994.9698324.
- Kumar, A., Khajuria, V., & Aggarwal, S., (2012). Secondary metabolites of *Mentha arvensis* and their biological activities. *Anal. Chem. Lett.*, 2(6), 373–400. doi: 10.1080/22297928.2012.10662623.
- Kumar, A., Shukla, R., Singh, P., Singh, A. K., & Dubey, N. K., (2009). Use of essential oil from *Mentha arvensis* L. to control storage moulds and insects in stored chickpea: Insecticidal and antifungal efficacy of *Mentha arvensis* essential oil. *J. Sci. Food Agric.*, 89(15), 2643–2649. doi: 10.1002/jsfa.3768.
- Kumar, D., Gupta, V., & Verma, V. S., (2013). First report of *Helminthosporium spiciferum* (Bainier) Nicot on mint (*Mentha arvensis*). *australas. Plant Dis. Notes*, 8(1), 73, 74. doi: 10.1007/s13314-013-0098-6.
- Kumar, R., Dubey, N. K., Tiwari, O. P., Tripathi, Y. B., & Sinha, K. K., (2007). Evaluation of some essential oils as botanical fungitoxicants for the protection of stored food commodities from fungal infestation. *J. Sci. Food Agric.*, 87(9), 1737–1742. doi: 10.1002/jsfa.2906.
- Kumar, S., et al., (1999). *Mini Plant Mentha Arvensis Himalaya*. Plant 10,935.



- Kumar, S., Suresh, R., Singh, V., & Singh, A. K., (2011). Economic analysis of menthol mint cultivation in Uttar Pradesh: A case study of Barabanki District. *Agric. Econ. Res. Rev.*, 24, 1–7.
- Lawrence, B. M., (2007). *Mint: The Genus Mentha*. Boca Raton, FL: CRC Press.
- Lin, K. H., et al., (2013). Antioxidant activity of herbaceous plant extracts protect against hydrogen peroxide-induced DNA damage in human lymphocytes. *BMC Res. Notes*, 6(1), 490. doi: 10.1186/1756-0500-6-490.
- Londonkar, R. L., & Poddar, P. V., (2009). Studies on activity of various extracts of *Mentha arvensis* Linn against drug induced gastric ulcer in mammals. *World J. Gastrointest. Oncol.*, 1(1), 82–88. doi: 10.4251/wjgo.v1.i1.82.
- Maia, N. B., Malavolta, Jr. V. A., Carvalho, R. V., Fancelli, M. I., & Carmello, Q. A. C., (1996). Ocorrência de *Pseudomonas cichorii* em *Mentha arvensis*. *Summa Phytopathol.*, 22(2), 185–188.
- Makkar, M. K., Sharma, S., & Kaur, H., (2018). Evaluation of *Mentha arvensis* essential oil and its major constituents for fungitoxicity. *J. Food Sci. Technol.*, 55(9), 3840–3844. doi: 10.1007/s13197-018-3291-y.
- Malik, F., et al., (2012). Phyto-chemical analysis, anti-allergic and anti-inflammatory activity of *Mentha arvensis* in animals. *Afr. J. Pharm. Pharmacol.*, 6(9), 613–619. doi: 10.5897/AJPP11.702.
- Margina, A., & Zheljazkov, V., (1994). Control of mint rust (*Puccinia menthae* Pers.) on mint with fungicides and their effect on essential oil content. *J. Essent. Oil Res.*, 6(6), 607–615. doi: 10.1080/10412905.1994.9699352.
- Margina, A., & Zheljazkov, V., (1996). Fungal pathogens from Uredinales on some medicinal and aromatic plants in Bulgaria and their control. *Int. Symp. Med. Aromat. Plants*, 426, 333–344. doi: 10.17660/ActaHortic.1996.426.38.
- Mekonnen, M., Manahile, B., & Mengesha, B., (2015). Screening of botanical extracts for the control of Japanese mint (*Mentha arvensis* L.) leaf rust (*Puccinia menthae*) in greenhouse and field condition. *Afr. J. Crop Sci.*, 3(7), 201–205.
- Mentha*, (2020). Kew Science: Plants of the World Online. Retrieved from: <http://www.plantsoftheworldonline.org/taxon/urn:lsid:ipni.org:names:30016176-2> (accessed on 02 September 2023).
- Mickienė, R., Ragažinskienė, O., & Bakutis, B., (2011). Antimicrobial activity of *Mentha arvensis* L. and *Zingiber officinale* R. essential oils. *Biologija*, 57(2), 92–97.
- Munsi, P. S., (1992). Nitrogen and phosphorus nutrition response in Japanese mint cultivation. *Acta Hortic.*, 306, 436–443. doi: 10.17660/ActaHortic.1992.306.58.
- Muthukumar, A., & Venkatesh, A., (2012). first report of stolon rot of mint caused by *Pythium aphanidermatum* from Tamil Nadu, India. *J. Mycol. Plant Pathol.*, 42(3), 394–396.
- Naseem, Z., Zahid, M., Hanif, M., & Shahid, M., (2020). Environmentally friendly extraction of bioactive compounds from *Mentha arvensis* using deep eutectic solvent as green extraction media. *Pol. J. Environ. Stud.*, 29(5), 3749–3757, Jun., doi: 10.15244/pjoes/114235.
- Nilo, M. C. S., et al., (2017). Chemical composition and antioxidant and antifungal properties of *Mentha x piperita* L. (peppermint) and *Mentha arvensis* L. (cornmint) samples. *Food Res.*, 1(5), 147–156. doi: 10.26656/fr.2017.5.104.
- Oh, H. A., Park, C. S., Ahn, H. J., Park, Y. S., & Kim, H. M., (2011). Effect of *Perilla frutescens* var. *acuta* Kudo and Rosmarinic acid on allergic inflammatory reactions. *Exp. Biol. Med.*, 236(1), 99–106. doi: 10.1258/ebm.2010.010252.

- Padalia, R. C., Verma, R. S., Chauhan, A., Sundaresan, V., & Chanotiya, C. S., (2013). Essential oil composition of 16 elite cultivars of *Mentha* from western Himalayan region, India. *Maejo Int. J. Sci. Technol.*, 7(1), 83–93.
- Pal, A. K., Mohanty, A. K., & Devarani, L., (2015). Gap analysis in adoption of scientific *Mentha* (*Mentha arvensis*) cultivation in Uttar Pradesh. *Indian Res. J. Ext. Educ.*, 15(2), 1–6.
- Pandey, A. K., Rai, M. K., & Acharya, D., (2003). Chemical composition and antimycotic activity of the essential oils of corn mint (*Mentha arvensis*) and lemon grass (*Cymbopogon flexuosus*) against human pathogenic fungi. *Pharm. Biol.*, 41(6), 421–425. doi: 10.1076/phbi.41.6.421.17825.
- Pandey, R. R., Dubey, R. C., & Saini, S., (2010). Phytochemical and antimicrobial studies on essential oils of some aromatic plants. *Afr. J. Biotechnol.*, 9(28), 4364–4368.
- Pandey, R., (2005a). Field application of bio-organics in the management of *Meloidogyne incognita* in *Mentha arvensis*. *Nematol. Mediterr.*, 33(1), 51–54.
- Pandey, R., (2005b). Management of *meloidogyne incognita* in *Artemisia pallens* with bio-organics. *Phytoparasitica*, 33(3), 304–308. doi: 10.1007/BF02979868.
- Pandey, R., et al., (2019). Diseases of mints and their management. In: *Diseases of Medicinal and Aromatic Plants and Their Management* (pp. 273–303). New Delhi, India: Today and Tomorrow Printers and Publisher.
- Pandey, R., Mishra, A. K., Tiwari, S., Singh, H. N., & Kalra, A., (2011). Enhanced tolerance of *Mentha arvensis* against *Meloidogyne incognita* (Kofoid and White) Chitwood through mutualistic endophytes and PGPRs. *J. Plant Interact.*, 6(4), 247–253. doi: 10.1080/17429145.2011.554892.
- Pandian, A., Kumar, S. D., Badoni, S. R., Malaiyandi, M., Chandrasekaran, S., & Sundaram, V., (2017). Total phenolic content, volatile constituents and antioxidative effect of *Coriandrum sativum*, *Murraya koenigii* and *Mentha arvensis*. *Nat. Prod. J.*, 7(1), 65–74.
- Park, J. H., Yang, J. Y., & Lee, H. S., (2014). Acaricidal activity of constituents derived from peppermint oil against *Tyrophagus putrescentiae*. *J. Food Prot.*, 77(10), 1819–1823. doi: 10.4315/0362-028X.JFP-14-107.
- Patil, D. B., Namrata, P., Patil, S. B., Chavan, S. S., Patil, P. J., & Bhamburdekar, S. B., (2015). Phytochemical investigation and antimicrobial activity of *Mentha Arvensis* L. [Pudina]. *World J. Pharm. Res.*, 4(9), 1829–1834.
- Patil, K., & Mall, A., (2012). Hepatoprotective activity of *Mentha arvensis* Linn. leaves against CCL4 induced liver damage in rats. *Asian Pac. J. Trop. Dis.*, 2, S223–S226. doi: 10.1016/S2222-1808(12)60156-X.
- Patra, N. K., et al., (2002). *Novel High Yielding Stable Mentha Arvensis Plant Named Damroo.* US PP12,791 P2.
- Perveen, K., & Bokhari, N. A., (2020). Management of Alternaria leaf blight in tomato plants by *Mentha* essential oil. *Plant Prot. Sci.*, 56(3), 191–196. doi: 10.17221/100/2019-PPS.
- Perveen, K., Haseeb, A., & Shukla, P. K., (2007). Efficacy of pesticides, neem seed powder and bio-control agents on *Meloidogyne incognita* and growth and oil yield of *Mentha arvensis*. *Nematol. Mediterr.*, 35(1), 75–79.
- Peter, K. V., (2006). *Handbook of Herbs and Spices* (Vol. 3). Boca Raton, Fla.: CRC.
- Pino, J. A., Rosado, A., & Fuentes, V., (1996). Chemical composition of the essential oil of *Mentha arvensis* L. var. *piperascens* malinv. from Cuba. *J. Essent. Oil Res.*, 8(6), 685, 686. doi: 10.1080/10412905.1996.9701043.

- PRAKASH Chemicals, (2018). Retrieved from: <http://www.prkchemicals.com/2018.html> (accessed on 02 September 2023).
- Prakash, O., et al., (2018). Novel process for isolation of major bio-polymers from *Mentha arvensis* distilled biomass and saccharification of the isolated cellulose to glucose. *Ind. Crops Prod.*, 119, 1–8. doi: 10.1016/j.indcrop.2018.03.063.
- PubChem., (n.d.). Retrieved from: <https://pubchem.ncbi.nlm.nih.gov/> (accessed on 02 September 2023).
- Ricupero, M., Desneux, N., Zappalà, L., & Biondi, A., (2020). Target and non-target impact of systemic insecticides on a polyphagous aphid pest and its parasitoid. *Chemosphere*, 247. doi: 10.1016/j.chemosphere.2019.125728.
- Roberts, D. D., (2018). *Method for Cultivation of Hybrid Mint Plant Designated 14 -27-71 for Production of Essential Oil Composition*. US 2018/0352767 A1.
- Roberts, D. D., (2019). *Method for Cultivation of Hybrid Mint Plant Designated 14 -27 -89 for Production of Essential Oil Composition*. US 2019/0112547 A1.
- Roy, D., & Mallick, B., (2017). Phytochemical analysis of field grown and tissue culture derived *Mentha arvensis* L. plants with special reference to antioxidative potentials. *Int. J. Eng. Technol. Sci. Res.*, 4(11), 1–7.
- Sagadevan, P., Suresh, S. N., Kumar, R. S., & Revathy, R. A. R., (2014). Studies on phytochemical composition, antibacterial and antioxidant potential of methanolic leaf extract of *Menthos arvensis*. *Int. J. Biosci. Nanosci.*, 1(1), 22–27.
- Saleem, M. N., & Idris, M., (2016). Podina (*Mentha arvensis*): Transformation from food additive to multifunctional medicine. *ARC J. Pharm. Sci.*, 2(2), 6–15. doi: 10.20431/2455-1538.0202002.
- Salehi, B., et al., (2018). Plants of genus *Mentha*: From farm to food factory. *Plants*, 7(3), 70. doi: 10.3390/plants7030070.
- Samad, A., Gupta, M. K., Shasany, A. K., Ajayakumar, P. V., & Alam, M., (2009). Begomovirus related to tomato leaf curl Pakistan virus newly reported in *Mentha* crops in India. *Plant Pathol.*, 58(2), 404. doi: 10.1111/j.1365-3059.2008.02003.x.
- Schuhmacher, A., Reichling, J., & Schnitzler, P., (2003). Virucidal effect of peppermint oil on the enveloped viruses herpes simplex virus type 1 and type 2 *in vitro*. *Phytomedicine*, 10(6, 7), 504–510. doi: 10.1078/094471103322331467.
- Sevik, M., (2012). Natural occurrence of cucumber mosaic virus infecting water mint (*Mentha aquatica*) in Antalya and Konya, Turkey. *Acta Bot. Croat.*, 71(1), 187–193. doi: 10.2478/v10184-011-0052-7.
- Sevindik, M., (2018). Pharmacological properties of *Mentha* species. *J. Tradit. Med. Clin. Naturop.*, 7(1), 1–4. doi: 10.4172/2573-4555.1000259.
- Sharma, S., Rasal, V. P., Patil, P. A., & Joshi, R. K., (2018). *Mentha arvensis* essential oil suppressed airway changes induced by histamine and ovalbumin in experimental animals. *Nat. Prod. Res.*, 32(4), 468–472. doi: 10.1080/14786419.2017.1311891.
- Sharma, V., Hussain, S., Gupta, M., & Saxena, A. K., (2014). *In vitro* anticancer activity of extracts of *Mentha* Spp. against human cancer cells. *Indian J. Biochem. Biophys.*, 51, 416–419.
- Shelepova, O. V., Voronkova, T. V., Kondrat'eva, V. V., Semenova, M. V., Bidyukova, G. F., & Oehnovich, L. S., (2014). Phenotypic and phytochemical differences between *Mentha arvensis* L. and *Mentha canadiensis* L. *Biol. Bull.*, 41(1), 19–23. doi: 10.1134/S1062359014010099.

- Shen, D., et al., (2011). A rapid LC/MS/MS method for the analysis of nonvolatile antiinflammatory agents from *Mentha* spp. *J. Food Sci.*, 76(6), C900–C908. doi: 10.1111/j.1750-3841.2011.02281.x.
- Singh, A. K., et al., (2005). Essential oil composition and chemoarrays of menthol mint (*Mentha arvensis* L. f. *piperascens* Malinvaud ex. Holmes) cultivars. *Flavor Fragr. J.*, 20(3), 302–305. doi: 10.1002/ffj.1417.
- Singh, D. K., Singh, S., Singh, S. K., Singh, D. K., & Kumar, K., (2014). Scientific cultivation of *Mentha* (Mint). *Pop. Kheti*, 2(3), 15–19.
- Singh, M. K., & Saini, S. S., (2008). Planting date, mulch, and herbicide rate effects on the growth, yield, and physicochemical properties of menthol mint (*Mentha arvensis*). *Weed Technol.*, 22(4), 691–698. doi: 10.1614/WT-08-027.1.
- Singh, P. P., Pandey, P., Singh, D., Singh, S., Khan, M. S., & Semwal, M., (2020). 'Mentha Mitra'—An android app based advisory digital tool for menthol mint farmers. *Ind. Crops Prod.*, 144, 112047. doi: 10.1016/j.indcrop.2019.112047.
- Siurkus, J., (2019). *The Oleo Gel Composition and Delivery System with Active Compounds from Cannabis Sativa and Mentha arvensis for Reduction of Inflammation and Pain in Deep Tissues*. US 2019/0167749 A1.
- Sonawane, H., Shinde, A., & Jadhav, J., (2016). Evaluation of anti-angiogenic potential of *Mentha arvensis* Linn. leaf extracts using chorioallantoic membrane assay. *World J. Pharm. Res.*, 5(2), 677–689.
- Štefanidesová, K., Špitalská, E., Csicsay, F., Friedländerová, V., Šáner, A., & Škultéty, L., (2019). Evaluation of the possible use of genus *Mentha* derived essential oils in the prevention of SENLAT syndrome caused by *Rickettsia slovaca*. *J. Ethnopharmacol.*, 232, 55–61. doi: 10.1016/j.jep.2018.12.005.
- Sturtz, G. D., (1994). *Low Menthol Mint Plant Mentha Spicata. L. Erospcata*. Plant 8,645.
- Sugandhi, B. R. M., & Bai, G. M., (2011). Antimicrobial activity of *Mentha arvensis* L. (*Lamiaceae*). *J. Adv. Lab. Res. Biol.*, 2(1), 8–11.
- Sultan, S. A., et al., (2017). *Community Analysis of Key Pests Associated with Mentha Crop at Sitapur, U.P. India*, 1(2), 6.
- Suresh, S. N., Rathishkumar, S., Rajeshwari, V., Sagadevan, P., Gayathri, S., & Vithya, E. D., (2012). Studies on phytochemical composition and antibacterial potential of methanolic leaf extract of *Mentha arvensis* Linn. *Int. J. Pharm. Res. Dev.*, 4(8), 1–4.
- Thawkar, B. S., Jawarkar, A. G., Kalamkar, P. V., Pawar, K. P., & Kale, M. K., (2016). Phytochemical and pharmacological review of *Mentha arvensis*. *Int. J. Green Pharm.*, 10(2), 71–76.
- Tian, W., et al., (2018). The anti-stress effect of *Mentha arvensis* in immobilized rats. *Int. J. Mol. Sci.*, 19(2), 355. doi: 10.3390/ijms19020355.
- Tiwari, P., (2016). Recent advances and challenges in trichome research and essential oil biosynthesis in *Mentha arvensis* L. *Ind. Crops Prod.*, 82, 141–148. doi: 10.1016/j.indcrop.2015.11.069.
- Tripathi, P., Dubey, N. K., Banerji, R., & Chansouria, J. P. N., (2004). Evaluation of some essential oils as botanical fungitoxicants in management of post-harvest rotting of citrus fruits. *World J. Microbiol. Biotechnol.*, 20(3), 317–321. doi: 10.1023/B:WIBI.0000023844.80464.59.
- Varma, J., & Dubey, N. K., (2001). Efficacy of essential oils of *Caesulia axillaris* and *Mentha arvensis* against some storage pests causing biodeterioration of food commodities. *Int. J. Food Microbiol.*, 68, 207–210.

- Verma, R. S., Rahman, L., Verma, R. K., Chauhan, A., Yadav, A. K., & Singh, A., (2010). Essential oil composition of menthol mint (*Mentha arvensis*) and peppermint (*Mentha piperita*) cultivars at different stages of plant growth from Kumaon Region of Western Himalaya. *Open Access J. Med. Aromat. Plants*, 1(1), 13–18.
- Vishwakarma, S., et al., (2019). L-menthol-based xanthate mediator for RAFT polymerization of vinyl acetate. *J. Macromol. Sci. Part A*, 57(299–309), 12. doi: 10.1080/10601325.2019.1691457.
- Vivek, S., Nisha, S., Harbans, S., Devendra, S. K., Bikram, S., & Raghbir, G. C., (2009). Comparative account on GC-MS analysis of *Mentha arvensis* L. ‘corn mint’ from three different locations of North India. *Int. J. Drug Dev. Res.*, 1(1), 1–9.
- Weller, S., Green, R., Janssen, C., & Whitford, F., (2000). *Mint Production and Pest Management in Indiana* (p. 103). Purdue Pesticide Programs, Purdue University Cooperative Extension Service, Bulletin.
- Yadav, Y., Kumar, R., Kumari, A., Vishuddha, N., & Verma, S. K., (2019). Effect of Herbicides on dry matter accumulation, fresh herbage yield, oil yield and profitability of Japanese mint (*Mentha arvensis* L). *J. Pharmacogn. Phytochem.*, 8(2), 49–53.
- Zachariah, T. J., & Leela, N. K., (2006). Volatiles from herbs and spices. In: *Handbook of Herbs and Spices* (pp. 177–218). Elsevier.
- Zhang, L., et al., (2015). Antibacterial activity and mode of action of *Mentha arvensis* ethanol extract against multidrug-resistant *Acinetobacter baumannii*. *Trop. J. Pharm. Res.*, 14(11), 2099. doi: 10.4314/tjpr.v14i11.21.



**Taylor & Francis**

Taylor & Francis Group

<http://taylorandfrancis.com>

## CHAPTER 2

---

# Neem-Drug Cabinet of Mother Nature

MOUMITA MALAKAR<sup>1</sup> and DEBASHIS MANDAL<sup>2</sup>

<sup>1</sup>*Department of Horticulture, Central University of Tamil Nadu, Neelakudy, Thiruvarur, Tamil Nadu, India*

<sup>2</sup>*Department of Horticulture, Aromatic and Medicinal Plants, Mizoram University, Aizawl, Mizoram, India*

---

### ABSTRACT

Neem (*Azadirachta indica*) resides to the family Meliaceae, well-known for its medicinal importance since time immemorial. Its contributions towards human civilization and culture are known to all generations. By habit it's a fast growing, evergreen, arborescent tree having strong highly branched trunk. Its tropical origin facilitates its cultivation in the Indian subcontinent. Major number of world's population keen to gain the medicinal importance of neem tree since it is easily available and cheapest source of wide array of active ingredients employed in medicinal products. According to World Health Organization (WHO) 80% population of developing countries trusts on natural medicines for their primary health care. It is also familiar as 'the wonder tree' and 'nature's drug store' owing to its immense ethnomedicinal, domestic, therapeutic, and agricultural significances. Almost all plant parts exclusively seed oil, bark, leaves, and its other purified products are quite potent to treat the most fatal disease like cancer which has been validated by several pre-clinical research reports during last decade. Wide range of phytochemicals (>60) including steroids and terpenoids have been obtained from neem. The isolated and purified crude bio-active compounds possess anticancer, antitumor, immunomodulatory, and apoptotic impacts which are effective properties against various fatal diseases and their respective

molecular mechanisms. Among numerous chemical compounds, Azadirachtin (AZ) ( $C_{35}H_{44}O_{16}$ ) is a key component. Genetic diversity study with aid of various advanced biotechnological tools (e.g., DNA-based markers like RAPD, AFLP) can furnish many worthy information especially will be useful to make relationship between their relatives.

## 2.1 INTRODUCTION

Meliaceae is the family of *Azadirachta indica* (neem). It is native to dry forests of South and Southeast Asia. 'Azadirachtin,' major phytoconstituent available in neem seed kernel contains notable pesticidal property, the root cause of its huge acceptance towards public. The concentration of bioactive compounds in neem leaves, bark, and fruit pulp are comparatively less than seeds. It's a vital component in agroforestry system for its multifunctionality. It is a medium to large stature tree (approx. 20 m in height). It has its adaptability to grow in varied soils and climatic conditions but preferably in acidic clay soils. Collaterally, it can also thrive well in soils having pH of 10. Congenial range of temperature is between 15 and 45°C with annual downpour of 750–1,000 mm. In India, it grows in tropical dry areas up to an elevation of 1,200 m. Among various establishment measures for neem plantation 'Stump Planting' is the most commercial one while seed plantation can be also opted but its low viability is the major hindrance. Neem seeds lose their viability within a month of storage. Neem tree starts to bloom in the month of April and within 80–120 days of flowering fruits start to attain maturity. This tree is not totally free from pests and diseases. Among range of post-harvest products produced from neem plant neem seed oil and neem seed cake are most vital whereas the former one used popularly as therapeutic oil and latter one as organic manure. Its kernel contains about 30–40% oil, which has the similar range of uses as that from other TBOS (therapeutic behavioral on-site). Removal of bitter constituents from its seed oil and cake broadened their use using recent advanced processing technology. The wood is strong and can be used for furniture, implements, and construction (Balaji, 2017).

The multifaceted use and medicinal importance of neem had been also mentioned in 'Charak-Samhita' and 'Sushruta-Samhita' considered as root of Indian System of natural treatment (known as 'Ayurveda'). In Sanskrit it has secured its name as 'SarvaRogaNivarini' (meaning 'the curer of all ailments') for its unique, versatile medicinal attributes (Bhuiyan et al., 1997;



Shrivastava & Swarnkar, 2014). In rural areas of Indian sub-continent, neem twigs are often used as chewing stick for having many active substances. Neem tree was pervaded all over the globe especially in South East Asia, Australia, South America and East and Sub-Saharan Africa took place by different esteemed Indian emigrants. Its potential to cure range of ailments influenced them to carry neem plant with them at their destination. But during the reign of Europeans in Indian subcontinent, the use of neem tree for theological purposes was totally prohibited while laterite was most acclaimed for its day-to-day use. Along with its therapeutic properties it has also enacted vital role in Indian agriculture, for example, after colonial's era the use of neem cake (scrap after oil extraction from neem seeds) as fertilizer and pesticide in sugarcane field was heightened during 1930s. IISc, Bangalore in 1920s first started to explore various possibilities of neem-based products and had taken initiatives to commercialize neem oil and cake. Many research investigations had been performed also by researchers during early 60s to isolate key active ingredients liable to its insecticidal properties and its successive use against major crop pests. Neem plant can control locust disturbances as reported by German entomologist in 1920s in Sudan, neem leaf extracted oil can cause insect sterility or inhibit egg-laying while seed borne 'azadirachtin' can interrupt metamorphosis of insect larvae. Hence, all these endorse the efficacy of neem plant against diversified pests. Thus, neem oil found great value as an organic-based pesticide. Barring the native tropical countries (like Myanmar, India, and Bangladesh), neem trees now colonized in Old World Tropics. Arid meteorological conditions favor neem trees' luxurious growth. Hence, Northern Australia, Sub-Saharan Africa (especially Ethiopia) and South-East Asian countries, are quite rich in neem germplasm. In Jijiga, Gambella, Amhara, Tigray region and afar – naturalized groves of neem are frequently found but the native people (Ethiopian) owing to lack of knowledge unable to use this 'Drug Reservoir' appropriately. But now-a-days, rural people, especially of Amhara, use leafy parts of neem for healing malaria and diabetes diseases. Neem oil could be effectively used in cosmetics, bath soap and also as a source of biofuel which prove its versatility and environment-friendly nature. Apart from this, its waste could be used as organic fertilizer, a value-added product. The history of neem endorses its significance during Harappa and Mohenjo Daro civilizations of India although it was successfully utilized for wide range of household purposes around 5,000 years ago also. Medical practitioners of those ancient era also used neem products for our traditional ayurvedic treatments owing to its huge therapeutic value. After that, its name was successfully enrolled in traditional Indian medicine

system as found in Indian scriptures of medicine – the ‘Charak Samhita’ and ‘Sushruta Samhita.’ Many internationally acclaimed organizations promote neem allied research owing to the growing fame of this ‘wonder tree.’ It was hugely accepted by Western countries for its therapeutic value and not having any side-effects. To unveil and tap the miraculous power and potential of neem tree researchers worked day and night, so that the derived benefits can be used commercially. The fascinating spiritual background story behind the neem tree can reveal that drops of heavenly nectar bestowed all curative properties in neem tree. Another story revealed that Amrita (Ambrosia known as elixir of immortality) passed by Garuda (part bird and part human; a creature of Hindu mythology) to the paradise poured on neem tree caused the miraculous effect while other mythological story narrated that Amrita once sprinkled by ‘Indira’ (the celestial kind) gave birth of neem tree with numerous therapeutic attributes could serve as beneficial for human civilization than ‘Kalpa-Vriksha,’ the wish fulfilling tree. It is saturated with its divine origin as muttered in the stories of ancient history of India. Not only this it was believed that afforestation using neem tree guaranteed a passage to heaven. It is also considered as ‘Dhanmantri’ (the Aryan God of medicine). Devi ‘Sithala’ (the Goddess of smallpox) resides in the neem tree as believed and scripture in ancient literatures (Retrieved from: file:///F:/PROJECT/neem/Neem\_history\_Neem\_and\_India.htm). The stalwart like Mahatma Gandhi (during 1869 to 1948) also gone through the neem diet (boiled neem leaf chutney) to resolve health issues. Neem oil massage paired with neem shampoo washing can effectively lower down the dandruff and hair fall problem. Barring enormous curative properties, neem oil and leaf extracts can be also used for cosmetic purpose which bestowed its name as ‘the village pharmacy.’ Neem oil can moisturize dry skin while quite effective for the treatment of acne and even boils. The remarkable contribution in of neem poultices could prove its potency in veterinary medicine as it can help to heal sores in elephants and horses. The Unani texts, which originated with Muslim doctors in Byzantine Greece, also recommend neem as a cure-all that is free of costs. The Unani recommends neem for inflammatory conditions, arthritis, gas, worms, wounds, leprosy, bile or phlegm, white patches on the skin, blood purification and as an antiseptic (Miah & Bhattacharjee, 2013).

India is famous for conserving large number of medicinal plants which show a synergistic effect in our ecosystem and are useful for human beings (Serrone et al., 2015) and plants besides being environmentally friendly. Climate change has some significant role on changes in biochemical profiling of this tree. More clearly, the content and types of secondary

metabolites can also vary according to adverse environmental conditions. These secondary metabolites have pharmacophoric and medicinal properties which are characterized as phenols, terpenes, alkaloids, and hence have used against human and plant pathogens besides their use in many antimutagenic and anticancerous studies. So, it could be deduced that the antimicrobial constituents of neem can effectively control human pathogens like *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Bacillus pumilus*) and plants pathogens (*Pythium*, *Rhizoctonia*, *Fusarium*, *Sclerotinia*, *Dematophora*). *A. indica* from as early as the Vedic times has held the interest of phytochemists all over the world for its rich source of alkaloids and terpenoids. It also possesses multitudinous biological activities like antiallergic, antidermatic, antibacterial, antifungal, and anti-inflammatory. Neem plant parts like roots, bark, leaves, flowers, seed, and fruit possess biological activities against human and plant pathogens. Girish & Shankara (2008) reported neem as 'Arista' – a name derived from Sanskrit which is considered the reliever of sickness hence called 'Sarbarogaribarini.' It is also used as a spermicidal and mouth wash. Oil that is extracted from neem leaves, seed, and bark has a broad range of antibacterial properties (both gram [+] and gram [-]) against *Mycobacterium tuberculosis* and some Streptomycin resistant strains. In Himachal Pradesh, the neem plant is grown in low hills. Shah et al. (2006) reported that this medicinal plant can be a source of drugs for having chemical moiety acts as hub of novel biomolecules.

'Heal All,' 'Panacea of All Diseases,' 'Divine Tree,' 'Village Dispensary' and 'Nature's Drugstore' are the colloquial names of neem tree due to the acknowledgement of its wide array of utilities in European and Chinese 'Materia Medica,' and 'Unani' (world's best ayurveda system). Extracts derived from various plant parts of neem are used to heal ophthalmia, leprosy, fever, tuberculosis, and malaria while as pediculicide, anthelmintic, diuretic, contraceptive, insecticide, febrifuge, antifeedant, parasiticide, emmenagogue, and antiseptic it is used since time immemorial. Neem extracts are conventionally used for curing purpose through oral, vaginal, and topical application. The semi-mature stems of neem are used by rural dwellers as natural tooth brush whereas its juice is used for some skin disorders and leaves to shoo away insects (Maithani et al., 2011). Among countless folk uses of neem tree, the followings are considered to be most vital:

- Bark, seeds, flowers, and leaves are used for making neem based medical formulations.

- Several neem formulations are popularly used in India and Pakistan for dental care.
- To cure acne and keep radiant skin, neem oil is indispensable.
- To treat chicken pox, patients are advised to lie down on neem leaves for getting its medicinal effect.
- To get relief from range of afflictions (pain), use of neem botanicals could be impactful as declared in ayurveda (Unani).

## 2.2 VERNACULAR NAMES

‘Dogon yaro’ (Nigerian), ‘Kohomba’ (Sinhala), ‘Neem’ (Hindi and Bengali), ‘Indian lilac’ (English), ‘Vaypum’ (Tamil), ‘Nimba’ (Sanskrit and Marathi), ‘Tamar’ (Burmese), ‘Nimtree’/’Vepu’/’Vempu’/’Vepa’ (Telugu), ‘Azadirakhta’ (Persian), ‘Bevu’ (Kannada), ‘Pokoksemambu’ (Malaysia), ‘Margosa’/’Neeb’ (Arabic), ‘Arya-Veppu’ (Malayalam) and ‘Mwarobaini’ (Swahili – East African language; semantically ‘the tree of the 40’).

## 2.3 ORIGIN AND DISTRIBUTION

### 2.3.1 ORIGIN

It is believed that neem tree had been originated either in the forest of Karnataka (South India) or in the dry island forest of Myanmar (Burma). But still controversies are there concerning its exact place of origin. According to Roxburgh (1874) India is considered as the primary center of origin for neem tree. In consonance with this information Brandis (1921); and Jacobs (1961) reported Upper Myanmar (Irrawaddy valley, upper region of Prome) as its place of origin. Its natural distribution range extends up to Shivalik hills in India (Koul, 2004).

### 2.3.2 DISTRIBUTION

1. **Nativeplaces:** Sri Lanka, India, Myanmar, Pakistan, Senegal, Thailand, Churu (state of Rajasthan), Indonesia
2. **Exotic:** Antigua, Argentina, Cuba, Gambia, Jamaica, Barbados, Mauritania, Nepal, Mexico, Kenya, Madagascar.

The established neem groves are now available in 30 countries worldwide while in India alone 18 million neem trees have been estimated. This expansive distribution in pan world (South-East Asia, East and Sub Sahelian

Africa, Australia, and South America) of neem tree by Indian emigrants is due to its wide array of utilities, easy-quick growing (usually attain 20 feet height in three years), wide climatic adaptability especially in arid condition (maximum temperature 120°C and annual downpour as low as 18 inches) and long productive phase (life span around 150–200 years). Few patches of neem plantation are also reported in USA and Europe (Venugopalan & Navaratnam, 2013). In different states of Malaysia (Perlis, Penang, Langkawi, Sungai, and Kedah) and China (Pan Zhi Hua and Sichuan province) neem trees are found in abundant. Neem tree was first introduced in China (at the hot river valley of Yunnan) from India in 1995 by researchers of Chinese Academy of Forestry (CAF) and now China is globally announced as hub of neem raw materials since ~4,00,000 artificial neem plantations have been established in Yunnan province. Then, again in 1997 from Africa, South-East, and South Asia neem trees had brought in China by CAF research groups and in 1998, commercial promotion on neem plantation was initiated. The existing topography and meteorological conditions favored thrive of neem trees in Yunnan province while CAF had also significant role for the dissemination of standard neem cultivation technology. Intensified cultivation and research on neem is reported since last two decades. Kenya is now going to be an emerging hub of neem raw materials. In Ghana and Nigeria (situated in West Africa) neem trees are cultivated extensively now. Earlier, they considered neem as shade providing plants but its global fame especially as medicinal tree ultimately influences its establishment. Now, to treat malaria, in all African countries neem formulations are widely used while the demand of neem trunks as firewood (in Ghana) is also quite high. The stretch of neem plantations have aided to keep the ecological equilibrium by interrupting the Southward spread (from Somalia to Mauritania) of Sahara Desert. For its bountiful importance, colloquially neem tree is known as ‘Green Gold’ in Africa and ‘Independence Tree’ in Senegal (name given by Senegal Neem Foundation [SNF]). In Saudi Arabia (in plains of Arafat), largest (10 sq. km. Areas with 50,000 neem trees) roadside neem plantations done by a Saudi philanthropist have been reported for the shade and comfort of pilgrims. Neem trees were introduced in last decade in Caribbean and Haiti too (Venugopalan & Navaratnam, 2013).

The major production of neem in India is found in 3 states principally, i.e., Andhra Pradesh (AP), Tamil Nadu (TN) and Karnataka. Several states of India (UP, WB, Gujrat, Bihar, Andhra Pradesh, Maharashtra, Delhi, Tamil Nadu and Orissa) now become the leading producer of neem. Mahabubnagar, Jedcherla, Shadnagar, Nalgonda, Bhongir, Vikarabad, Pargi, Tandur,

Warangal, Jangaon, Hyderabad, Jogipet, Zaheerabad, Ongole, Khammam – these districts of AP; Salem, Dindigal, Madurai, Thene, Thirunamalai – these districts of TN; and Bangalore and Tumkur districts of Karnataka meet the entire domestic need of neem and its value-added products (Anon, 2012b). Mahabubnagar, Medak, Nalgonda, Warangal, Khammam, Ananthapur, Chittoor, Vizianagaram, Srikakulam – these districts of AP also secured highest rank for neem fruit production (Anon, 2012a). Different districts of TN viz. Virudunagar (34.34 ha), Thoothukundi (22.80 ha), Tirunelveli (11.53 ha), and Madurai (9.72 ha) occupy notable territory for neem cultivation while other 2 states occupy 21.58 hectares of land for neem plantation. Maithani et al. (2011) reported about the existence of 20 million neem trees in India. It's an evergreen tree but during February-March leaf fall starts. Blooming takes place during January-March in Southern parts while bit later in Northern parts. At the juvenile stage, neem trees need full sunlight condition. Their frost susceptibility has been confirmed by Arid Forest Research Institute (AFRI), Jodhpur. Balaji (2017) stated that 'coppicing' and 'pollarding' – as plant rejuvenation strategy could be adopted in case of neem while propagation using root suckers could be an alternative of conventional seed propagation.

## **2.4 MARKETING AND TRADE**

Neem fruits and seeds prices range from Rs. 50–150/– and 20–250/– kg<sup>-1</sup>. Major importers of these are Karnataka, Tamil Nadu and Kerala used for production of bio-pesticides and oil extraction. The fruiting age of neem is 35 yrs. It turns fully productive in 10 yrs. So, the normal production of neem is 30–50 kg of fruit/tree/annum (Balaji, 2017).

### **2.4.1 NEEM PRODUCTS TRADED IN THE WORLD MARKET**

Value added products of neem are traded throughout the world. The leading producers of these products are India, United States and Australia.

#### **2.4.1.1 NEEM OIL IN INDIA**

'Neem oil' is a vital value-added product. It is traded throughout the world but still neem trees growing in India and the production of neem oil are impropportionate. The estimated yield quantity of neem kernels (principle oil

source materials) in India is 3.5 million tons, hence, approximately 7,00,000 tons of neem oil could be produced but the actual production is ~1,50,000 tons out of which 34 tons of 3,00,000 INR worth are exported.

In 1920, first neem soap and in 1929, neem toothpaste were manufactured by 'the Calcutta Chemical Company.' After that, 'Sunida Exports' and 'Plasma Power P Ltd.' – these 2 Indian private companies had launched variety of neem products like neem-based food supplements, agricultural, and veterinary products, neem oil, soap, neem leaf granules, neem soap nut powders, neem cake and neem bark powders. Among these value-added products, neem leaf granules, bark powders and soap nut powders are sold in the market at high price rate of US\$ 1.8 kg<sup>-1</sup>, US\$ 1.26 kg<sup>-1</sup>, and US\$ 4.68 kg<sup>-1</sup> respectively while 'Plasma oil' has not only high domestic demand rather exported throughout the world (like Netherlands, UK, Hawaii, New Zealand, Panama, Switzerland, etc.) (Retrieved from: <http://www.calchemico.com>).

There is different methods like 'Ghani' and 'Expeller' used for neem oil yielding while whole fruit, developed seed and kernels – these 3 raw materials are basically used for neem oil yield. The percentage of oil yield also varies according to the method of crushing like in 'Expeller' method of crushing, 4–6, 12–16, and 30–40% of oil yielding is possible from whole fruits, developed seed and kernels respectively while in 'Ghani' method only neem kernels are appropriate for yielding 25–35% of oil; rest 2 types of raw materials are inappropriate for this method (Anon, 2012c).

The extract of neem seed was first commercialized by 'Thermo-Trilogy Corporation' (a USA based company) as non-edible product being approved by U.S. Environmental Protection Act (EPA), 1985. 'Margosan-O' – a neem-based product used to check leaf miners and gypsy moths in plants (trees and shrubs), manufactured by Vikwood Botanical but the patent, registration, and technology of this product was purchased by W.R. Grace in 1988. Later, its formulation was changed before successful greenhouse crops application. 'Neemix' is 'azadirachtin' (0.25%) (a chemical constituent of neem extract) based product got approval from U.S. EPA in 1993 to use on agricultural crops in Florida. Later, a collaborative approach had been established between Florida and India for commercial cultivation of neem tree and production of 'Neemix' product. This product can effectively control pests (army worms, leaf miners and aphids) in citrus and range of vegetable crops. W.R. Grace also purchased the patent of 'Neemix' and got registration after changing its formulation by increasing the concentration of azadirachtin from 0.25% to 4.5% (18 times more concentrated) in 1994 and launched in the agricultural market. The upgraded formulation of 'Neemix'

made it easy to-handle and to-package. 'Thermo Trilogy Corporation' is the new name of 'Biopesticide Group of Companies' which was earlier owned by W.R. Grace. In 1996, W.R. Grace sold his company. 'Thermo Trilogy' then renamed the product 'Margosan-O' into 'Neemazad.' Among several neem-based products manufactured by 'Thermo Trilogy,' key are broad spectrum fungicides to check agricultural and horticultural diseases and mite populations. These fungicides basically contain hydrophobic extract of neem oil (application rate 5.46 lb US gallon<sup>-1</sup>) to control 'greasy spot,' '*Alternaria* leaf spot' and 'mildew' diseases, 'post bloom fruit drop' disorder and mites (Retrieved from: <http://www.neemfoundation.org>).

Barring these companies, 'Agro Logistic Systems,' Inc. Of USA also produce diversified neem-based products which are as follows:

#### 2.4.1.2 AGRONEEM

This product contains 0.15% of azadirachtin (AI) and neem biomass [neem lipids] @ 15%. In other words, it's an emulsified product. Around 1 ton of seeds (raw material) are needed for 220 l of oil yielding (approx. 22% oil recovery). According to Tinghui et al. (2001), the yield of oil from the same amount of seeds could be enhanced up to 314 l by using the proportion of oil and emulsifier@ 70:30 (tentative return could be \$22,400 ton<sup>-1</sup>). These compositions made this product as an effective pest management tool (2–3 liters hec<sup>-1</sup> is an effective dose rate). Key merits of this product are its non-toxic, biodegradable, eco-friendliness (obtained registration by U.S. EPA) while it could be used also as anti-feedant, insecticide, insect repellent and growth regulator. Its compatibility with broad array of fertilizers, fungicides, and insecticides is noticeable (Singh et al., 1996, 1999). It is currently manufactured by Agro Logistics Systems and price range of 32oz (1 quart) plastic bottle is ~\$400-\$600. In Australian market this product is available at comparatively cheap rate of \$15–\$18 lit<sup>-1</sup>.

#### 2.4.1.3 NEEM CAKE

The key ingredients of this product are NPK. It's commonly known as 'Soil supplement.' It enhances the porosity of the soil which consequently increases the nutrient uptake and improves soil structure. It could also be used to control soil borne nematodes. Marz (1989) reported that the price



rate of 50 lb. bags of neem cake was around \$300-\$600 (data is based on the Australian market survey).

#### 2.4.1.4 *AGROMORE FOLIAR*

It is basically used as plant growth promoter which enhances the crop yield. This foliar fertilizer is equipped with phosphorous (Ph), magnesium (Mg) and zinc (Zn). The chemical constituents of neem help in rapid absorption of essential nutrients which in turn assist in photosynthesis. Several authors (Marz, 1989; Tinghui et al., 2001) had reported about its poor market price and selling percentage. The approximate price of 12 bottles of this product is \$192 which supports the above report.

'Neem Aura Naturals' is a new product (like 'Toothpaste,' 'Wild-Craft Neem Oil,' 'Organic Neem Leaf,' 'Neem Cream,' 'Neem hand and Body Lotion,' 'Neem Herbal Spray,' 'Organic Neem Leaf Extract,' and 'Neem Soap') crafted using leaves of organically grown neem trees.

Another, popular neem oil-based products' manufacturer is 'Bio Neem' company of New South Wales, Australia. This company produces highly concentrated emulsified 'Neem Seed Oil' which contains 3,000 ppm of key active ingredients of neem. It is highly effective to control broad spectrum of pests. The price ranges from \$13 to \$154 (Retrieved from: <http://www.bion neem.aunz.com>). Several other neem-based products like 'Neem Facial Moisturizing Lotion,' 'Neem Shampoo' for all hair types, 'Neem Soaps,' 'Cold Pressed Neem Oil,' 'Neem Toothpaste,' 'Neem Seedling,' and 'Neem Meal Cake' are manufactured, and exported by Neem Co-operative established in 1996 in Northern NSW, Australia (Retrieved from: <http://www.nor.com.au>). For further flourishing of neem bio-business and before large-scale capital investments in this field, qualitative, and quantitative evaluations of the products are quite vital. The products must be economical; otherwise unrealistically high price may lead to the commercial failure. The annual turnover was of US \$125 million year<sup>-1</sup> by Thermo-Trilogy' in the year of 2001 (Tinghui et al., 2001).

#### 2.4.1.5 *NEEM POTENTIAL IN CHINA*

The huge annual loss (ranged from 16–30 million tons) of agricultural products due to diseases and insect-pest infestations were evident in China since 1980. Even after applying the farm chemicals (quantity ~2,50,000

tons) sufficiently, the loss ranged like the above. Several cons like non-environmentally friendly nature, toxicity, and growing resistance against broad array of biological threats of using the chemical fertilizers made the Chinese Central and Local Governments bound to ban them to use which paved the position of bio-chemicals. China started to cultivate neem tree in Waning County of Hunan province and use neem-based products from 1986 but increased developmental activities have significantly reduced the neem populations. Again in 1995, new neem plantations were started by Luxi Biological Resources Development (a research institute) situated in Yunan province. This institute also produced 1 million micropropagated plantlets during 1999 to strengthen neem cultivation in Yunan province and other prefectures. It had received various governmental aids in this regard too. The provincial government had also aided by US \$2.8 million funding to develop a processing factory for neem named 'Yunan Guangming Neem Development Company' (YGND) which targeted to produce 2.8 million seedlings and their subsequent plantation at 3,300 hectares of land per year. Currently, a joint venture between YGND and Australia is about to made for azadirachtin extraction and production of neem-based pesticide formulations. The organic fertilizers are now receiving much attention by several government, research, and business organizations. China's first neem-based formulation was neem oil (raw materials used neem seeds; imported from India, Thailand, and Burma) with 0.3% azadirachtin, released during 1997 and was successfully registered by the Ministry of Agriculture of China. This product also received much appreciation from other relevant ministries owing to its qualitative attributes. Yunan and Hainan based few companies (Xinkian Eco-Science and Technology Company) are also in the process of establishing few neem processing factories. They are targeting to produce 6,70,000 liters of 0.3% azadirachtin preparation and 250 tons of neem oil per annum. The popularization of neem-based value-added products are for its diversified application such as:

- Application as biopesticides at cheap rate which in turn may enhance the export rate and quantity of horticultural products for 'Green' production strategy.
- Serve as source of income for rural people.
- Conducive climatic condition for abundant production and environmental benignity of products.
- Used as non-toxic, natural, cost-effective contraceptive, also potentially impacting the population control.

#### 2.4.1.6 EXPORT POTENTIAL

Neem is known for its versatility. In one side, it could be used for pharmaceutical purposes while on other side, as forest produce. It is one of the forest species from which diversified value added products are produced and exported. These reasons compulse many countries (like Japan, USA, Netherlands, Germany, and France) to establish research laboratories exclusively for neem (Retrieved from: [http://agritech.tnau.ac.in/banking/PDF/Forestry%20Wasteland\\_Neem.pdf](http://agritech.tnau.ac.in/banking/PDF/Forestry%20Wasteland_Neem.pdf)) but even after having abundant neem wealth in India, very little systematic research have been made. ‘Azadirachtin,’ the key biologically active constituents extracted from neem seeds (yield rate 3 g kg<sup>-1</sup> of neem seeds), has huge export potential but in India, millions of neem trees are abandoned and grow in scattered way. Hence, to reap the export benefits at the best, several initiatives by government organizations (ICAR, ICFRE, NGOs, and Agricultural Universities) should be adopted for organized and commercial cultivation of neem.

## 2.5 COMPOSITION AND USES

### 2.5.1 CHEMISTRY OF NEEM

Among uncountable number of chemical constituents (like meliacin, gedunin, nimbolides, nimbidin, nimbin, salanin, valassin, etc.) obtained from neem, terpenoids, and azadirachtin are of special interest. The former one is obtained from different plant parts while the latter one from neem seeds. Azadirachtin is the most well studied compound (types A-K) and employed for preparing almost every neem formulation (e.g., pesticides, medicine, etc.) as active ingredient. The chemical compounds of neem are accumulated and synthesized at secretory cells, found to be present in seed kernels. Barring, terpenoids, and azadirachtin, 20 sulfurous compounds had been also identified by Lokanadhan et al. (2012). Along with these, tignic acid are also responsible for the distinctive odor of neem crushed seeds and oil while biologically active substances cause bitter taste of neem oil. The oil recovery percentage from neem seed kernel is 30–50%. It contains different active chemical ingredients, together known as ‘triterpene’ or ‘limonoids.’ Azadirachtin, salannin, nimbin, and meliantriol are 4 best limonoids used exclusively for pesticidal and insecticidal properties (Mondal & Mondal, 2012; Hashmat et al., 2012).

Different plant parts of neem are rich in chemical compounds like neem bark contains tannins (gallic acid), catechin (epicatechin), diterpenoids (margolone, margolonone, isomargolonone), polysaccharides (GlaGlb, GllaGlla), and glycoside. All these bio-chemical constituents possess antibacterial, antitumor, antiulcer, and anti-inflammatory properties. 'Ethanol extract' of neem has hypotensive, spasmolytic, and diuretic properties while its 'Chloroform extract' has inflammation activity and 'Aqueous extract' possesses anti-complement property and act as an immune stimulant. Overall, all these chemical substances obtained from neem bark are analgesic in nature.

Cyclic trisulfide, tetra sulfide, flavonoid, quercetin – these bio-chemical constituents are available in neem leaf and possess anti-fungal and hyperglycemic features. Furthermore, 'Methanolic extract' of neem is antipyretic in nature and has anti-plaque property while the 'Aqueous extract' of neem leaf is hypoglycemic in nature, possesses antiulcer, antifertility, and antiviral properties and also stimulates the immune system. 'Acetone extract' of neem is anticarcinogenic in nature. Barring, these activities, these neem leaf constituents also aid to heal eye problem, epistaxis, intestinal worms, leprosy, anorexia, biliousness, skin ulcers and also act as CNS depressant.

'Nimbidine,' 'Nimbine,' 'Nimbolide' and 'Az' – all these chemical compounds are available in neem oil and contain anti-inflammatory, antipyretic, antifeedant, anti-malarial properties. These can also cure leprosy and intestinal worm issues.

To heal the urinary disorder, piles, epistaxis, intestinal worm, diabetes, and leprosy, neem fruits are infallible since it contains phytosterols (Maithani et al., 2011).

### **2.5.2 ACTIVE INGREDIENTS**

Different plant parts of neem tree are the sources of range of bio-active compounds. Among these, azadirachtin (AZ) ( $C_{33}H_{44}O_{16}$ ), a steroid like tetranotriterpenoid (limonoid) is the key compound. It was first isolated from neem seeds by Butterworth & Morgan (1968) from *A. Indica* while the detailed insecticidal properties and complete elucidation of chemical structure of AZ were reported by Chopra (1928); and Kraus et al. (1987) for the first time. Isman et al. (1990) stated the correlation between the AZ content and the degree of insecticidal activity which determines the efficacy of neem oil. Several authors (Schmutterer & Zebitz, 1984; Chirathamjaree et al.,

1997; Sidhu & Behl, 1996) found the impact of eco-geographical conditions and origin of individual species on the total yield of AZ. Based on the minor variations in chemical structure of AZ, it is classified into Azadirachtin-A-Z (different analogs of AZ). AZ-A is the major component while AZ-B (3-tigloylazadirachtol) occupies 15% of the total concentration of AZ and AZ-C to AZ-Z analogs is found to be available in least quantity (Rembold, 1989). One more AZ analog, i.e., AZ-K had been isolated from neem seeds by Govindacharu et al. (1992) while Ramji et al. (1996) found a novel tetra-terpenoids compound, i.e., 1-epiazadirachtin from the same source. Other species of Meliaceae family also contain AZ (Morgan & Thornton, 1973). Schmutterer (1990) mentioned about the other bio-active compounds like salannol, salannolacetate, 3-deacetylsalannin, azadiradion, gedunin, nimbinen, salannin, 23-dihydro-23p-methoxyazadirachtin, 1-tigoloyl-3-acetyl-1-methoxyazadirachtin, deacetylnimbinen, 14-epoxyazadiradion, 3-tigoylazadirachtol, meliantriol, 14-apoxyazadiradione, vilasinin derivatives, azadiradione, deacetylazadirachtinol, 6-0-acetylnimbandiol, and 3-deacetylsalannin obtained from oil of neem seed kernels. Siddiqui et al. (1986) isolated isonimocinolide and nimocinolide from fresh neem leaves and later (Siddiqui et al., 1988) alkanes from desiccated leaves while Chavan (1984); and Chavan & Nikam (1988) recovered non-terpenoidal constituents, saturated hydrocarbons, coumarins, and isocoumarins from juvenile, whole neem twigs. The bark, whole fruits, heartwood could be also the source of key biocidal components but extensive investigations are required in this field.

### **2.5.3 MINERAL CONSTITUENTS OF NEEM KERNELS**

Magnesium@ 0.29–0.46%, phosphorous@ 0.24–0.38%, calcium@ 0.2–0.4% and chemically enriched neem oil@ 40% could be obtained from neem seed kernels summoned from different agro-ecological conditions.

### **2.5.4 USES**

Zoonotic food and waterborne pathogens are becoming resistant to antibiotics and thus is an environmental problem. Neem is a viable option in 21<sup>st</sup> century for its great use in pest management, environmental protection and medicine. Neem leaf extract increases the blood platelet and white blood cell counts which work effectively against the ZIKA virus and fortifies the immune

system of a patient. Gum degeneration problem could be also solved using tooth paste containing neem formulations. Scalp condition problems respond to treatment with neem shampoo and conditioner. The antibiotic principles are the defensive mechanism of these plants against different pathogens. It has a role in anti-inflammatory, antiarthritic, antipyretic, hypoglycemic, antigasteric ulcer and antitumor activities (Paul et al., 2011). Neem formulations may be used in antibiotics as an adjuvant to get synergistic effect and to treat opportunistic infections which are the cause of death in HIV infected patients. Wheat and paddy crops are glazed with neem-based urea (a source of  $N_2$ ) could give significant yield. It facilitates Vit N, P, and K uptake. The health promoting effect of neem is for its antioxidant richness. Due to chemicals like nimbin, nimbidin, nimbolide, and limonoids of neem plant parts, it is of significant importance in agricultural fields and horticultural sciences (Dohroo & Gupta, 1995). Quercetin and  $\beta$ -sitosterol, polyphenolic flavonoids possess antifungal and antibacterial properties. *Staphylococcus aureus* and *Pseudomonas aeruginosa* are sensitive to neem plant extract. *Candida albicans* was inhibited more often by neem plant extract (Dohroo et al., 2016).

Insecticidal properties of neem extracts had been elucidated by several authors but Balaji et al. (2017) emphasized the ways of its action. They revealed that the extracts don't perish insects directly but it alters their life cycle (like feeding and breeding incapability, inability to metamorphose, etc.) which in turn make their action very subtle.

Neem oil (as foliar spray) and litter compost (as green manure) is used extensively in rice cultivation to control various pests while neem residues (obtained after oil extraction from seeds) by soil application could enrich the soil organic matter and nitrogen content by inhibiting nitrification. Grounded neem leaves could be also used to store grains and horticultural seed components. To check fleas and sucking pest populations in rice field, neem bark and root in powdered form are also used while neem bark and root extracts could also act as nematicide (Lokanadhan et al., 2012).

#### 2.5.4.1 THERAPEUTIC USES

Wide array of neem formulations are well-known for its therapeutic uses. For example, oral intake (as tonic) by adult females of neem bark extract (using hot water) could work as emmenagogue, extracts containing anthraquinone fraction prepared using dehydrated neem blooms, fruits, and leaves

could be used for leprosy, to heal hysteria (a psychological disorder), fever, and deep wounds hot water extract of neem flower and leaf could be effective, for diabetic patients dried neem flowers work fabulously, to heal piles, dermatological issues (itching, eczema, etc.) and ulcers hot water extract of dried neem fruits is infallible, as insecticide, anthelmintic, and purgative the whole plant extract (using hot water) is useful, to treat gonorrhoea, leucorrhoea, and dyspepsia neem leaf and flower juice are very useful, to soothe boils use of neem leaves as poultice is effective, for ring worm infestation and to treat eczema neem leaf paste is unparalleled, to control nasal worm infestation use of neem leaf juice (as nasal drop) is impactful, for throat inflammation treatment steam inhalation of neem bark has gathered praise, to restore the appetite and cure intermittent fever, neem decoction could be used, for long term storage purpose of woollens neem leaves could be used, and to treat filariasis oral intake of neem bark juice is very effective (Chatterjee & Pakrashi, 2010; Kabeeruddin & Mufradat, 2007). A neem fruits, flowers, and root-based formulation is prepared by using the stated neem parts, 'Triphala' and dried ginger to treat common flu. Several authors (Hashmat et al., 2012; Chatterjee & Pakrashi, 2010) recommended the intake of neem flower decoction for general debility convalescent. To get rid of oral bad odor, use of juvenile neem twigs is in age old practice (Siddiqui et al., 1988; Chavan, 1984; Kabeeruddin & Mufradat, 2007; Tandon & Sirohi, 2010).

#### 2.5.4.2 *NEEM AND ITS INDUSTRIAL USES*

In cosmetic, pharmaceutical, ayurvedic drug, fertilizer, animal-feed, textile, and rubber industries the uses of neem value-added products (especially neem oil) are mentioned worthy. Neem oil and grounded neem leaves is the major ingredient for the preparation of several neem-based commercial formulations like nail polish and oil, shampoos, conditioners, and face creams. Among these products, neem shampoo is highly effective to control hair lice problem. Neem toothpaste to care about the oral-hygiene and dental issues has been acknowledged by European countries (Aneesa, 2016).

#### 2.5.4.3 *AZADIRACHTIN*

It is the key bio-active ingredient of neem. It is the outright killers of insects and pests.

#### 2.5.4.4 FUNGICIDES

Fungicidal properties of neem extracts are also evident. Its action is far significant as compared to the synthetic fungicides.

#### 2.5.4.5 ANTIBACTERIALS

The use of neem oil as anti-bactericide (e.g., *Staphylococcus* sp., *Salmonella* sp., etc.) is authenticated by different research institutions.

#### 2.5.4.6 ANTIVIRAL AGENTS

Several empirical information(s) on antiviral properties neem extracts are available. Since time immemorial, the efficacy of neem leaf paste to heal small pox and chicken pox viruses have well been acknowledged. Rubbing of neem leaf paste directly on infected skin usually give better results (Balaji, 2017).

#### 2.5.4.7 DERMATOLOGICAL USES

For range of skin problems like itching, dry, and scaly skin, redness of patchy skin, etc., neem oil is infallible. It's considered as wonder drug to cure psoriasis.

#### 2.5.4.8 NEEM AS PESTICIDE

The roles of neem-based products to control pest infestations are well known due to the presence of 'Azadirachtin' component. Its organic nature is the key reason of its huge popularity and acceptance as compared to the synthetic pesticides since the harmful impacts of synthetic ones on soil microorganisms, plants, and human beings are well evident. The upward trend of uses of natural or organic pesticides, is motivating different research communities to dig up its range of potency (Anis Joseph et al., 2010; Venthanayagam & Rajendran, 2010). Barring, the efficacy of this herbal pesticide against broad array of germs and bacteria, another key merit is their non-residual nature.



#### *2.5.4.9 DENTAL TREATMENTS*

The use of neem twigs as ‘Organic Toothbrush’ is an age-old practice in India, in fact, it is endorsed by dentists for the efficacy to heal periodontal diseases.

#### *2.5.4.10 MALARIA*

Ayurvedists, Charaka (during 2000 BC) and Sushruta (during 1500 BC) had stated the potential of neem formulations to cure malaria, a fatal disease in Africa and India. To date, every medical practitioner also recommend neem-based pills as antimalarial drug.

#### *2.5.4.11 PAIN RELIEF AND FEVER REDUCTION*

The potency of neem products as cheap source of analgesic, antipyretic, and anti-inflammatory is evinced since long ago.

#### *2.5.4.12 CONTRACEPTIVE AGENTS*

The bio-active components like DK-1, DNM-5, and DNM-7 are effective contraceptive agents, isolated from neem oil by DIPAS (Defense Institute of Physiology and Allied Sciences). The oral administration of these components especially DNM-7 is highly impactful for abortion after implantation. ‘Sensal’ is a neem-based abortifacient used popularly in India.

#### *2.5.4.13 VETERINARY MEDICINE*

Various neem-based products are also useful to prevent wide array of live-stock diseases. This aspect could further prosper neem’s usages.

#### *2.5.4.14 COSMETICS*

For facial cream, body oil, nail polish and other cosmetics, the uses of neem oil and leaf powder are infallible.

#### 2.5.4.15 LUBRICANTS

The non-drying nature and prolonged shelf life of neem oil influenced its uses as greasy agent. To grease cart wheels, the use of neem oil in rural India is most abundant.

#### 2.5.4.16 FERTILIZERS

The potency of neem fertilizers for growth enhancement of sugarcane (cash crop) and various vegetables and rice (food crops) has been well proven. The most common form of using neem fertilizer is neem cake, prepared using the neem seed residues after oil extraction. Neem cake, also synonymously known as eco-friendly ‘Soil Conditioner,’ ‘Nutrient Supplement,’ and ‘Growth Promoter.’ In neem cake manure maximum 10% of moisture, 2.5% of water-soluble organic nitrogen, 13% of total ash and 5% of acid insoluble ash contents are found. The limonoid content of neem helps to check root nematodes and other pest (white ants) populations in diversified agronomical and horticultural crops. The broadcasting of raw neem leaves or its powdered form (as bio-fertilizer) in flooded rice field of Karnataka helps to improve the qualitative and quantitative parameters. It basically meets the demand of macro nutrients.

#### 2.5.4.17 NEEM USED AS MANURE

The necessity of using manures in soil is for the necessary improvement of soil structure, that's why the use of animal feces are very common. The soil structure is improved by the uptick of  $N_2$ , Ph, S, K, and Ca content. The use of neem-based manure could effectively contribute for these. The use of this environmentally benign and bio-degradable manure not only boost plants' growth by providing almost all macro and essential micro-nutrients but also totally harmless for soil microflora and plants. The integrated use of neem-based extracts (like blending with urea, FYM or sea weed) could fetch best outcomes. To finetune its efficacy, cold pressing or solvent extraction methods could be adopted. Its cost-effective nature, capacity to eliminate denitrifying soil bacteria and antifeedant traits also equally contribute towards its worldwide acceptance as manure (Lokanadhan et al., 2012).

#### *2.5.4.18 NEEM AS UREA COATING AGENT*

To enhance the efficacy of urea, neem products are used as coating agents (either in liquid or powdered form), especially it makes the denitrifying bacteria non-functional (growth and activities are seized) and uplifts the soil NPK content. In one hand, it minimizes the degradation of urea in the soil and control range of pests (caterpillars, beetles, leaf hoppers, borer, mites, etc.), on other hand. Antifeedant, antifertility, and anti-growth – these 3 are chief properties of neem urea coating barring its other multifaceted qualities (Lokanadhan et al., 2012).

#### *2.5.4.19 NEEM AS SOIL CONDITIONER*

Neem seeds are used as raw materials for this purpose. The powdered neem seeds are sprinkled during plantation followed by immediate irrigation, vital for its easy penetration into the soil and absorption by plant roots. As a safe organic soil conditioner, it has gained fame internationally (like USA, UK, and Australia). It gives wholesome protection to the plants. The multifunctional approaches of this product immensely help in soil fertility enhancement (Lokanadhan et al., 2012).

#### *2.5.4.20 NEEM AS FUMIGANT*

To eradicate the household, storage, and crop pests, the usefulness of neem products are indescribable. In pan world, its usages have impressively increased for its non-toxic nature (100% natural) which can effectively control human deaths led by consumption of synthetic pest fumigants. Neem based fumigant can deter oviposition, mating, and growth of insects while its antifeedant properties influence the death of pests and also disallowed the resistance development among pests. Azadirachtin – the active ingredient of neem formulations is liable to disrupt the growth cycle of insects, pests, fungi, etc. Its full proof usefulness is acknowledged throughout the world (Lokanadhan et al., 2012).

#### *2.5.4.21 NEEM TREATED UREA AND COAL-TAR TREATED UREA*

These formulations could be made by blending urea with grounded neem seed or neem cake (size 2 mm). Urea could be mixed with gypsum and neem cake@ 5:4:1 to enhance N<sub>2</sub> efficiency. Coal tarred urea (100 kg of urea, 1 kg

of coal, 1.5 liters of kerosene and a handful of powdered neem cake) could be used as soil basal dose (Lokanadhan et al., 2012).

#### **2.5.4.22 OTHER PRODUCTS**

##### **2.5.4.22.1 Resin**

‘Neem glue’ has recently fame as a food additive and is in use in South Asia. Exudate released by the wounds made in bark is used as glue, generally not used as substitute of polysaccharide gum.

##### **2.5.4.22.2 Bark**

The coarse fiber of neem bark used to make ropes in rural India. Not only that, neem barks contain 14% of tannins which is equal to the amount obtained from conventional tannin yielding tree (e.g., *Acacia decurrens*)

##### **2.5.4.22.3 Honey**

The high qualitative values and rich flavors of neem nectars contribute to the apiary industry.

##### **2.5.4.22.4 Neem Fruits**

The dry neem fruits after smashing into water are useful to cure piles, urinary diseases, leprosy, intestinal worms and other cutaneous diseases.

##### **2.5.4.22.5 Soap**

Neem crude oil is an essential ingredient for soap manufacture industries due to its cost-effective nature. Basically, it is used prolifically in coarse laundry soap manufacturing industries.

##### **2.5.4.22.6 Neem Leaf Tea**

It is another value-added product of neem prepared by using processed neem leaves. The health benefits of ‘Neem Leaf Tea’ have surpassed its bitter taste and consequently, have been accepted by health-conscious people

(Source; <http://www.keralaagriculture.gov.in/html/bankableagriprojects/fw%5Cneem.htm>).

### **2.5.5 IMPACT OF NEEM PRODUCTS ON INTEGRATED CROP MANAGEMENT (ICM) AND PEST MANAGEMENT (IPM)**

Its eco-friendly, non-toxic, and pesticidal properties have been already discussed earlier. Several value-added products of neem could play impactful roles for ICM and IPM. Its uses in IPM helps to check the oviposition of pests and insects, affects their life cycle while the antifeedant properties of neem-based products hinder the resistance building capacity. The environmentally benign nature of these products has replaced many synthetic pesti- and -insecti-cides. Along with its non-harmful nature towards the target pests (chiefly sucking and chewing insects) and also the other biological predators of target pests, its water-soluble nature is highly beneficial for plants (nourishment) and soil (conditioning). Thus, it is widely used in ICM system. In several cash (e.g., rice, pulses, cotton, oil seeds, etc.) and horticultural crops (e.g., broad ranges of fruits, vegetables, flowers, etc.) production system, it is used widely. Its popularity as 'bio-pesti'-and-'insecti-cides' and 'organic growth component' in current, commercial agriculture systems is noteworthy. 'Azadirachtin' (belongs to the organic molecule class namely 'Tetranortriterpenoids') – the active ingredient of neem extracts, is the key ingredient of insect-pest repellent because of the structural similarity of it with 'Ecdysones' (a type of insect hormone aids in metamorphosis of insects from larva to pupa stage). This active ingredient inhibits the growth of young insects and pests (Lokanadhan et al., 2012). Different plant parts and seed extracts which are used for the formulation of neem-based insecticides have been tabulated below.

#### **2.5.5.1 MODE OF ACTION**

The neem-based products not directly bring the cidal effects on insects or pests but they act as fecundity suppressor, oviposition deterrent, antifeedant, and growth inhibitors (Schmutterer, 1988, 1990). The mode of action as antifeedant is like that the presence of bio-constituents (e.g., salaninand-melandriol and azadirachtin) choked the peristaltic movement of insects' esophagus and alimentary canal causes reverse peristalsis which reduce the desire for food (leaves which are treated with neem products). Moreover,

anyhow after ingestion of neem treated plant parts, they lose their mating wishes as side effects and as a consequence, their life cycle gets hampered. As an oviposition deterrent, it blocks the egg laying potential of females. To protect seeds, they're usually treated with neem kernel powder or neem oil. The unique property of affecting on juvenile hormones of insects or pests of neem extracts makes them suitable as insect/pest growth retardant (Lokanadhan et al., 2012).

#### 2.5.5.2 ANTIFEEDANCY

The chemical activity as antifeedant of neem products had been studied in several phytophagous like Isoptera, Hemiptera, Orthoptera, Lepidoptera, Coleoptera, and Diptera (Mordue & Blackwell, 1993). According to several authors (Chapman, 1974; Schoonhoven, 1982), the feeding inhibition in insects is due to the chemical signaling. Either the increased amount of phagostimulants or the stimulation of few specific deterrent cells or both of these mechanisms causes antifeedancy. They also stated that chemoreception act as 'Primary Antifeedancy' while loss of appetite due to toxic effects of AZ-containing extracts act as 'Secondary Antifeedancy.' But the degree of effects depends on the quantity and concentration of active ingredient (AZ) consumption.

#### 2.5.5.3 GROWTH REGULATION

The role of AZ and several other neem-related products as Insect Growth Regulators (IGRs) are known. The application for larval growth inhibition could be by topical application or oral ingestion or through injection. The impact of treatments depends on type of insects/pests genus. As for example, the oral ingestion treatment found impactful in Orthoptera, Hemiptera, Lepidoptera, and Diptera (Ascher, 1993; Mordue & Blackwell, 1993; Schmutterer, 1988, 1990). IGR efficacies also depend on plant parts. For example, to inhibit the growth of diamond-black-moth (*Plutella xylostella* L.), neem seed extract is highly effective as compared to the extracts of leaves, bark, twigs, and wood as suggested by Tan & Sudderuddin (1978). Ascher (1993) reported that the secretion of PTTH (Prothoracicotropic Hormone), morphogenetic peptide, and allatotropins from brain-corpora cardiacum complex are stopped which results in reduction of juvenile hormone titer and modify hemolymph ecdysteroid.

#### 2.5.5.4 *FECUNDITY SUPPRESSION AND STERILIZATION*

Several authors (Ascher, 1993; Mordue & Blackwell, 1993; Schmutterer, 1988, 1990) had studied the fecundity issues of Orthoptera, Hemiptera, Heteroptera, Coleoptera, Lepidoptera, Diptera, and Hymenoptera. AZ-induced inhibition in the release of PTH and allatotropins not only decreased the growth rate of insects but also negatively effect on their fertility, fecundity, and ovary development since AZ modifies ecdysteroid hormone (it regulates vitellogenesis). The sperm production (Shimizu, 1988), sexual behavior, hormonal disbalance, and release of sexual pheromones (Dorn et al., 1987) also get affected by AZ treatment.

#### 2.5.5.5 *OVIPOSITION REPELLENCY*

As suggested by Schmutterer (1988, 1990); and Dhar et al. (1996), the neem treated oviposition sites effectively cause oviposition repellency especially in Coleoptera, Lepidoptera, and Diptera.

#### 2.5.5.6 *BLOCKING THE DEVELOPMENT OF VECTOR-BORNE PATHOGENS*

To block the development of triatomine vectors, single treatment using AZ was very useful as reported by Mulla & Su (1999). This treatment caused the complete blockage of *Trypanosoma cruzi*.

#### 2.5.5.7 *CHANGES IN BIOLOGICAL FITNESS*

The biological fitness in the sense of reduced lifespan (Wilps, 1989), high mortality rate (Dorn et al., 1987), flying inability (Wilps, 1989), immunodepression (Azambuja & Garcia, 1992), enzyme inhibition, interrupted biological rhythms (Mulla & Su, 1999), and reduced nutrient absorption rate (Wilps, 1989) had been also evident to be lowered by AZ treatment. The toxic effect of AZ treatments, affect the mitosis cell division of midgut epithelial cells, ovarian, and testisidal cells and epidermal cells.

## 2.6 BOTANY AND TAXONOMY

### 2.6.1 MACROSCOPIC DESCRIPTION

#### 2.6.1.1 TREE

It is a tropical, evergreen tree attains the height of 12–18 meter and width of 1.8–2.4 meter, possesses clear, erect trunk with a spreading crown of 20 meter in diameter. Under the congenial condition, it can attain the height of 20 feet within three years of time. The wide adaptability of growing make them suitable to grow almost in all places with tropical climatic condition but arid to semi-arid conditions especially the places which experience little downpour (18 inches) and high heat (120°F), are also suitable for its growing. It is well known for its long life (Maitgani et al., 2011).

#### 2.6.1.2 LEAVES

Leaves are compound, range from pinnate to imparipinnate (8–9 leaflets generally found), texture glabrous, alternate phyllotaxy clustering near the distal end of branches, rachis (15–25 cm long and 0.1 cm thick) and petiole (2–7 cm long; very short lengthwise) are subglabrous in texture, leaf shape ovate to lanceolate (size range 3.5–10 x 1.2–4 cm), glossy in texture, margin serrated, exstipulate, leaf base unequal, apex acuminate, yellowish-green in color with bitter taste and indistinct odor.

#### 2.6.1.3 STEM BARK

Its bark is rusty gray in color although the hue and thickness depend on the age of tree and *in vivo* collection site. Its rough textured and fissured (longitudinal in nature) bark has its characteristic odor and bitter taste. The inner surface of its bark is laminated with yellowish foliaceous, fractured structure. The gum (commonly known as ‘East Indian Gum’) secretory tubercles (color ranges from gray to dark reddish brown) usually scatter throughout the trunk’s bark surface. The specific gravity of timber ranges from 0.56–0.85 proves its heavy nature (Balaji, 2017).

#### 2.6.1.4 FLOWER, FRUITS, AND SEEDS

The color of delicate, minute, axillary neem tree flowers (blooming season early summer, i.e., March–April) ranges from white to pale yellow. It



possesses honey like fragrance to attract pollinators (honey bees). Inflorescence is drooping panicle type (length up to 25 cm). Botanically, neem fruits are drupe type while anatomical studies revealed the existence of thin epicarp, pulpy mesocarp and cartilaginous endocarp. Morphologically, fruits are ovoid to ellipsoidal in shape with blunt end. This olive sized (1–2 cm long) fruits (green colored during immature stage and yellow at full ripe stage) possess some garlic like odor along with oil. Fruits are basically 1 seeded (shape ovoid/spherical). Histologically, it has found that the Testa is thin and consists of a shell and a kernel (number ranges from 2–3). Seed kernels are the key source of oil. Fruiting (season April to August) starts usually after 3–5 years and could yield 110 lbs of medicinally and botanically significant oil (Parotta, 2001; Ross, 2001).

## **2.6.2 MICROSCOPIC DESCRIPTION**

### **2.6.2.1 LEAF MIDRIB**

Anatomically, it has found that the midrib of neem leaf has thick cuticle on any one side followed by 4–5 layered collenchyma cells and stele (consists of 1 crescent shaped vascular bundle at lower position and 2/3 small sized bundles at upper position). Leaflets are outlined along with the midrib in convex manner. The other tissues are parenchymatous, thin walled with secretary cells and calcium oxalate crystals in rosette form are also found to be evident. These crystals are also present in phloem parts which are surrounded by non-lignified fiber strand (Maithani et al., 2011).

### **2.6.2.2 LAMINA**

It is dorsiventral in nature. Anatomically, lamina is composed of thin walled, tangentially elongated, single layered palisade cells (cell ration 3–4.5) and multilayered (5–6) spongy parenchyma cells. Leaf surface is covered by thick cuticle. Especially, at ventral surface of leaf anomocyticstomatas (stomatal index on ventral and dorsal surface 13–14.5 and 8–11.5 respectively) are found to be present. The internal ground tissue is traversed by veins and also calcium oxalate crystals (in rosette form) (Maithani et al., 2011).

### **2.6.2.3 STEM BARK**

This part is very thick in nature. It's composed of multilayered, regularly spaced stone cells which are in sandwiched condition with phloem elements

contain brown contents. The older barks are made up of dead elements of secondary phloem (cork cambium). The stone cells alternately present in between the irregular, tangential compressed band of cork tissues. In between the gaps of cork tissues, multilayered (3–5 layered) fiber groups are often found to be present. These intervened with thin-walled phloem elements and also frequently compressed with thick-walled cells (Maithani et al., 2011).

#### 2.6.2.4 INFLORESCENCE

Neem possesses indeterminate, thyrus type inflorescence (30 cm long (approx.)). The bisexual, actinomorphic, minute, pentamerous, sweet scented, white to pale yellow-colored flowers are axillary in position. Bracts are minute and caducous (drop off early and easily) in nature, calyx lobes are ovate shaped and thin textured, puberulous internally, aestivation imbricate. Corolla aestivation is imbricate, spatulate, polypetalous in nature and ciliolate internally. Petals are oblanceolate in shape (Parotta, 2001; Ross, 2001).

#### 2.6.3 TAXONOMICAL CLASSIFICATION

- Kingdom: Plantae
- Order: Rutales
- Suborder: Rutinae
- Family: Meliaceae
- Subfamily: Melioideae
- Tribe: Melieae
- Genus: *Azadirachta*
- Species: *indica*

### 2.7 CULTIVATION

Generally, 400–1,200 mm of annual rainfall is needed for its successful thrive but <400 mm rainfall is also moderately sufficient for neem growing although ground water level play some role in this case. Tropical to subtropical climatic condition is conducive for its growing. Temperature range between 21 and 32°C is optimum although it can tolerate more high temperature but not too low temperature like <4°C as its detrimental for plant health (cause untimely leaf shedding and death).

### **2.7.1 SOIL**

Wide ranges of soils (clayey, saline, and alkaline) except black cotton soil are suitable for neem trees. Hard calcareous and stony saline soils are also suitable for its growth to some extent. Low ground water level as well as inundated land is almost suitable for neem trees. But for its luxurious growth well drained, sandy soil with 6.2–7 pH is optimum. To change soil pH (from acidic to neutral) neem tree plays some vital role due to its calcium (Ca) mining properties while alkaline nature of shredded neem leaves also found useful for soil acidity neutralization.

### **2.7.2 PRICKING**

Seedlings of 7–10 cm tall with 15 cm long tap root system are appropriate for transplantation while 45 cm seedling height is found best for transplantation in dry areas to tide over the adverse meteorological conditions. Good soil health and weed free land is suitable during this operation.

### **2.7.3 PLANTING TECHNIQUES**

Direct seed sowing, polypot growing and root-shoot cuttings – these are the most common planting techniques adopted for neem plants. The 1<sup>st</sup> method may be carried out by dibbling, broadcasting, line or ridge-furrow and aerial sowing methods. These methods are useful for commercial production of neem. The 2<sup>nd</sup> planting method is generally used in agro-forestry or Silvi pasture while the 3<sup>rd</sup> one is useful for road side avenue plantation. Moreover, the selection of planting methods also largely influenced by biotic, edaphic, and climatic factors and also by the purpose of growing neem populations. For root-shoot cutting method, pit planting using 20–45 cm tall seedlings are used. Sometimes, stump plantings also show good results.

### **2.7.4 ENTIRE OR POLYPOT PLANTING**

The required details for this method are as follows:

- Seedling height: Generally, 20–25 cm but in Tamil Nadu condition 45 cm height is best to cope with drought stress condition.
- Planting time: Early of monsoon.

- Pit size: 30 cubic cm.
- Optimum spacing: 3 x 3 mtrs.
- Leaf and root tips pruning found beneficial under Nagpur (Maharashtra district) condition.

### **2.7.5 PLANTING ROOT-SHOOT CUTTINGS**

The required details for this method are as follows:

- Cuttings Specification: 1–1.1-year-old seedlings with 2.5 cm shoot and 2.3 cm roots are used while in Tamil Nadu, 2-year-old stumps with 12 months old root are used for getting better growth.
- Planting Time: Off time of rainy seasoning crow bar holes.

### **2.7.6 FARM FORESTRY PLANTATIONS**

The required details for this method are as follows:

- For block plantation, spacing of 5 × 5 m to accommodate 400 trees ha<sup>-1</sup> are usually followed.
- Wider spacing of 7 × 7 m to accommodate 200 trees ha<sup>-1</sup> also practiced but depends on availability of land and target of plantation.

### **2.7.7 CARE OF YOUNG PLANTATION**

During the establishment stage (1<sup>st</sup> year), 2 times weeding year<sup>-1</sup> is usually effective but from 2<sup>nd</sup> year onwards, one-time weeding year<sup>-1</sup> is sufficient. Strip weeding is generally followed for young plantation while mechanical weeding could be continued up to five years of plant age.

### **2.7.8 PLANTATION GROWTH**

Fast growth is being noticed up to 5<sup>th</sup> year of plant age while from the successive years it gets slow although the growth rate significantly depends on quality of soil and climatic factors. For example, in Karnataka 6.58 m height and 68.1 cm girth size are attained within 10 years of growth while in UP, the neem trees grown under alkaline soil could attain the height of 1.7 m and 2.64 m after the 1<sup>st</sup> and 2<sup>nd</sup> seasons of plantation, respectively. Within

five years, neem trees could attain 4 m of height while only 10 m of height it could attain after 25 years of growth. The range of girth size increment is 2.3–3 cm. Provenance trial at AFRI (Arid Forest Research Institute), Jodhpur during 1992 and in Bangkok during 1993 had been conducted. The outcomes epitomize that genetic factors play vital role for neem trees growth, hence, investigations on genetic improvement of neem are vital. Furthermore, root suckers could also affect the plant growth (for example, 210 days old sucker plantation could help neem tree to attain 65.7 cm of height).

### **2.7.9 PROPAGATION**

Neem tree could be propagated both by sexual (by seeds) and asexual (cuttings) means. Rainfall, wind, and also birds/bats could be the agents of seed dispersal. Generally, asexual mode of propagation is encouraged due to recalcitrancy of neem seeds.

#### **2.7.9.1 SEXUAL PROPAGATION**

##### **2.7.9.1.1 Seed Harvesting**

According to Nagaveni et al. (1987), neem fruits immediately after shedding on ground should be summoned for necessary processing in order to avoid the loss of seed viability. Other authors (Chaturvedi, 1993; Gunasena & Marambe, 1998) had stated that before the dropping of mature fruit, it could be collected at immature stage (yellowish-green color) also followed by depulping and drying under shade for consecutive 2 days. This can lower down the chance of losing seed viability as well as risk of fermentation of closed cotyledons and high germination percentage. Moreover, the time of harvesting and seed maturity affect the AZ and oil content. In green fruits collected after 20, 30, and 40 days after anthesis (DAA) found devoid of any AZ content while in yellow fruits which were collected after 60 DAA found to contain 0.112% of AZ. 0.051% of AZ had been also evident in green fruits collected after 50DAA (Rengasamy & Parmar, 1994). According to Johnson et al. (1996), except AZ content, limonoid content also vary depending on seed maturity. They reconfirmed the relation between seed maturity and AZ content (10 mg of AZ per gm of seed kernels of green newly ripened fruits could be obtained).

### 2.7.9.1.2 Seed Storage

Neem seeds are intermediate type (Berjak et al., 1995; Bharadwaj & Chand, 1995, Mohan et al., 1995). Ambient to low temperature storage conditions could enhance the seed viability up to 6 months without affecting the germination rates (Singh et al., 1997). According to these authors, drying under shaded condition for about a week could increase its viability by reducing the moisture content up to 11%. Gamene et al. (1996) studied the storage behavior of neem seeds and found that at 55 and 75% level of RH, 70% of germination capacity could be obtained after 2.1 months of storage period while at lower (32–25%) and higher (95%) level of RH, the germination percentages were deteriorated noticeably. They also found that 20–30°C temperature is optimum for neem seed storage while Sacande et al. (1998) recommended 10–15°C temperature and 10% moisture content but low (<3°C) and high (>50°C) storage temperature could affect the viability seriously. Sacande et al. (1998) mentioned several reasons for complex storage behavior of neem seeds like:

- Low moisture content (10%) and low temperature (10°C) enhance the sensitivity of neem seeds.
- Imbibitional stress during storage at 8% moisture content also enhances its sensitivity.
- Higher level of temperature range and moisture content could induce metabolic stress condition.

Generally, the range of neem seed moisture content is between 10 and 24%. The types of neem seeds, i.e., orthodox, intermediate, and recalcitrant had been documented by several authors endorse the obvious variations of neem seed moisture content during the storage. According to Chamberlain et al. (2000), the sources of seeds also affect the seed moisture content. For example, the seeds namely *A. indica* var. 'Siamensis' summoned from Kenya, the optimum seed moisture content was 10% while for the seeds of the same variety from Myanmar, 20% moisture content found optimum. 'Siamensis' seed variety collected from Thailand and Malaysia showed best viability performance at 24% moisture content during storage. Thus, it corroborates the earlier statement. It had found that the storage of shade dried seeds with 30% moisture content and without pulp in earthen pots could retain 62% of viability for 90 days (Surendran et al., 1992). In fact, storing of seeds in airtight containers reduce the seed respiration rate and aid to maintain the amount of storage resources which influence the viability

status of seeds (Jindal et al., 1994). Dod et al. (1997) found that neem seeds (9% moisture content) could be preserved successfully for 2 months in cloth, paper, polyethylene, and polylined jute bags under ambient condition but best outcome had been obtained in cloth bag storage. During storage, AZ content may also vary as reported by Yakkundi et al. (1995). They found the variations in AZ content of seeds which were preserved at room temperature and under ambient RH for 1 month. The AZ content varied 68% in dark and 55% in light as compare to the original content as it is proved by HPLC analysis. Johnson et al. (1996) also found the variation in AZ and salanin content during storage period of 180 days.

### **2.7.9.1.3 Seed Germination**

Maturity status of seeds affects the germination rate as reported by Bharati et al. (1996). They found the higher germination percentage in semi-mature (greenish yellow) seeds as compared to the young (green) and over mature (yellow) ones. Singh et al. (1995) found that the germination rates of freshly harvested seeds are more as compared to the stored ones. Pre-soaking of seeds may also have some effect on germination rate. Kumaran et al. (1996) found that imbibition of seeds in 2%  $\text{KH}_2\text{PO}_4$  solution could enhance shoot length, leaf number and germination percentage while 1%  $\text{KH}_2\text{PO}_4$  solution could give maximum root length. Several other authors (Hegde, 1993; Fagoonee, 1984) found improved germination rate due to soaking of de-pulped seeds in normal water from 30 mins to 3 days. Deshelling of seed coat may also enhance the germination rate as suggested by Radwanski & Wickens (1981).

### **2.7.9.2 VEGETATIVE PROPAGATION**

Asexual or vegetative propagation using 'Grafting,' 'Root Cuttings,' 'Stem Cuttings' and 'Stump Cuttings' is useful for getting genetically identical offspring although now-a-days tissue culture technique had got huge admiration for mass multiplication.

#### **2.7.9.2.1 Macropropagation**

Neem propagation using 'Stump Cuttings' is popular in Ghana, and Winneba. Generally, healthy, mature twigs or stem cuttings (length: 2.5 cm) with root mass (length ~23 cm) are the best propagation materials (Childs, 1999) for this method usually collected from two-year-old plants. To boost the root

emergence from cuttings use of PGRs like IAA and IBA also played some significant role. Sivagnanam et al. (1989) stated that treatments using aforementioned PGRs are effective for mist propagation and can cause easy rooting within 135 days of planting. Coppice shoots can more efficiently response in IBA treatment than stem cuttings prepared from woody trunk (Tomar, 1998). According to Palanisamy et al. (1998), IBA@1000 ppm is most effective for increasing number of roots and root biomass while a positive correlation between rhizogenesis and emergence of shoots using stem cuttings had also been noted. Kamaluddin & Ali (1996) found some positive impact of auxin and IBA (0.2% and 0.4% solution) on root emergence from cuttings and increased leaf area of leaves which were developed from emerged shoots. Endogenous auxin level may also influence the rooting rate from stem cuttings (Palanisamy & Kumar, 1997). Gupta et al. (1998) found that 800 ppm of IBA was optimum for air layered cuttings.

#### **2.7.9.2.2 Micropropagation**

For neem micropropagation, young leaf segments are most commonly used explants (Puri, 1999; Narayan & Jasiwal, 1985; Rao et al., 1988). Tissue culture technique is in vogue since 1980s or 90s for producing healthy, disease-free seedlings. Joshi & Thangane (1996) used woody explants of neem for *in vitro* propagation while Drew (1993) used stem nodal sections as explants component. In both cases, successful development of roots and shoots had been obtained. The survival rates of plantlets under open field condition were high when axillary buds and embryos were used as explants as reported by Thiagarajan & Murali (1993); and Joarder et al. (1993). Venkateswarlu (1999) revealed that biochemical content viz AZ and other seed attributes could be obtained as identical as vegetatively propagated plantlets in case *in vitro* generated plantlets. But further investigations are needed to get better performance of micropropagated plantlets under open field condition as recommended by Bahuguna (1997). Several authors (Sarkar & Datta, 1986; Ramesh & Padhya, 1988; Stephen et al., 1998; Allan et al., 1994; van der Esch, 1999) had also targeted tissue culture methods for easy isolation of limonoids and AZ.

#### **2.7.10 HARVESTING AND YIELD**

Ovoid shaped neem fruits (size 1–2 cm, contain resinous pericarp and 1 kernel [weight 0.2 g approx., fat content ranges from 30–50%]) are used for



multifaceted purposes which determine its importance. According to Shinde & Biswas (2011), maximum 30 kgs of neem fruits per tree could be obtained after 10 years of growth of neem tree. For the harvesting quantity of neem fruits, UP (55.7%), TN (17.8%), and Karnataka (5.5%) ranked first. Healthy trees could also yield 10–15 kgs of fruits on 5<sup>th</sup> year onwards. According to Kumar & Gupta (2002), in a fully grown neem tree up to 50 kgs of fruits could be also harvested annually. The price of neem fruits are usually Rs. 5 kg<sup>-1</sup>. Good management practices could significantly enhance the yield of fruits (Balaji, 2017). The value-added products of neem fruits are seed coat (4.5% of total weight of fruits), husk (25% of total weight of fruits), and kernel (23% of total weight of fruits). Kernels also yield 2.5 kgs of neem oil and 3 kgs of neem cake (Subbulakshmi et al., 2012).

### **2.7.11 ECONOMICS OF CULTIVATION**

Spacing 5 m × 5 m could accommodate 400 plants ha<sup>-1</sup> and the tentative cost for the plantation is Rs. 2070.00 ha<sup>-1</sup> although the cost depends on area of plantation.

#### **2.7.11.1 FINANCIAL ANALYSIS**

The cost:benefit ratio of neem-based products are very economical as evident by financial analysis ([http://agritech.tnau.ac.in/banking/PDF/Forestry%20Wasteland\\_Neem.pdf](http://agritech.tnau.ac.in/banking/PDF/Forestry%20Wasteland_Neem.pdf))

### **2.7.12 POLICY SUGGESTIONS**

- Scientific cultivation.
- Train the farmers pertain to package practices of neem.
- Research has to be strengthening in the area of new variety suitable to all factors.
- Pest and disease control measures to increase the yield.
- Formation of Farmers Producers Company/Farmers Group to increase the price of the product.
- Government sponsored loan facilities are needed to develop, establish, and support the neem farmers for getting good price.

- Farmers having organized plantation of tree crops may be given with carbon credit by the State/Central government. It provides some encouragement to the farmers for establishing neem populations.

## 2.8 MICROFLORA AND DISEASES OF NEEM

The insect-pest repelling potential of neem makes them eligible to use for insect-pest management practices. Range of bioconstituents available from fruits, seeds, and leaves are proved to be effective to inhibit some kind of fungal growth, to restrict viral infection, etc. Despite these, few threats have been identified in neem which is as follows:

### 2.8.1 INSECTS

Broad array of insects have been found to attack all neem plant parts (Schmutterer, 1990; Tewari, 1992; Ciesla, 1993; Boa, 1995) but among them few serious threats have been summarized below:

#### 2.8.1.1 LEAF DEFOLIATORS (SCIENTIFIC NAME: SOLENOPSIS SPP.; COMMON NAME: FIRE ANTS)

It causes severe damage to the juvenile leaves of neem. Its prevalence is found in Andhra Pradesh (India), and also in Central and South America. Except *Soleonopsis* spp., few other species like *Ascotisselenaria*, *Eurema* spp. are also cause damage to the immature leaves (Chamberlain et al., 2000).

#### 2.8.1.2 STEM AND WOOD BORERS (COMMONLY KNOWN AS BEETLE)

Different species of beetles like *Apatemonachus*, *A. terebrans*, *Cydia* spp., *C. aurantiana*, *Hypsipyla* sp., and termites are liable to wood, stem, and shoot bore problems. Most vulnerable stage is the juvenile phase of plant growth. They easily attack the young shoots and in severe cases plants die also (Ciesla, 1993). In India, 55% death of neem plants caused for this reason (Madhavan & Gopi, 1990). In Haryana, shoot, and leaf borers cause 97.75% of young plant death (Chaudhary, 1997).

### 2.8.1.3 SUCKING INSECTS

According to Ciesla (1993), these insects belong to the Hemiptera and Homoptera order and parasitically dwell on neem plant (host) to take nutrition from leaves, branches, and stems. The common symptoms are desiccation injury of leaves and young shoots, defoliation, dieback of stem, etc. Not only it affects the flowering and fruiting of neem plants but may also lead to death due to severity of infestation. In India, *Helopterus antonii* (Common name: Tea mosquito) is a serious threat for neem trees and cause dried foliage and shoots. During sucking, this insect secretes a phytotoxic saliva which causes drying of plant parts (Madhavan & Gopi, 1990). *Aonidiella orientalis* (Oriental yellow scale) causes serious threat for young neem trees. Heavy infestation gives a burnt appearance to the plants. This species is found mostly in Africa and India (Schmutterer, 1998). *Pulvinaria maxima* (known as Neem Scale) mostly spotted in India causes drying of young shoots due to sucking sap by nymphs and adults and results in dieback of young shoots as reported by Tewari (1992). In case of heavy infestation, development of white patches in whole plant also occurs.

### 2.8.1.4 MITES (SCIENTIFIC NAME: PHYLLOCOPTES FRUCTIPHILUS KEIFER)

This eriophyid mite also attacks tender shoots and foliage and results in chlorotic, puckered, and desiccated leaves (Madhavan & Gopi, 1990; Tewari, 1992).

### 2.8.1.5 MOLLUSKS

Several authors (Tewari, 1992; Ahmed, 1998; Kumar et al., 1998) found 2 species of mollusks viz. *Laevicaulis alte* and *Macrochlamys indica* cause serious damages to the tender stem and shoots. Lack of sap results in desiccated and burnt appearance of plants. Heavy feeding of young leaves consequently make bald tree. Sometimes, they can also cause girdling at the root collar region. The prevalence of mollusks is abundant during monsoon season.

### 2.8.1.6 MAMMALS

Mammals like domestic goat, cows, red flanked duiker (*Cephalophus rufilatus*), Nigerian hare (*Lepus crawshayi*) pose notable problems especially for young neem trees (Browne, 1968).

## 2.8.2 DISEASES

They key sites of infections are leaves, stems, and roots. ‘Damping off’ (causal organism: *Rhizoctonia solani*), a serious disease for neem tree causes threatful damage to the seedlings. Around 20% mortality rate of seedlings had been reported in Dehra Dun (Ciesla, 1993). Maximum infection takes place during the transplantation and leads to heavy loss. ‘Leaf web blight’ (causal organism: *Rhizoctonia solani*) developed gray-brown spots on foliage while old and severe infestation allow the development of fungal hyphae. ‘Leaf spot’ and ‘Leaf blight’ (causal organism: *Colleototrichum gloeosporide*) also cause complete damage to the plants while ‘Powdery mildew’ (causal organism: *Oidium azadirachtae*) affects the mature and immature leaves threatfully. Several other bacterial strains like *Xanthomonas azadirachtii*, *Pseudomonas viticola*, *P. Azadirachtae*, etc., also cause leaf spot disease (Chakravarti & Gupta, 1975; Moniz & Raj, 1967; Mehrotra, 1990, 1989; Sankaran et al., 1986; Tewari, 1992; Uniyal & Uniyal, 1996). Brown (1968); and Tewari (1992) reported another disease namely ‘Pink disease’ of neem caused by *Corticiumsalmonicolor*. This disease is characterized by the formation and spreading of pink mycelia throughout the neem bark and wood. Severe infestation may also affect the heartwood. Furthermore, wilting, and blackening of shoots and foliage also happen as side effects. *Ganoderma lucidum*, the causal organism of ‘Root rot’ disease of neem, characterized by the formation of white, spongy root rot. It affects the health (defoliation, dieback of branches, chlorotic leaves, etc.) of whole neem tree (Ciesla, 1993). Some serious fungal diseases like ‘Shoot shot hole,’ ‘Twig canker’ (caused by *Phomajolyana*), leaf spot (caused by *Pseudocercospora-subsessilis*), ‘Blight and stem rot’ (caused by *Sclerotium rolfsii*), ‘Leaf spot and blight’ (caused by *Alternaria alternata*) are often found in neem tree (Singh & Raheja, 1996; Castellani & Mohamed, 1984; Sankaran et al., 1986; Mehrotra & Pandey, 1991).

*Aspergillus ochraceus*, *A. niger*, *A. flavus*, *Penicillium* sp., *Xylariaazadirachtae*, *Phomopsis azadirachtae*, *Fusarium oxysporum*, *Mycelia sterilia*, *F. avenaceum*, etc., are few neem seed mycoflora found (Verma & Srivastava, 1993; Tewari, 1992). According to Shenoj et al. (1996), total 77 endophytic fungal strains had been reported in the inner bark of neem.

### 2.8.2.1 PARASITIC PLANTS

Neem tree has been found to be a host plant for many other parasitic floras. As for example, *Tapinanthus* sp. found to dwell on neem tree in Nigeria

and sometimes cause its complete death while *Cassytha filiformis* (a semi-parasitic plant) found to be enough potential to kill a mature neem tree in Kenya as reported by Schmutterer (1998). In Indian continent and Solomon Islands, *Dendrothoe falcata* was often found to choose neem tree as its host plant (Ciesla, 1993).

### 2.8.2.2 NEEM DECLINE AND GENETIC IMPROVEMENT

This disorder is characterized by defoliation, development of chlorotic leaves, and emergence of leaves in clustered form at the branch tips. Due to this symptomatic appearance, this physiological disorder is often known as ‘Giraffe Necked Neem.’ It is mostly reported in some countries of West Africa (Ciesla, 1993). The reason of this physiological disorder is unknown but several authors (Ciesla, 1993; Thomsen & Souvannavong, 1994) had suspected that abiotic stresses (like insufficient soil moisture level, low genetic diversity and high nutritional competition) and cultural management practices (like soil sanitation, biotic stress management practices, etc.) may be few of the reasons. *Hitherto*, any bio-engineered neem varieties which are resistant to this physiological disorder or range of fungal or bacterial diseases have not been developed (Chamberlain, 1999) but growing of them at exotic places beyond their native places by provenance trials may aid in the development of resistance.

### 2.8.2.3 DIE-BACK DISEASE OF NEEM

Major sites of attack are leaves, twigs, inflorescence of neem. The occurrence of symptoms of die back (caused by *Phomopsis azadirachtae*) may appear on shoots and leaves of neem tree of any age, size, and height. This disease may also cause severe fruit losses which consequently lead to economic loss (Anon, 1997). Neem trees from Mysore region severely affected by this disease. Some effective control measures need to be adopted.

## 2.9 PROCESSING AND EXTRACTION

‘Decortication’ is the actual method used for the processing of neem fruits. Khadi and Village Industries Commission (KVIC) used decorticators and found it very useful. Decorticators (may be manual or power or mobile operated) provide 70% shell, and 25% kernel for seeds with pulp while 45%

**TABLE 2.1** Endophytic Fungi Isolated from Inner Bark of Neem (*Azadirachta indica*)

<b>Endophytic Fungi</b>	
<b>Ascomycetes</b>	<b>Hyphomycetes</b>
<i>Chaetomium crispatum</i>	<i>Cochlonema verrucosum</i>
<i>C. globosum</i>	<i>Curvularia lunata</i>
	<i>Fusarium clamydosporum</i>
<b>Coelomycetes</b>	
<i>Pestalotiopsis</i> spp.	<i>Fusarium moniliformae</i> var. <i>subglutinans</i>
<i>Phomaeupyrena</i>	<i>Fusarium oxysporum</i>
<i>Phyllosticta</i> spp.	<i>Fusarium solani</i>
<b>Hyphomycetes</b>	
<i>Acremonium acremonium</i>	<i>Gliomastix</i> spp.
<i>Aspergillus flavus</i>	<i>Nigrospora oryzae</i>
<i>Aspergillus niger</i>	<i>Penicillium</i> spp.
<i>Aspergillus oryzae</i>	<i>Trichoderma</i> spp.
<i>Cladosporium acaciicola</i>	<i>Verticillium albo-atrum</i>
<i>Cladosporium cladosporioides</i>	<i>Sterile mycelia</i>

shell and 50% kernel for depulped seeds. Highest quantum of oil could be obtained after 2–5 months of collection (Anon, 2012c).

## 2.10 BIO-PROSPECTATION OF *AZADIRACHTA INDICA*

The potential of neem-based products prepared using its barks, foliage, fruits, and blooms as bio-control agents are acclaimed throughout the world. Its broad array of usages like as antiallergic, antifeedant, antifungal, anti-inflammatory, immune-modulatory, antiulcer, antimalarial, and anti-dermic made it as ‘Green Treasure.’ The antioxidant properties and free radical scavenging potential are the major causes of its capacity to control wide varieties of agricultural pests. Besides all these merits, the simple, cost-friendly, and non-technical ways of its processing also responsible for its wide popularity at rural societies. Raissa et al. (2019) studied the bio-constituents of Indonesian and Philippines varieties of neem using TLC, LC-MS, and other chemical tests. For this study, they used the ethanolic extracts of neem leaves. By TLC and LC-MS, the presence of diversified bio-compounds (like flavonoid, tannin, saponin, terpenoid, etc.) had been proved by the appearance of bands in long UV 366 and m/z value, respectively. Researchers found the Indonesian

varieties as superior ones than the Philippines varieties. Sonale et al. (2019) also investigated on the availability of bio-compounds from neem seed kernels using SCF (Supercritical fluid carbon dioxide) process (experiment specification[s]: 300 bar pressure, 50°C temp., mixture of 30% methanol and acidified methanol). Their initiative was due to the antiproliferative potential of chemical compounds present in kernel extracts against *Candida albicans*, *C. tropicalis*, *C. parapsilosis*, *Trichophyton rubrum*, *T. mentagrophytes* (group of dermatophytes). SCF-Me showed the inhibition against *T. rubrum* (21.53±0.23), *T. mentagrophytes* (18.1±0.1), *C. parapsilosis* (18.46±0.25), *C. albicans* (16±0.26). The effect of SCF-MeA extracts on growth inhibition of any dermatophytes was not noticeable. Researchers also applied SCF-Me extract on foodborne bacteria, fungi, and yeast to study its effect on them. Consequently, they found the inhibition zone of 27.26±0.25, 24.36±0.35, 16.7±0.60, 15.2±0.43, and 15.93±0.20 against *Pseudomonas aeruginosa*, *Bacillus subtilis*, *Aspergillus ochraceus*, *A. niger*; and yeast, respectively. The optimum concentration of SCF-Me was 80 mg for yeast while for others 70 mg. Researchers found that the presence of AZ (50.7%), nimbin (0.08%), salannin (1.83%), triterpenoids (50.7%), epoxy azadiradione (1.58%), and 6-deacetyl nimbin (0.14%) [confirmed by LC and LC-MS methods] are the key reasons of the inhibition.

## 2.11 CONTEMPORARY MEDICINAL USES OF NEEM IN MANKIND

According to Venugopalan & Navaratnam (2013), the uses of neem plant parts as traditional medicine are in age old practices. Initially, these were used as household remedies later by the intervention of science and technologies these are in use of modern medical system also. Its multifaceted usages have already elucidated earlier of this chapter. About a decade earlier, King Institute of Preventive Medicine, Chennai had first implemented the decoction of neem leaves to treat dengue patients and the success story endorsed the synonym of neem tree as ‘Wonder Tree.’

### 2.11.1 NEEM IN COMBATING DISEASES

*A. indica* is indigenous to Southern Asia used to combat broad array of human and plant diseases. To evaluate phytochemical screening of *A. indica* the methods given by Trease & Evans (1989) are followed generally. The chemicals in neem were analyzed and found as alkaloids, tannins, phenolics,

glycosides, saponins, flavonoids, steroids, phlobatanins, and triterpenes. Hugo & Russell (1983) performed studies related to minimum inhibitory concentration using bacteria strains like *Pseudomonas aeruginosa*, *Klebsiella eozane*, *Staphylococcus aureus* and *Escherichia coli*. Silver et al. (1997) undertook antimicrobial susceptibility testing and found in their studies that *P. aeruginosa* showed the highest zone of inhibition followed by *S. aureus* and then by *E. coli*. Neem extract contains the chemical Azadirachtin which is effective against pests besides a deformatal effect on viruses, mites, fungal pathogens, plant parasite nematodes, bacteria, mollusks, and protozoan parasites such as coccidian species. Azadirachtin, which is one active ingredient of neem, is extracted from neem seed kernels. The activity of azadirachtin is affected by a number of factors viz., humidity, sunlight, storage, pH, and method of extraction. Khan et al. (1974) reported the beneficial role of neem cake when applied to soil. It releases beneficial chemicals upon decomposition and inhibits many diseases of fruit, vegetable, ornamental, and spice crops. Dohroo et al., 2016 reported that the application of neem oil has been beneficial in combating fungal pathogens like *Fusarium oxysporum*, *Rhizoctonia solani* and *Macrophomina phaseolina* causing various diseases in plants as well as the tungro virus of rice seedlings.

### **2.11.2 NEEM USE IN BIOCONTROL CONSORTIUM**

To have better control over plant viral diseases, the bioproducts obtained from *Trichoderma* sp., *Gliocladium* sp., and *Bacillus thuringiensis* could be mixed with neem extracts as reported by Tripathi & Tripathi (1982). Ethanolic and methanolic leaf extracts of neem (used concentrations were 25, 50, 75, and 100%) were proved to be useful to control *Aspergillus flavus*, *Alternaria solani* and *Cladosporium* species of fungus [disc diffusion method had been adopted] (Shrivastava & Swarnkar, 2014). The researchers also used Ketoconazole to evaluate its antifungal activity and toxicity.

### **2.11.3 NEEM AGAINST BACTERIAL PATHOGENS**

El Mahmood et al. (2010) studied the antibacterial activity of seed extracts of neem (*A. indica*) against ear and eye infection causing bacterial pathogens. They reported that various neem plant parts could be used as herbal medicine due to having therapeutic values. They tested the crude extract of *A. indica* against various bacteria like *S. aureus*, *E. coli* and *S. pyogenes*. These clinical



microbes were obtained from patients suffering from eye and ear infections. The agar well diffusion method was adopted and the growth of these bacteria was restricted to various degrees than the control strain which was more sensitive to the toxic effect of the corresponding bacteria. Jahan et al. (2007) studied the effect of neem oil on some pathogenic bacteria like *S. aureus*, *E. coli*, *S. typhi*, *P. aeruginosa* by the agar disc diffusion method and found that *S. aureus* has a minimum zone of inhibition. Thakurta et al. (2007) reported in their study on the antisecretory, antihemorrhagic, and antibacterial activity of *A. indica* to heal diarrhea and cholera in India. To have antibacterial effect against *E. coli* and *B. subtilis*, methanolic, and acetic extracts of neem could be used as reported by Winee et al. (2013). Other researchers (Irshad et al., 2011) had also corroborated the same. Ethanolic extracts of neem leaves were screened for antibacterial properties. Ranganathans et al. (1996) found the antidermatophytic activities of neem leaves through their *in vitro* investigation while Rao & Rao (1999) revealed the antifungal properties of 'Gedunin' biochemical isolated from neem leaf extract Plant et al. (1986) reported on a sulfurous compound from *Azadirachta* leaves that showed antifungal activity against *Trichophyton metagrophytes*. Dua et al. (1995) reported its use as mosquito repellent while Pillai & Santhakumari (1984) evaluated the potency of neem extracts on acute and chronic gastro duodenal ulcer in animal models.

#### **2.11.4 ANTI-CARCINOGENIC AND ANTI-MUTAGENIC EFFECT OF NEEM**

The efficacy of neem extracts obtained using several of its plant parts to treat cancerous cells have been explored long back in Asian countries, especially in India and recently in abroad. Chaimuangraj et al. (2006) used dietary doses of aqueous neem leaf extract to treat 3H-B- $\alpha$ -P (benz- $\alpha$ -pyrene) induced cancer. They studied on *in vivo* murine system and measured the level of cancer induction in terms of 3H-B- $\alpha$ -P-DNA adduct formation. They found significant chemopreventive outcomes which were proved by the reduced level of metabolic activation of 3H-B- $\alpha$ -P-DNA and also its production. The same authors also investigated the impact of neem leaf extract (rate of dietary doses were 20, 100, and 250 mg kg<sup>-1</sup> of body weight) on azoxymethane-induced aberrant crypt foci (ACF) and proliferating cell nuclear antigen (PCNA) inhibition. They conducted the experiment on animal (rat) model. They found noticeable inhibition in colon epithelium cells of rats by low

ACF and PCNA labeling indices ( $p < 0.0006$ ). The extracts made from neem blooms also possess preventive potential against DMBA and B- $\alpha$ -P induced neoplastic cell development. Further discovery of novel drug molecules and unraveling of mechanistic principles through cutting edge ethnomedicinal studies using several neem plant parts may significantly contribute for healing several fatal diseases. Scientific interpretations of anticancerous impact of neem extracts have already been elucidated above. Further, Niture et al. (2006) unveiled the anti-mutagenic- and -carcinogenic potential of ethanolic and aqueous extracts of neem. From physiological point of view, MGMT (O-6-methylguanine-DNA-methyltransferase), an enzyme which detoxify O-6-alkylguanines. Neem extracts increase the activity of MGMT enzyme through time dependent demethylation of O-6-alkylguanines and consequently enhance the cell integrity. The elimination of cytotoxic lesions is one of the useful chemoprevention strategies. The positive activities of procarcinogen, oxidative DNA damage and upregulation of antioxidant led to DMBA-induced Hamster Buccal Pouch (HBP) carcinoma disease which could be inhibited by dose-dependent usages of 'Nimbolide' and 'AZ' biomolecules (Priyadarshini et al., 2009).

#### **2.11.5 EFFECT OF NEEM ON DRUG METABOLIZING ENZYMES**

The antitumor characteristics of neem extracts made it usable to shield from the scary side effects (especially programmed cell death of blood cells) of chemotherapeutic agents (viz. Cisplatin [cis] and 5-fluorouracil [5-FU]). Granulocyte colony stimulating factor (GCSF) are often used to modulate the cis and 5-FU led side effects. Manikandan et al. (2008) studied the antitumor potential of neem leaf extract on Swiss mice model. They found that pre-treatment with this significantly have suppressed leucopenia and neutropenia while also fastened the antitumor activities of cyclophosphamide concomitantly. Authors reported that neem leaf fractions could also modulate the phase I and II xenobiotic metabolizing and antioxidant defense enzymes, and lipid and protein oxidation mechanisms which resulted in attenuation of DMBA-induced HBP carcinoma as evident in Swiss mice model. Hence, researchers concluded that neem leaf extract could be an alternative of GCSF not only for its organic nature but also regarding the cost effectiveness. Other researchers (Paul et al., 2011) had also mentioned that repeated use of GCSF could also led to angiogenesis and development of tumor as evident in animal models. Several enzymes like

alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, etc., found liable to skin tumor induction which made them considered as 'marker' enzymes. Koul et al. (2006) reported that Aqueous *A. indica* Leaf Extract (AAILE) could attenuate the activity of aforementioned marker enzymes by decreasing lipid peroxidation level, enhancing glutathione and other allied antioxidant enzymes' level. Diethyl nitrosamine and acetylaminofluorene led pre-neoplastic nodules in male Sprague Dawley Rat model could be inhibited by oral administration of neem leaf extract @ 5% (w/v) (Hanachi et al., 2004). Researchers mentioned that the reasons may be due to the enhanced distribution of antioxidant elements and GST activity while protection against hepatocarcinoma could be also obtained to some extent. Phase II hepatic enzymes (like glutathione S-transferase, DT-diaphorase, etc.) detoxify certain chemical carcinogens (like BaP, and DMBA) cause the carcinogenesis. Interestingly, Sithisam et al. (2005) found that 80% ethanolic extract of neem leaf not only could increase phase II hepatic enzymes level but also increase the level of hepatic antioxidant enzymes (glutathione reductase, glutathione peroxidase, and superoxide dismutase) level. Aqueous and ethanolic foliar, flower, and stem bark extracts of Siamese neem could also result in identical ways as reported by Dasgupta et al. (2004). The active ingredients of Neem are liable to all of its functional mechanism. 'Nimbidin,' 'Azadirachtin A' (Az-A), and 'Nimbolide' – these 3 are active ingredients (ai) while the 'Leaf glycoprotein' and 'Ethanolic leaf extracts' also play carry out some vital mechanisms. The chief function of neem 'Nimbidin' is its inhibition capacity against phagocytosis while its inflammatory stimulatory potential prevents the migration of peritoneal macrophages (a type of white blood cell component provide shield against microorganisms) which results in quick healing. It causes the induction of inducible NO (Nitrous Oxide) synthase (iNO) and also inhibits the prostaglandin E2 (PGE2) and NO production in LPS (lipopolysaccharide) induced macrophages. Furthermore, it also lowers down the release of myeloperoxidase, isozyme, and  $\beta$ -glucuronidase enzymes and causes the attenuation of neutrophil degranulation. Az-A causes the over-expression of Cyclin E and rearrange the actin filaments. 'Nimbolide,' another vital active ingredient (ai) of neem not only enhances the ROS (reactive oxygen species) production but also causes a decrease in Bax ratio with over-expression of Apaf-1, Caspase-3 and ADP-ribose polymerase. It also reduces and enhances the rate of proliferation of cell nuclear antigen and antioxidant and carcinogen detoxification enzyme levels, respectively. Collaterally, it also induces apoptosis by fragmentation and condensation process. The upregulation of antioxidant level prevent the

procarcinogen activation and oxidative DNA damage which in turn inhibit the tumor invasion and angiogenesis. Barring these 3 'ai,' ethanolic leaf extract is another significant active component of neem. It has multifaceted functions like it helps to increase the number of erythrocytes in bone marrow, causes enhancement of lipid peroxidation in stomach and liver and stimulates human peripheral blood mononuclear cells (PBMC) activity. The later activity causes the upregulation of Caspase-3 and downregulation of Bcl2 (Bax ratio) and Cyclin D1. The production of cytotoxic cytokines, IFN- $\gamma$  and TNF- $\alpha$  restrict the tumor cell proliferation and apoptosis. Lastly, leaf glycoprotein, another ai of neem maintains the balance between CXCR3 and CXCL10 during proliferation, angiogenesis, and apoptosis. This balancing helps to restore the impaired chemotactic activity of head and neck squamous cell carcinoma of PBM cells. This wholesome mechanism (Paul et al., 2011) proves its functionality and impact on the health system.

### **2.11.6 NEEM ARRESTS TUMOR CELL GROWTH AND PROLIFERATION**

Neem extracts could be also used as tumor suppressor. The chemical constituents like polysaccharides and limonoids are found in neem bark, seed oil and leaves as reported by Indian, European, and Japanese researchers. The extract of these plant parts is effective enough to act against lymphocytic leukemia. Neem extracts can perform better than any anticancer agents. For example, hot water extract of neem bark is effective enough against solid tumors as proved in an investigation carried out in Japan, 80% ethanolic extract at the dose rate of 250–500 mg kg<sup>-1</sup> body weight could suppress BaP and DMBA induced tumor formation as evident in Swiss albino mice model (Dasgupta et al., 2004), the triterpenoid bio-constituent, i.e., nimbolide available in edible parts of neem could restrict the HT-29 (human colon carcinoma cells) cell growth at G2/M and G0/G1 stages of cell growth by upregulation of p21 gene (it is a down-stream effector of p53 gene, an anticancer protein) (Paul et al., 2011). Paul et al. (2011) also stated that 'nimbolide' impede the expression of cyclin A, and E, Cdk2 and Rad17 by upregulating cyclin D2 and Chk2. Many other researchers also reported the antiproliferative and apoptotic effect of 'nimbolide' being studied its effect on U937, HL-60, THP1 and B16 cell lines. These 2 effects are caused due to the mediation of enhanced expression of Apaf-1 and Caspase-3 and inhibition of bcl-2/bax ratio which prove the molecular mode of mechanism of 'nimbolide.'

The upregulation of pro-cancer agents like p53 gene, bcl2 gene, and PCNA (proliferating cell nuclear antigen) could effectively control (by restricting cell proliferation and differentiation) the DMBA-induced carcinogenesis which can again prove the anticancerous impact of ethanolic neem leaf extract as reported by Subapriya et al. (2006). The *ex vivo* application of neem seed oil@ 50 µl on female mice model could restrict the growth of breast cancer cell line (MCF-7) and consequently suppress the tumor development up to 50% (Bieberich et al., 2006). All these examples endorse the antitumor and anticancerous efficacy of neem extracts.

### **2.11.7 NEEM INDUCES APOPTOSIS IN CANCER CELLS**

Genetically driven ‘programmed cell death’ is known as ‘Apoptosis.’ It is natural way to discard redundant, irreparable, wayward, unwanted body cells. These natural biochemical blades carry out this kind of biological process with aid of caspase enzyme without hampering the equilibrium of essential body materials. These traits of apoptosis have made it appropriate to use in cancer treatment. Recent research reports have revealed the utility of neem extract to treat cancer through apoptosis method. Ethanolic extract of neem (dose dependent manner) is potential enough to treat prostate cancer by inducing apoptosis of the target cells (PC-3). Ganguli (2002) explored the mechanism of neem extract induced apoptosis where he found that the neem extract enhances the expression of pro-apoptotic Bax protein and reduce bcl-2 protein expression (a pro-survival factor of cancer cells). Hence, researcher also had endorsed the efficacy of neem extract against prostate cancer. Kumar et al. (2009) affirmed the potential of ‘nimbolide’ (an active bio-ingredient of neem extract prepared using its leaf and flowers) as an anticancer agent. They revealed that by modulation of mitochondrial pathway being upregulating the Apaf1 and caspase3 enzymes and decreasing bcl2/bax ratio, ‘nimbolide’ induces apoptosis. Nimbolide induced disruption of cell cycle at G2/M, G0/G1 and G/S check points cause the induction of apoptosis, which is very useful for treatment of U937, HL-60, THP1, and B16 cells. Kumar et al. (2009) stated that sometimes, disrupted cell cycle also results in immunity against apoptosis, that’s why the exact molecular interactions between cell cycle disruption and apoptosis have not been fully unraveled. Sah et al. (2006), in their report, mentioned in the same tune with additional information that p53 and p21 genes also play some role in this regard. Ethanolic neem leaf

extract suppresses bcl2, PCNA, p53 genes of DMBA induced cancer cells while boost the expression of Bim, caspase-8, and 3 genes (pro-apoptotic genes) which yield convincing results to heal the target issues and also deletion of neoplasm (Subapriya et al., 2005, 2006). Conclusively, neem extracts of various plant parts could be a viable option of chemical agents for treating some fatal diseases.

### **2.11.8 THE ROLE OF NEEM IN BIOIMMUNOTHERAPY OF CANCER**

To get protection from several fatal diseases, strong immunity system, may be innate or acquired, is the only out since not only it vigils the overall body defense mechanism but also reduce health risks by gearing up the immunity. 'Bio-immunotherapy' now-a-days has received attention of medical practitioners due to its dependable activity especially against cancer and other fatal diseases. Interferons (IFN), a therapeutic cytokine are used *in vitro* or *in vivo* to treat cancer cells but its efficacy could increase manifold through blending with some natural anticancer agents. Lowered immune and genetic systems could results in onset of cancer but earlier by several authors the anticancerous potential of neem extracts has been proved already. Gearing up of immunity, orchestration of TAA (tumor associated antigen), B and T cells and APC (Antigen Presenting Cells) cells are three of the most vital mechanisms. For generation of anti-serum C57BL/6 against B16MelSAg (vaccine) in mice, neem leaf extract (NLE) as an adjuvant function fantastically (Baral et al., 2004) by inhibiting the growth of b16 melanoma tumor cells. The synergistic impact of B16MelSAg + NLE lowered 50% of the tumor burden as reported by Baral et al. (2004). NLE may also react with CEA (carcinoembryonic antigen) and peptide protein which can influence to consider it not only as 'immune adjuvant' but also as 'immune booster antigen' (Sarkar et al., 2007). These reports broaden the application of neem extracts for many tumor treatments. Perforin protein induced tumor generation could be handled effectively by modulating the p38 MAPK pathway. In this case, NLE by enhancing human cancer cells (K562) cytotoxicity through CD40-CD40L dependent endogenous production of IL-12 could control perforin-induced the tumor growth (Baral & Chattopadhyay, 2004). Simply, the attenuated concentration of perforin eliminates tumor cells. Neem leaf glycoprotein (NLGP), an active ingredient has some immunomodulatory role to restore the impaired chemotactic movement of peripheral blood mononuclear cells (PBMC) (Chakroborty et al., 2008). NLGP also

showed some antitumor potential and it restricts tumor cell growth through immunomodulation. Bose et al. (2009) to explain the mode of action of NLGP stated that the downregulation of CXCR3B (liable to lymphocyte apoptosis) and enhanced expression of IFN $\gamma$  results in restoration of chemotaxis of PBMCs and decrease the tumors growth. According to the same researchers, upregulation (CD<sub>69</sub> and CD<sub>45</sub>RO) and downregulation (CD<sub>45</sub>RA and CD<sub>62</sub>L) of marker genes of lymphocyte, monocyte, and dendritic cells cause the activation of immune system. NLGP also facilitates the activation of T cells and secretion of T-helper 1 cytokines (e.g., IFN $\gamma$ ). NLGP also expedites the response of type II cells than type I which are proved through IL4 secretion. The NLGP led activation of NK-cells and cytotoxic T-cells (isolated from head and neck squamous cell carcinoma) are enough potent to kill K562 cells (erythroleukemia) and KB cells (oral cancer cells). According to Bose et al. (2009) the cytotoxic T lymphocyte (CTL) response (get induced by NLGP action) is dependent on perforin enzyme while independent of NK cells. Ghosh et al. (2006) mentioned about the capacity of NLP (neem leaf preparation) to aid in the production of WBC. The same researchers also found that pre-treatment with NLP of CYP-induced tumor cells could also yield some positive results as proved in mice model. Paul et al. (2011) demonstrated that NLP induced activation of NK and NK-T cells and secretion of TNF $\alpha$  and IFN $\gamma$  could suppress murine B16 melanoma cells as found in Swiss albino mice model. According to Prasad et al. (2010), the mechanism of TNF $\alpha$  (a controversial cytokine) depends on several factors viz. type of cell line, external, and internal stimuli while it is responsible for activation of NF $\kappa$ B (a strong transcription factor) which in turn stimulates many genes ultimately favor the cancer cell growth. The activation of different markers like CD<sub>44</sub>, CD<sub>47</sub>, CD<sub>8</sub>, and CD<sub>25</sub> using subcutaneous aqueous neem extract led to the reduced activation of peritoneal macrophage activity while attenuated metastatic activity of sarcoma L-1 and lymphosarcoma RAW cells could be also achieved using the same extract (Beuth et al., 2006). IFN $\gamma$ , and TNF $\alpha$  are the potent inducer of nitric oxide (NO) while NO could regulate T-cell proliferation, cell signaling, apoptosis, and cytokine production as it is a major tumoricidal agent. NO production could be also enhanced by NLGP treatment may be alone or with tumor antigen vaccination. Moreover, NLGP treatment enhances the antitumor immunity by induction of T and B cells, causes maturation of myeloid based DCs and also optimizes T cells functions (Paul et al., 2011). Hence, conclusively, neem extracts may be considered as 'Candidate Vaccine Tool' for immunotherapeutic treatment of cancer.

### **2.11.9 TOXICOLOGICAL RISK FACTORS INVOLVED IN THE USE OF NEEM EXTRACTS**

Along with all the therapeutic benefits of neem extracts, its toxicological effects should be also taken into consideration. Its luxuriant use may cause some allergic symptoms like swelling of throat and mouth, itching, breathing problems, etc. Sometimes, prolonged use of neem products may also cause some damage to the liver cells and kidney and results in jaundice and urinary trouble. Collaterally, damage of RBCs, generation of neurotoxicity, permanent damage to the reproductive systems (as proved in rat model by decreasing the methylated deoxycytidine level) (Tsarev, 2010; Khillare & Shrivastav, 2009), etc., are few cons of using neem-based products miserliness. Albeit any major harmful events have not been encountered by the users yet but still use of these products judiciously may help to eliminate some untoward issues.

### **2.11.10 VITILIGO**

It is an autoimmune disorder. Patchy skin with faded color is its key symptoms. Intaking of 4 g of raw neem leaves before meal is effective enough to heal this skin disease. Collaterally, application of neem oil on patchy, discolored skin may restore the normal skin color (Kumar et al., 2019).

### **2.11.11 ANTIDIABETIC EVALUATION**

It is proved in rat model that the use of neem-based products at the single dose rate of 250 mg kg<sup>-1</sup> could effectively decrease blood glucose (18%), triglycerides (32%), urea (13%), cholesterol (15%), lipids (15%) and creatinine (23%) (Shravan et al., 2011; Hashmat et al., 2012) after 15 days of neem products administration. Multiple doses will be indeed more effective.

### **2.11.12 LARVICIDAL ACTIVITY**

Aditi et al. (2011) at Zoology laboratory of DAV college, Kanpur has conducted an experiment to evaluate the larvicidal properties of neem extracts. They used 1, 2, 3, 4, and 5 ppm aqueous extract solutions of neem (Ne), *Gymnema sylvestre* (Gs), *Nerium indicum* (Ni) mill and *Datura metel* (Dm) L. They found that the mortality percentages of culex larvae were



70–99%, 44–89%, 41–74%, and 19–54% in *Ne*, *Gs*, *Ni*, and *Dm*, respectively. These outcomes prove the efficacy of neem aqueous extract to check larvae populations.

### **2.11.13 TO CURE PEDICULOSIS**

The findings of the study indicate that the pediculosis is a major health problem faced by the school children which need a non-pharmacological healing approach. Application of neem oil is simple and easy to implement, easily available, no notable side effects and most acceptable to reduce the degree of pediculosis among school children. The excavated results supported that the incorporation of neem oil application among school children is the best intervention to treat pediculosis (Isac, 2011).

### **2.11.14 LIVER PROTECTANT**

The usefulness of neem extracts to heal biliary diseases and for blood purification purpose are well known. It enhances the level of antioxidants, ascorbic acid (Vit C), Vit E and carotenoids which gear up the immunity by neutralizing free radicals and also stabilize the serum marker enzymes to check liver damage (Dubey & Kashyap, 2014; Biswas & Chattopadhyay, 2002):

1. **Azadirachta indica Use in Bilioussness:** Bilioussness is a medical condition which cause a disorder of gall bladder or liver. Excessive secretion of bile causes this gastric distress. Bilioussness is characterized by headache. Neem has been found to be very useful in curing this condition (Biswas & Chattopadhyay, 2002).
2. **Azadirachta indica in Jaundice:** *Azadirachta indica* plant is very useful in liver problem, particularly it is very helpful in curing jaundice disease. To cure jaundice, intake of neem leaf extracts + ½ teaspoon of honey for 7 days are very effective (Dubey & Kashyap, 2014).

### **2.11.15 ANTI-ALLERGIC**

1. **Azadirachta indica in Urticaria:** ‘Urticaria’ commonly known as ‘Hives,’ a type of dermatological ailment causes red, bumpy, and itchy patches on the skin. The allergic and non-allergic reasons may lie behind for this disease but healing of this is a complex due to

non-availability and side effects of chemical agents. Hence, intake of decoction prepared using neem bark, sandal paste and guduchi could be an easy and safe remedy (Katsayal & Nadabo, 2008).

- 2. Cures Asthma:** According to Katsayal & Nadabo (2008) the use of neem oil (dose rate ranges from 1 drop to 1 tea spoon) on thong or swallowing of neem oil may improve asthma problem.

### **2.11.16 PESTICIDE**

Neem oil extracted from neem seeds (color: yellow to brown; taste: bitter; odor: garlic/sulfur smell) are known for its utility as pesticide due to having AZ bio-constituent. It is potential to control broad range of agricultural pests and insects (like bed bugs, cockroaches, mites, ants, Cherry and Pear slugs, etc.) which ascertained its utility as organic pest-and-insect-icide in India (Tiwary & Pandey, 2010). For example, Agroneem is one of the popular organic pesticides for agricultural pest management program since it contains 0.15% AZ and 15% of neem biomass (neem lipids) while its non-toxic and bio-degradable nature and compatibility with wide range of chemical fertilizers, insecticides, and fungicides also contribute as add on merits. The antifeedant properties of AZ affect the hormonal system and reproductive system of insects. The neem extracts could be also used as a major component in insect repellent, shampoo, soap, toothpaste, food supplement, face wash, body lotion, etc. (Dubey & Kashyap, 2014).

## **2.12 PHYTOCHEMICALS AND PHARMACOLOGICAL ACTIVITY INVOLVE**

The age-old practice (>2000 years) of using different neem plant parts for medicinal purposes are known in pan world. In our traditional health system, the position of neem tree is at the pinnacle (Chatterjee & Pakrashi, 1994). Different plant parts of neem contain varied percentages of phytoconstituents (Kaushik & Singh, 2001). >135 chemical compounds have been found from neem extracts. They are classified into 2 major classes like 'Isoterpenoids' (diterpenoids, triterpenoids, limonoids, azadirone, gedunin, vilasinin) and non-isoterpenoids (Octadecanoic acid [9–24%] alpha linoleic and 9-hexadecenoic acids, proteins [amino acids], carbohydrates [polysaccharides], flavonoids, glycosides, tannins, dihydrochalcone). The multifaceted uses of different neem plant parts have been enumerated below:

### **2.12.1 BARK**

Tannins are the chief chemical content of bark. Gallic acid, catechin, epicatechin, galocatechin, etc., are different forms of tannins. Tanin is responsible for the prevention of oxidative burst of PNN (Polymorpho Nuclear Neutrophil) cells during carrageenin-induced inflammation as reported by Maithani et al. (2011); and Chopra & Nayer (1959). Furthermore, margo-lone, margolonone, diterpenoids, and isomargolonone are competent enough to control *Klesiella*, *Staphylococcus*, and *Serratia* species (Maithani et al., 2011). Bark extract of neem (dose rate: 50 mg kg<sup>-1</sup> for continuous 4 days at subcutaneous position) also contains GIa and b (2 water soluble polysaccharides) which possess antitumor effect (Chopra & Nayer, 1959) while GIIaa and GIIIa are another 2 polysaccharides possess anti-inflammatory effect (Fujiwara et al., 1982). The aqueous extract of neem bark could also cause the complement activation in human serum. To gear up the immune system, as antiacid, antiulcer, spasmolytic, hypotensive, diuretic, analgesic, and curative agents its contribution is undeniable (Maithani et al., 2011).

### **2.12.2 LEAF**

Sulfur containing compounds (like cyclic trisulfide, and tetrasulfide) are the key constituents found from neem leaf. Pant et al. (1986) revealed that the extract prepared from mature, fresh neem leaves by steam distillation method, possess antifungal activity against *Trichophyton mentagrophytes*. Several researchers have reported the analgesic, immunity stimulant (proved by humoral and cell-mediated responses both) and antipyretic properties of neem leaf extracts. Murty et al. (1978) exhibited that neem leaf administration @100 mg kg<sup>-1</sup> for 21 days could increase IgM and IgG (antibodies) levels. The oil obtained from neem leaf activates cell-mediated immune mechanisms to elicit mitogenic/antigenic challenge. According to Murty et al. (1978) neem leaf aqueous extract lowers down blood glucose and control adrenaline secretion as evident in induced diabetic rat model. Flavonoids and quercetin – these 2 compounds are responsible for the antidiabetic (hypo and hyperglycemia) effect (Maithani et al., 2011). Oral administration of neem leaf extract (NLE) could also prevent mucus depletion and degranulation of mast cell which result in restriction of ethanol-induced ulcer problem while antifertility and abrogate effect of NLE are also evident in animal models. Maithani et al. (2011) stated about the antiviral activity of NLEs

against *Vaccinia*, Chikungemya, and Measlesvirus *in vitro*. Badam et al. (1999) reported about the efficacy of methanolic NLEs @ 1 mg ml<sup>-1</sup> for 96 hours against Coxsackie virus (Group B) by inhibiting plaque formation. Methanolic NLEs could also interfere in the replication cycle of Coxsackie virus (Group B). Balasenthil et al. (1999) reported about the potential of NLEs (aqueous) against DMBA induced squamous cell carcinoma. They also mentioned that these significantly reduce the neoplastic incidence. The chemopreventive mechanism of NLEs against MNNG (N-methyl-N-nitro-N-nitroso-guanidine) by reducing and increasing the level of lipid peroxide and antioxidant respectively and also through the modulation and metabolization of glutathione and enzymes respectively had proved in the experiments carried out by Arivazhagan et al. (2000). This result could confirm the use of NLEs for enzyme detoxification purpose of human stomach. Furthermore, paracetamol induced liver necrosis, chronic liver damage issues (i.e., increased level of AST [Aspartate aminotransferase], ALT [Alanine aminotransferase], and GGT [Gamma glutamyl transpeptidase]), and depressant activity of different complex neural disorders, acetonic NLEs could be utilized efficiently (Arivazhagan et al., 2000). To get anxiolytic activity NLE administration @ 200 mg kg<sup>-1</sup> of body weight could be effective as proved in rat model. Barring these, to heal leprosy, epistaxis, anorexia, biliousness, and skin ulcers potential of NLEs are unparallel.

### 2.12.3 SEED

Basically, the hexane-based extract of neem seeds is used to interfere in the reproductive cycle of rodents. Different bio-constituents of it cause the pregnancy aggregatory effect in rodents due to oral administration of neem seed extracts (NSE) @ 10% concentration without posing any side effects. It is for cell-mediated immune reaction. Hence, it can be a viable option as an organic contraceptive since it doesn't pose any side effects like other steroidal contraceptives and also it causes non-hormonal, spermicidal effects (Khalid et al., 1989). Alcoholic NSEs could also act against the chloroquine-resistant malarial parasites as reported by the earlier researchers. Furthermore, purified forms of alcoholic NSEs could also interfere in the sexual and asexual reproductive cycles of human malarial parasite of *P. falciparum*. *Trichophyton*, *Epidermophyton*, *Microsporium*, *Trichosporon*, *Geotricum*, and *Candida*— the growth inhibition of these could be effectively made using extracts prepared from neem seeds (Table 1) (Maithani et al., 2011).

Oil extracted from neem seeds also impactful against gram (+) and gram (-) microorganisms (like *Mycobacterium tuberculosis*, *Vibrio cholerae*, *Klebsiella pneumoniae*, *M. pyogenes*, *Streptococcus mutans*, *S. faecalis*, etc.) (Maithani et al., 2011). The horse grain germination *in vivo* could be improved by NSE pre-treatment by enhancing the antioxidant activity and lowering the lipoxygenase and lipid peroxidation activities. For healing of leprosy, intestinal worms and vaginal infections, NSEs will be an indispensable option. NIM-76 is a novel vaginal contraceptive which prevents broad array of vaginal issues (Maithani et al., 2011).

#### **2.12.4 FRUIT**

Neem fruit extracts (NFEs) are the repository of phytosterols which exhibit antiulcer activity. Stress induced gastric lesion could be healed by using NFEs as reported by Maithani et al. (2011). Moreover, NFE could be useful to treat piles, urinary disorder, diabetes, wound, leprosy, and intestinal worms also.

#### **2.12.5 OIL**

The biological efficacies of neem oil have already been demonstrated by several researchers. ‘Nimbidin,’ is a principal component found to be present in neem seed kernel-based oil. It is mostly used as anti-inflammatory and antipyretic agent. Nimbin, nimbidinin, nimbolide, and nimbidic acid – these are chemically grouped into tetranotriterpene and have isolated from neem seed crude extract (Mathani et al., 2011). In general, these biochemical compounds possess antimalarial features while antibacterial potential against *S. aureus* and *S. coagulase* of nimbolide had been proved by Khalid et al. (1989). Other biochemical compounds like campesterol,  $\beta$ -sitosterol, stigmasterol, and plethora of triterpenoids especially AZ also function cancer and tumor related issues. Application of AZ@300–2,000 ppm could also act as antifeedant as evident in several animal models (Khalid et al., 1989). Khosla et al. (2000) reported that for alloxan-induced diabetic rabbits neem oil is very effective and could also bring hypoglycemic effect. As natural contraceptive (prior application of neem oil at intravaginal position before coitus), spermicidal (in case of rhesus monkey and human spermatozoa), antifertility and antipyretic, the potential of neem seed oil is noteworthy (Mathani et al., 2011).

## 2.13 SEXUAL AND BREEDING SYSTEMS

Neem is cross-pollinated tree. Bisexual (male and female both) and staminate (functionally male) flowers have found to be present in the same flower in case of neem (Singh et al., 1996). Botanically, it is known as 'Andromonoecious.' Gupta et al. (1996) in their literature mentioned that 'Protandry,' a form of sexual hermaphroditism has been found in neem flowers. Anthers mature first and then stigma starts to be receptive. The mature anthers dehisce around 8 hrs. in the morning within the nyctinasty flowers. Neem flowers are entomophilous and seeds dispersal taken place by birds and mammals. Anatomically, its ovary is trilobular, polycarpic in nature (Singh et al., 1995). Selfing operation could successfully produce viable seeds as reported by Gupta et al. (1996); and Solanki (1998). The rate of outcrossing was estimated through isozyme analysis (Solanki, 1998). Chamberlain et al. (2000) at Arid Forest Research Institute, Jodhpur carried out an investigation on the hybridization of *A. indica* and *A. indica* var. 'Siamensis' but the crossing was not fruitful in terms of formation of any viable seeds.

### 2.13.1 MOLECULAR VARIATION

A large number of methodologies exist for assessment of genetic diversity in the plant species. A combination of morphological traits and protein profiling methods, such as isozyme has been carried out in neem (Kundu, 1999). However, such traits are influenced by environmental factors as well as development stage of the plants. Hence, the studies don't provide accurate measure of the existing genetic diversity. Molecular markers are useful to study genetic diversity between diversified accessions.

Farooqui et al. (1998) studied the diversity analysis of 17 neem accessions using RAPD marker. Around 49 random DNA primers they had used. The high similarity index among different Indian accessions of neem had proved very narrow diversity while the clustering pattern, the researchers found by dendrogram analysis, also didn't manifest the geographical variation. They found that the accessions from different geographical region had not always clustered together. The clustering pattern was ambiguous. Hence, they suggested to take assistance of other genetic analysis to get clear interpretation. Kundu (1999) carried out the isozyme analysis of banana cultivars of 3 different provenances, i.e., Bangladesh, Thailand, and Kenya. The researcher found difference at inter and intra provenance level. This

result corroborated the efficacy of isozyme analysis for ascertaining different origin of neem cultivars. Wickramasinghe & Simons (1994) also affirmed the efficacy of isozyme analysis for understanding the genetic diversity since they found the differences between neem varieties from India, Sri Lanka, Nepal, and *A. indica* var. 'Siamensis' from Thailand. Dhillon et al. (2007) also carried out the genetic diversity analysis of 40 neem varieties summoned from different eco-geographical regions using RAPD molecular marker. Out of 152 total reproducible bands, 104 (68.4%) bands were found polymorphic. Cluster analysis using dendrogram formed by Jacard's similarity coefficient (UPGMA) proved the variations among different neem varieties. The range similarity indices were 0.60 to 0.94 which proved the broad genetic base among the Indian neem varieties. In Principal Component Analysis (PCA) the scattered plotting proved the wide genetic base. Deshwal et al. (2005) used RAPD to study the genetic diversity in the Indian neem. But the level of variation and reproducibility detected by the RAPD marker is comparatively lower than the other markers. Amplified fragment length polymorphism (AFLP) technique permits to analyze large number of loci in a single experiment and detects more polymorphism (Powell et al., 1996). Singh & Randhawa (2008) assessed the genetic divergences exist among 14 indigenous neem accessions and 8 exotic neem clones collected from Haryana, Punjab, and Rajasthan using AFLP (Amplified Fragment Length Polymorphism) marker. A total of 758 amplicons were produced after the PCR analysis using 14 selective AFLP primers. The similarity indices value (range 0.21 to 0.89) proved the wide genetic base obtained by Jaccard's Similarity Coefficient Analysis. The phylogenetic diagram clearly showed the separate clusters of indigenous and exotic gene pools. PCA proved 74% variation among indigenous and exotic neem varieties.

### **2.13.2 THE INTERNATIONAL NEEM NETWORK**

International Neem Network (INN) was established in 1994 for venturing wide array of approaches needed for further genetic improvement and to obtain wide adaptability for its growing (Thomsen & Souvabbavong, 1994). Another purpose of this organization is to conduct some outreach programs for further facilitation of neem cultivation and for publicizing its multifaceted usages, so that its benefit could be utilized by most of rural people. Furthermore, seed collection, provenance exploration, knowledge exchange at international level, research on seed physiology and technology, diversity

analysis, biochemical markers, and reproductive biology were also other target of INN. Around 21 countries of Asia, Latin America, Europe, and Africa were collaborated with INN while FAO and IPGRI also participated in various international and national activities. Moreover, few significant projects like ‘Improved productivity of man-made forests through tree breeding’ (Philippines based project), ‘Afforestation and reforestation – formulation of national policies’ (Vietnam based project), and ‘Forestry research support program for Asia-Pacific region’ (Thailand based project) were proposed by FAO/UNDP under the INN mission. In India, a training workshop had been conducted to familiarize with different norms and benefits of INN during July 1994 at Coimbatore, Tamil Nadu, India. Conclusively, the global collaboration with major neem growing countries for further facilitation and exchange of neem allied research are the chief mission of INN.

### **2.13.3 PROVENANCE EXPLORATION, COLLECTION, AND TESTING**

According to Hansen et al. (1996); and FAO (1998), the first approach made by INN in 1995 was the collection of seeds of 25 different neem accessions from the collaborators distributed throughout the world. The purpose of this initiative was to conduct a trial to ascertain the appropriacy of certain accessions under different eco-geographical regions. Based on the report found in the document of FAO (1995a), seed collection initiative was started between March and August. During seed plantation programs, 100 m distances between seeds had been provided for successful establishment of neem trees. Development of neem nursey was another motto of INN (FAO, 1995b). This mission also helped to supply quality planting materials and *ex situ* conservation of neem accessions.

### **2.13.4 THE DESIGN AND ESTABLISHMENT OF INTERNATIONAL PROVENANCE TRIALS**

Trial design for provenance trials and establishment had been formulated by FAO (1996). As mentioned in the preceding paragraphs that the key objectives of international provenance trials are to evaluate the adaptability of neem accessions under different eco-geographical regions and to study the genetic variation. Considering the local meteorological conditions and availability of resources, the numbers of seedlings are usually decided but definitely the trial designs, and establishments should be statistically sound



and robust. The international trials were initiated during 1995–1997 and out of 36 international provenance trials, 25 trials were successful. Owing to low survival rates, trial in Nicaragua, Sudan, and Chad had been stopped. INN acts as a funding source required for the maintenance and establishment of international provenance trials.

### ***2.13.5 SUPPORTIVE RESEARCH COMPONENTS***

Seed physiology and technology, genetic divergence study in terms of molecular characterization and biochemical compounds, and reproductive biology – these are considered as supportive research components of INN activities. These components except the fundamental objectives like seed exchange and establishment of neem populations at international provenance trials can extensively foster the INN missions and visions.

### ***2.13.6 GENETIC VARIATION AND REPRODUCTIVE BIOLOGY***

The research proposals under this component are decided by CIRAD-Forêt, France in collaboration with INN (Thomsen & Souvannavong, 1994).

### ***2.13.7 SEED PHYSIOLOGY AND TECHNOLOGY***

DANIDA Forest Seed Centre, Denmark is the major coordinator for this research component. This organization mainly concentrates on storage and handling practices of recalcitrant and intermediate tropical forest tree seeds. INN, IPGRI, and DANIDA itself are considered as funding agencies here. The seed storage and desiccation studies of 30 neem tree accessions are considered under this research component (Chamberlain et al., 2000).

### ***2.13.8 COMPONENT ON GENETIC VARIATION IN CHEMICAL COMPOUNDS***

ICFRE (Indian Council for Forest Research and Education) is the principal coordinator under this component. Research activities are fully concentrated under this component are basically AZ content estimation, determination of fatty acid content of neem seeds and characterization of active bio-chemical

ingredients (used as bio-chemical markers). Research experiments under this usually start only after the initiation of flowering and fruiting. Here, INN is the only funding source and key collaborator.

### **2.13.9 NETWORK PROGRAM AND FUTURE ACTIVITIES**

Management and establishment of neem plantations by international provenance trials are the main activities of INN as mentioned earlier. According to Hansen et al. (1996), the assessment of tree characters and research methodologies had been started in 1997. AZ (key bio-constituent) content assessment and study of neem seeds morphology are usually carried out at an interval of four years (Chamberlain, 2000). Emmanuel (1998) reported that under INN provenance trials mission, AFRI had conducted trials (number of replications: 4; statistical design: RBD) at Jodhpur, Palampur, and Jaipur. Morphological data obtained under this program are tree height 0.57–2.05 m and stem girth 8.04–13.36 cm after one year of growth. Chamberlain (2000); and Sharma (1998) revealed that the tree height and stem girth varied from 1.63–5.49 m and 3.6–6.63 cm respectively under the provenance trial at Jabalpur. According to Wickremasinghe & Gunasena (1998), out of 11 provenance trials, the trials at Tanzania, Thailand, Sri Lanka, India, Pakistan, and Nepal were successful in terms of height, stem girth and branch numbers.

### **2.13.10 FUTURE ACTIVITIES OF THE INN**

- Extensive study of genetic diversity of neem;
- Germplasm conservation of neem genetic resources;
- Breeding program for development of genetically improved neem varieties;
- Further investigations on bio-chemical constituents of neem in search of some novel bio-compounds.

### **2.13.11 OTHER IMPROVEMENT ACTIVITIES**

- Establishment of neem clonal gene bank using 32 exotic neem accessions by research section of Royal Forest Department, Thailand (Boontawee et al., 1993).

- Indigenous neem tree accessions (28 nos) collection by the Forest College and Research Institute of TNAU, Tamil Nadu, India (TNAU, 1999; Mishra, 1995).
  - High rate of seed harvest and extraction of oil and AZ – the major objectives of this improvement activity.
  - Evaluation of adaptability of indigenous neem accessions under varied agro-climatic conditions was another objective.
- Collaborative project by CAZRI and AFRI (funding agency: NOVOD Board) for provenance trials at Rajkot (Hijarat), Gandhi Nagar (Gujarat), and Ameawati (Maharashtra) (). The objectives are as follows:
  - Evaluation of neem seed resources;
  - Evaluation of tree morphologies for consideration as breeding selection traits;
  - Estimation of AZ and oil contents from seeds.
- Provenance trial by NRCAF in 1994 (Solanki, 1998). The objective(s) are as follows:
  - Selection of trees based on bole straightness, high fruit yield and canopy arrangement.

## 2.14 PATENTS ON NEEM

Japan (35 nos), USA (54 nos), Australia (23 nos), India (14) and few European countries had started to make patents since 1980 on neem-based products and its processing. The areas of patents are health care (13%), crop protection application (63%), veterinary care (5%), cosmetics (6%), industrial (5%) and others (8%) while majority of patents had been owned by CSIR-India (14), Bayer (8) and Certis W.R. Grace (49) (Anonymous, 1993, 2006). The most vital and 1<sup>st</sup> patent is US patent on ‘Therapeutic formulation using Neem Stem Bark’; Year 1983; Organization Temuro Corporation (Anon, 1985).

## 2.15 FUTURE PERSPECTIVES

- The demand of alternative medicine in current era is about ~10.895 billion USD (Source: WHO) while herbal medicine is 5 trillion USD (Retrieved from: [www.timesjobs.com/candidate/careerresources/medicines.jsp](http://www.timesjobs.com/candidate/careerresources/medicines.jsp)).

- Great potential for increased sustainable use of household neem pesticides (Paul et al., 2011; Hellpap & Leupolz, 1999).

## 2.16 NEEM CONFERENCES IN INDIA (SOURCE: ANON, 1993)

1. 2<sup>nd</sup> World Neem Conference, Queensland, Australia, 1996.
2. 1<sup>st</sup> World Neem Conference, Bangalore, India, 1993.
3. 4<sup>th</sup> World Neem Conference, Mumbai, India, 2002.
4. 3<sup>rd</sup> International Neem Conference, Nairobi, Kenya, 1986.
5. 3<sup>rd</sup> World Neem Conference, Vancouver, Canada, 1999.
6. 2<sup>nd</sup> International Neem Conference, Rauschholzhausen, Germany, 1983.
7. 1<sup>st</sup> International Neem Conference, Rottach-Egern, Germany, 1980.
6. 5<sup>th</sup> World Neem Conference, Coimbatore, India.

## 2.17 CONCLUSION

‘Herbal Panacea,’ another popular name neem. This name is because of its ability to treat wide range of diseases. AZ, Nimbidin, Nimbolide, etc., are its major active bio-constituents possess different kind of biological properties. But still, exploration of all of its therapeutic abilities have yet to be made. Hence, to get its utmost effect in-depth molecular investigations are highly needed. Collaterally, overdose or luxuriant uses of neem products may be detrimental for health. Thus, it is advisable to use at prescribed dose rates.

**TABLE 2.2** Specifications for Neem Kernel Oil

Characteristic	Requirement
Maximum moisture and insoluble impurities	0.3% by weight
Lovibond color (1/4 in cell), expressed as Y + 5R, not deeper than	–
Refractive index at 40°C	45.0
Specific gravity,	1.4615–1.4705
Saponification value	0.908–0.934
Iodine value (Wij’s method)	180–205
Maximum acid value	65–80
Maximum unsaponifiable matter	15
Minimum titer	2% by weight
	36°C

**TABLE 2.3** Recommendations for Use of Neem Oil and NSKE for Different Pest Management

Common Name	Zoological Name	Effective Measures to Control
Brown plant hopper	<i>Nilaparvata lugen</i> sp.	Neem oil @3% and neem seed kernel extract @5% could be used; soil application using neem seed residue @25 kg ha <sup>-1</sup> could be also useful.
Black bug	<i>Scotinophoralurida</i> sp.	Spraying of neem seed kernel extract @5% or soil application using neem seed residue @25 kg ha <sup>-1</sup> could be also useful.
Ear head bug	<i>Leptocorisa acuta</i>	Neem seed kernel extract @5% or soil application using neem seed residue @25 kg ha <sup>-1</sup> could be also useful.
Sheath rot	<i>Saroclodiumoryzae</i> sp.	Neem seed kernel extract @5% or neem oil @3% could be useful.
Sheath blight	<i>Rhizoctonia solani</i>	Foliar spray using neem oil @3% is beneficial.
Bacterial leaf blight	<i>Xanthomonas oryzae</i> var. <i>Oryzae</i>	Neem seed kernel extract @5% or neem oil @3% could be useful.

## KEYWORDS

- **azadirachtin**
- **breeding**
- **DNA-based marker**
- **international neem network**
- **neem**
- **phytochemicals**
- **therapeutics**
- **tropical forest**

## REFERENCES

- Aditi, G., Bhandari, B. S., & Rai, N., (2011). Antimicrobial activity of medicinal plants *Azadirachta indica* A. Juss, *Allium cepa* L. and *Aloe vera* L. *International Journal of Pharma Tech Research*, 3(2), 1059–1065.

- Ahmed, S., (1988). *Farmer Pest-Control Practices in India: Some Observations*. Final Workshop of IRRI-ADB-EWC Botanical Pest Control in Rice Based Cropping Systems, IRRI, IRRI, Los Banos, Philippines.
- Allan, E. J., Eeswara, J. P., Johnson, S., Mordue, A. J., Morgan, E. D., & Stuchbury, T., (1994). The production of azadirachtin by *in-vitro* tissue-cultures of neem, *Azadirachta indica*. *Pesticide Science*, 42(3), 147–152.
- Anesa, N., (2016). Beneficial effects of neem oil-an updated review. *Journal of Pharmaceutical Science and Research*, 8(8), 756–758.
- Anon., (1985). *The Wealth of India*. Raw materials publication and information directorate. CSIR. New Delhi, India.
- Anon., (1993). *World Neem Conference- Abstracts*. Indian Council of Agricultural Research. Bangalore, India.
- Anon., (1997). World of Neem- Neem foundation's exhibition and conference. *Global Neem Update*, 2, 2, 3.
- Anon., (2012a). Retrieved from: <https://www.oilseedcrops.org/wp-content/uploads/2012/11/Indian-Neem-Growth.pdf> (accessed on 02 September 2023).
- Anon., (2012b). Retrieved from: <https://www.oilseedcrops.org/wp-content/uploads/2012/11/Indian-Neem-Growth.pdf> (accessed on 02 September 2023).
- Anon., (2012c). Retrieved from: <https://www.oilseedcrops.org/wp-content/uploads/2012/11/Indian-Neem-Growth.pdf> (accessed on 02 September 2023).
- Arivazhagan, S., Balasenthil, S., & Nagini, S., (2000). Modulatory effects of garlic and neem leaf extracts on N-methyl-N'-nitro-N-nitrosoguanidine (MNNG)-induced oxidative stress in Wistar rats. *Cell Biochemistry and Function: Cellular Biochemistry and its Modulation by Active Agents or Disease*, 18(1), 17–21.
- Ascher, K. R. S., (1993). Nonconventional insecticidal effects of pesticides available from the neem tree, *Azadirachta indica*. *Archives of Insect Biochemistry and Physiology*, 22, 433–449.
- Ayurvedic Pharmacopeia of India, Government of India, (n.d.). 1(2), 131, 132.
- Badam, L., Joshi, S. P., & Bedekar, S. S., (1999). 'In vitro' antiviral activity of neem (*Azadirachta indica*, A. Juss) leaf extract against group B coxsackieviruses. *Journal of Communitive Disease*, 31, 79–90.
- Bahuguna, V. K., (1997). Silviculture and management practices for cultivation of *Azadirachta indica* (neem). *Indian Forester*, 123, 379–386.
- Bakshi, B. K., (1976). *Forest Pathology: Principles and Practice in Forestry*. Forest research institute. Dehra Dun, India.
- Balaji, P., (2017). *Fruit Yield and Economic Analysis of Selected Tree Species (STS) Under Agro-forestry System in Tamil Nadu* (pp. 1–45). TN State Forest Department Final Report on Neem (*Azadirachta indica*).
- Balasenthil, S., Arivazhagan, S., Ramachandran, C. R., & Nagini, S., (1999). Chemopreventive potential of neem (*Azadirachta indica*) on 7,12-dimethylbenz[a]anthracene (DMBA) induced hamster buccal pouch carcinogenesis. *Journal of Ethnopharmacology*, 67, 189–195.
- Baral, R., & Chattopadhyay, U., (2004). Neem (*Azadirachta indica*) leaf mediated immune activation causes prophylactic growth inhibition of murine Ehrlich carcinoma and B16 melanoma. *International Immunopharmacology*, 4, 355–366. doi: 10.1016/j.intimp.2003.09.006.

- Berjak, P., Campbell, G. K., Farrant, J. M., Omondi, O. W., & Pammenter, N. W., (1995). Responses of seeds of *Azadirachta indica* (neem) to short-term storage under ambient or chilled conditions. *Seed Science and Technology*, 23(3), 779–792.
- Beuth, J., Schneider, H., & Ko, H. L., (2006). Enhancement of immune responses to neem leaf extract (*Azadirachta indica*) correlates with antineoplastic activity in BALB/c-mice. *In Vivo*, 20, 247–251.
- Bharathi, A., Umarani, R., Karivaratharaju, T. V., Vanangamudi, K., & Manonmani, V., (1996). Effect of drupe maturity on seed germination and seedling vigor in neem. *Journal of Tropical Forest Science*, 9(2), 147–150.
- Bhardwaj, S. D., & Chand, G., (1995). Storage of neem seeds: Potential and limitations for germplasm conservation. *Indian Forester*, 121(11), 1009–1011.
- Bhuiyan, M., Nishimura, M., Matsumura, S., & Shimono, T., (1997). Antibacterial effects of the crude *Azadirachta indica* Neem bark extract on *Streptococcus sobrinus*. *Pediatric Dental Journal*, 71, 61–64.
- Bieberich, E., Sebastian, A., & Sarkar, N. H., (2006). Neem-seed oil inhibits the growth of breast cancer cells. *Proceedings of American Association of Cancer Research*, 47, 19–34.
- Biswas, K., & Chattopadhyay, I., (2002). Biological activities and medicinal properties of neem (*Azadirachta indica*). *Journal of Current Science*, 82(11), 1336–1345.
- Boa, E. R., (1995). *A Guide to the Identification of Diseases and Pests of Neem (Azadirachta indica)* (p. 71). FAO, RAPA, Bangkok, Thailand.
- Boontawee, B., Kanchanaburagura, C., & Boonsermsuk, S., (1993). Studies on neem in Thailand. In: Read, M. D., & French, J. H., (eds.), *Genetic Improvement of Neem: Strategies for the Future* (pp. 41–45). Winrock International, Bangkok, Thailand.
- Bose, A., Chakraborty, K., Sarkar, K., Goswami, S., Chakraborty, T., & Pal, S., (2009). Neem leaf glycoprotein induces perforin-mediated tumor cell killing by T and NK cells through differential regulation of IFN $\gamma$  signaling. *Journal of Immunotherapy*, 32, 42–53.
- Bose, A., Chakraborty, K., Sarkar, K., Goswami, S., Haque, E., & Chakraborty, T., (2009). Neem leaf glycoprotein directs T-bet-associated type 1 immune commitment. *Human Immunology*, 70, 6–15.
- Browne, F. G., (1968). *Pests and Diseases of Forest Plantation Trees*. Clarendon Press, Oxford, UK.
- Butterworth, J. H., & Morgan, E. D., (1968). Isolation of a substance that suppresses feeding in locusts. *Chemical Communications (London)*, 1, 23, 24.
- Castellani, E., & Mohamed, M. I., (1984). Diseases of *Azadirachta indica* in Somalia. 1 *Cercospora* disease. *Rivista di Agricoltura Subtropicale Tropicale*, 78, 733–739.
- Chaimuangraj, S., Arakaki, J., Suzui, M., Morioka, T., Kinjo, T., & Kaneshiro, T., (2006). Antioxidative and modifying effects of a tropical plant *Azadirachta indica* (neem) on azoxymethane-induced preneoplastic lesions in the rat colon. *Asian Pacific Journal of Cancer Prevention*, 7, 467–471.
- Chakraborty, K., Bose, A., Pal, S., Sarkar, K., Goswami, S., & Ghosh, D., (2008). Neem leaf glycoprotein restores the impaired chemotactic activity of peripheral blood mononuclear cells from head and neck squamous cell carcinoma patients by maintaining CXCR3/CXCL10 balance. *International Immunopharmacology*, 8, 330–340. doi: 10.1016/j.intimp.2007.10.015.
- Chakravarti, B. P., & Gupta, D. K., (1975). A non-pigmented strain of *Xanthomonas azadirachtii* Moniz and raj causing leaf spot of neem (*Azadirachta indica* A. Juss.). *Current Science*, 44, 240, 241.

- Chamberlain, J. R., (1999). *Improvement of Neem (Azadirachta indica) and Its Potential Benefits to Poor Farmers in Developing Countries* (p. 13). Report on a visit to India. CNRD, Green College, Oxford, UK.
- Chamberlain, J. R., Childs, F. J., & Harris, P. J. C., (2000). An introduction to neem, its use and genetic improvement. In: *Improvement of Neem (Azadirachta indica) and its Potential Benefits to Poor Farmers in Developing Countries* (pp. 1–41). Article No. R7348.
- Chapman, R. F., (1974). The chemical inhibition of feeding by phytophagous insects: A review. *Bulletin of Entomological Research*, 64, 339–363.
- Chatterjee, A., & Pakrashi, S. C., (2010). *The Treatise on Indian Medicinal Plants* (Vol. 3, pp. 75–78). New Delhi: National Institute of Science Communication (CSIR).
- Chatterjee, A., & Pakrashi, S., (1994). *The Treatise on Indian Medicinal Plants* (Vol. 3, p. 76).
- Chaturevedi, A. N., (1993). In: Randhawa, N. S., & Parmar, B. S., (eds.), *Silviculture in Neem Research and Development, Society of Pesticide Science* (pp. 38–49). India.
- Chaudhary, O. P., (1997). New record of a shoot borer on neem. *Insect Environment*, 3, 8.
- Chavan, S. R., & Nikam, S. T., (1988). Investigation of alkanes from neem leaves and their mosquito larvicidal activity. *Pesticides*, 22(7), 32, 33.
- Chavan, S. R., (1984). Chemistry of alkanes separated from leaves of *Azadirachta indica* and their larvicidal vs. insecticidal activity against mosquitoes. In: Schmutterer, H., & Ascher, K. R. S., (eds.). *Proc. 2<sup>nd</sup> International Neem Conference* (pp. 59–65). GTZ, Eschborn, Germany.
- Childs, F., (1999). *Improvement of Neem (Azadirachta indica) and its Potential Benefits to Poor Farmers in Developing Countries* (p. 16). Report on a visit to Ghana. HDRA, Coventry, UK.
- Chirathamjaree, C., Ermel, K., & Sangwanich, A., (1997). Azadirachtin content of neem seed kernels from selected locations in Thailand. In: Rodcharoen, J., Wongsiri, S., & Mulla, M. S., (eds.). *Proceedings 1<sup>st</sup> Symposium on Biopesticides* (pp. 192–195). Chulalongkorn University Press, Bangkok, Thailand.
- Chopra, R. N., Nayer, S. L., & Chopra, I. C., (1956). *Glossary of Indian Medicinal Plants*/CSIR, New Delhi.
- Chopra, R., (1928). *Annual Report of the Entomologist to the Government, Punjab, Lyallpur, for the Year 1925–1926* (pp. 67–125). Report of Department of Agriculture of Punjab, 2 l.
- Ciesla, W. M., (1993). Pests and diseases of neem. In: Read, M. D., & French, J. H., (eds.), *Genetic Improvement of Neem: Strategies for the Future* (pp. 95–106). Winrock International, Bangkok, Thailand.
- Dasgupta, T., Banerjee, S., Yadava, P. K., & Rao, A. R., (2004). Chemopreventive potential of *Azadirachta indica* (Neem) leaf extract in murine carcinogenesis model systems. *Journal of Ethnopharmacology*, 92, 23–36. doi: 10.1016/j.jep.2003.12.004.
- Deshwal, R. P. S., Singh, R., Mallik, K., & Randhawa, G. J., (2005). Assessment of genetic diversity and genetic relationship among 29 populations of *Azadirachta indica* A. Juss. using RAPD markers. *Genetic Resources and Crop Evolution*, 52, 285–292.
- Dhar, R., Dawar, H., Garg, S., Basir, S. E., & Talwar, G. P., (1996). Effects of volatiles from neem and other natural products on gonotrophic cycle and oviposition of *Anopheles stephensi* and *Anopheles culicifacies*. *Journal of Medical Entomology*, 33, 195–201.
- Dhillon, R. S., Mohapatra, T., Singh, T., & Boora, K. S., (2007). Assessment of genetic diversity in *Azadirachta indica* based on DNA fingerprinting. *Indian Journal of Biotechnology*, 6(4), 1–8.
- Dod, V. N., Gabhane, V. V., Patil, B. N., & Pagar, P. C., (1997). Storability of neem (*Azadirachta indica* A. Juss.) seeds as influenced by storage containers. *Crop Research Hisar*, 14(2), 289–292.



- Dohroo, A., Karnwal, A., & Ghai, M., (2016). Recent developments in Neem (*Azadirachta indica* – A. Juss) derived antimicrobial constituents for control of human and plant diseases – a review. *Annales Academiae Medicae Siles*, 70, 220–223.
- Dohroo, N. P., & Gupta, S. K., (1995). Neem in plant disease control. *Agricultural Reviews*, 16(3), 133–140.
- Dorn, A., Rademacher, J. M., & Sehn, E., (1987). Effects of azadirachtin on reproductive organs and fertility in the large milkweed bug, *Oncopeltus fasciatus*. In: *Proc. 3<sup>rd</sup> Int. Neem. Conf.* (pp. 273–288).
- Drew, R. A., (1993). *Clonal Propagation of Neem by Tissue Culture*. World Neem Conference, Bangalore, India.
- Dua, V. K., Nagpal, B. N., & Sharma, V. R., (1995). Repellent action of neem cream against mosquitoes. *Indian Journal of Malaria*, 32, 47–53.
- Dubey, S., & Kashyap, P., (2014). *Azadirachta indica*: A plant with versatile potential. *Journal of Pharmaceutical Sciences*, 4(2), 39-46. doi: 10.5530/rjps.2014.2.2.
- El-Mahmood, A. M., Ogbonna, O. B., & Raji, M., (2010). The antibacterial activity of *Azadirachta indica* (neem) seeds extract against bacterial pathogens associated with eye and ear infection. *Journal of Medicinal Plants Research*, 4(14), 1414–1421.
- Emmanuel, C. J. S. K., (1998). Progress and present status of the provenance trial at AFRI, Jodhpur. In: *Proceedings of a Workshop of Neem (Azadirachta Indica)* (p. 5). AFRI, Jodhpur, India, (ed.) U.K. Tomar.
- Ermel, K., Pahlich, E., & Schmutterer, H., (1986). In: Schmutterer, H., & Ascher, K. R. S., (eds.) *Proceedings of 3<sup>rd</sup> International Neem Conference* (p. 171). Nairobi, Kenya.
- Fagoonce, I., (1984). Germination tests with neem seeds. In: Schmutterer, H., & Ascher, K. R. S., (eds.), *Natural Pesticides from the Neem Tree and Other Tropical Plants*. GTZ Press, Ecshborn, Germany.
- FAO., (1995a). *Procedures for Seed Collection and Exchange*. The Yellow Booklet).
- FAO., (1995b). *Revised Procedures and Design in Trial Establishment: 1. Nursery phase* (The Green Booklet).
- FAO., (1996). *Revised Procedures and Design in Trial Establishment: 2. Field trial* (The Red Booklet).
- FAO., (1998). *Seed Sources for the International Provenance Trials of Neem (The Blue Booklet)*.
- Farooqui, N., Ranade, S. A., & Sane, P. V., (1998). RAPD profile variation amongst provenances of neem. *Biochemistry and Molecular Biology International*, 45, 931–939.
- Fujiwara, T., Takeda, T., Ogihara, Y., Shimizu, M., Nomura, T., & Tomita, Y., (1982). Studies on the structure of polysaccharides from the bark of *Melia Azadirachta*. *Chemical Pharmaceutical Bulletin*, 30, 4025–4030.
- Gamene, C. S., Kraak, H. L., Van-Pijlen, J. G., & De-Vos, C. H. R., (1996). Storage behavior of neem (*Azadirachta indica*) seeds from Burkina Faso. *Seed Science and Technology*, 24(3), 441–448.
- Ganguli, S., (2002). Neem: A therapeutic for all seasons. *Current Science*, 82, 13, 14.
- Ghosh, D., Bose, A., Haque, E., & Baral, R., (2006). Pretreatment with neem (*Azadirachta indica*) leaf preparation in Swiss mice diminishes leukopenia and enhances the antitumor activity of cyclophosphamide. *Phytotherapeutic Research*, 20, 814–818.
- Girish, K., & Shankara, B. S., (2008). Neem-A green treasure. *Electronic Journal of Biology*, 4(3), 102–111.

- Govindachari, T. R., Sandhya, G., & Raj, S. P. G., (1992). Structure of azadirachtin K, a new tetranortriterpenoid from *Azadirachta indica*. *Indian Journal of Chemistry- Sect. B Organic and Medicinal Chemistry*, 31, 295–298.
- Gunasena, H. P. M., & Marambe, B., (1998). *Neem in Sri Lanka: A Monograph* (p. 62). University of Peradeniya, Peradeniya, Sri Lanka.
- Gupta, V. K., Solanki, K. R., Gupta, R., Kumar, R. V., & Datta, A., (1996). Reproductive biology of neem (*Azadirachta indica* A. Juss). *Range Management and Agroforestry*, 17(2), 187-192.
- Gupta, V. K., Solanki, K. R., Kumar, R. V., & Datta, A., (1998). Propagating neem (*Azadirachta indica*) by air layering. *Forest, Farm, and Community Tree Research Reports*, 3, 29-31.
- Hanachi, P., Fauziah, O., Peng, L. T., Wei, L. C., Nam, L. L., & Tian, T. S., (2004). The effect of *Azadirachta indica* on distribution of antioxidant elements and glutathione s-transferase activity in the liver of rats during hepato carcinogenesis. *Asia Pacific Journal of Clinical Nutrition*, 13, 170.
- Hansen, C. P., Thomsen, A., & Souvannavong, O., (1996). Recent activities of the international neem network. *Forest Genetic Resources*, 24, 33–39.
- Hashmat, I., Hussain, A., & Ahmed, A., (2012). Neem (*Azadirachta indica* A. Juss) – A nature's drugstore: An overview. *International Research Journal of Biological Sciences*, 1(6), 76-79.
- Hegde, N. G., (1993). *Improving the Productivity of Neem Trees* (pp. 69–79). World Neem Conference, Bangalore, India.
- Hellpap, C., & Leupolz, W., (1999). Influence of socio-economic factors on the use of neem insecticides by farmers. *Proceedings of the International Neem Conference*. University of Queensland, Australia.
- Hugo, S. B., & Rusell, A. D., (1983). *Pharmaceutical Microbiology* (Vol. 3, pp. 105–125). Blackwell Scientific Publication.
- Irshad, S., Butt, M., & Younus, H., (2011). *In vitro* antibacterial activity of two medicinal plants neem (*Azadirachta indica*) and peppermint. *International R. J. Pharmaceuticals*, 1(1), 9–14.
- Isac, L., (2011). *Effectiveness of Neem Oil Upon Pediculosis*. M.sc Thesis. Retrieved from: <http://repository-tnmgrmu.ac.in/4586/1/3004128lincyissac.pdf> (accessed on 02 September 2023).
- Isman, M. B., Koul, O., Luczynski, A., & Kaminski, J., (1990). Insecticidal and antifeedant bioactivities of neem oils and their relationship to azadirachtin content. *Journal of Agricultural Food and Chemistry*, 38, 1406–1411.
- Jahan, T., Begum, Z. A., & Sultana, S., (2007). Effect of neem oil on some pathogenic bacteria. *Bangladesh Journal of Pharmacology*, 2, 71, 72.
- Jindal, S. K., & Vir, S., (1994). Effect of different types of seed containers: Seed versus fruit storage on germination and seedling characteristics in neem. *Journal of Tropical Forestry*, 10, 301-304.
- Joarder, O. I., Naderuzzaman, A. T. M., Islam, R., Hossain, M., Joarder, N., & Biswas, B. K., (1993). *Micropropagation of Neem Through Axillary Bud Culture*. World Neem Conference, Bangalore, India.
- Johnson, S., Morgan, E. D., & Peiris, C. N., (1996). Development of the major triterpenoids and oil in the fruit and seeds of neem (*Azadirachta indica*). *Annals of Botany*, 78, 383–388.
- Joshi, M. S., & Thangane, S. R., (1996). *In vitro* propagation of *Azadirachta indica* A. Juss. (neem) by shoot proliferation. *Indian Journal of Experimental Biology*, 34, 480–482.

- Kabeeruddin, H., & Mufradat, M., (2007). pp. 400–411. New Delhi: Aijaz Publishing House.
- Kamaluddin, M., & Ali, M., (1996). Effects of leaf area and auxin on rooting and growth of rooted stem cuttings of neem. *New Forests*, 12(1), 11–18.
- Katsayal, U. A., & Nadabo, Y. A., (2008). Effects of methanol extract of *Azadirachta indica* leaves on the histology of liver and kidney of Wister rats. *Nigerian Journal of Pharmaceutical Sciences*, 7(1), 9–14.
- Kaushik, N., & Singh, B. G., (2001). In: Sener, B., (ed.), *Proc 3<sup>rd</sup> IUPAC International Conference on Biodiversity (ICOB-3)* (pp. 283–286). Antalya, Turkey. Kluwer Academic.
- Khalid, S. A., Duddect, H., & Gonzalez-Sierra, M. J., (1989). Isolation and characterization of an antimalarial agent of the neem tree *Azadirachta indica*. *Journal of Natural Products*, 52, 922–927.
- Khan, A. M., Alam, M. M., & Ahmad, R., (1974). Mechanism of the control of plant parasitic nematodes as a result of the application of oil cakes to the soil. *Indian Journal of Nematology*, 4, 93–96.
- Khillare, B., & Shrivastav, T. G., (2003). Spermicidal activity of *Azadirachta indica* (neem) leaf extract. *Contraception*, 68, 225–229. doi: 10.1016/S0010-7824(03)00165-3.
- Khosla, P., Bhanwra, S., Singh, J., Seth, S., & Srivastava, R. K., (2000). A study of hypoglycemic effects of *Azadirachta indica* (neem) in normal and alloxan diabetic rabbits. *Indian Journal of Physiology and Pharmacology*, 44, 69–74.
- Koul, A., Mukherjee, N., & Gangar, S. C., (2006). Inhibitory effects of *Azadirachta indica* on DMBA-induced skin carcinogenesis in Balb/c mice. *Molecular Cell Biochemistry*, 283, 47–55. doi: 10.1007/s11010006-2269-7.
- Koul, O., (2004). Neem: A global perspective. In: Koul, O., & Wahab, S., (eds.), *Neem: Today and in the New Millennium*. Springer, Dordrecht. [https://doi.org/10.1007/1-4020-2596-3\\_1](https://doi.org/10.1007/1-4020-2596-3_1).
- Kraus, W., Bokel, M., Bruhn, A., Cramer, R., Klaiber, I., Klenck, A., Nagl, G., et al., (1987). Structure determination by NMR of azadirachtin and related compounds from *Azadirachta indica* (*Meliaceae*). *Tetrahedron*, 43, 2817–2830.
- Kumar, A. R., Karthika, S., Gopalasatheeskumar, K., & Arulkumaran, G., (2019). Neem (*Azadirachta indica*): A miraculous medicinal plant from India. *International Journal of Universal Pharmacy and Bio Sciences*, 8(4), 48–59.
- Kumar, H. G., Mohan, C. K. V., Rao, J. A., & Nagini, S., (2009). Nimbolide a limonoid from *Azadirachta indica* inhibits proliferation and induces apoptosis of human choriocarcinoma (BeWo) cells. *Investigation on New Drugs*, 27, 246–252. doi: 10.1007/s10637008-9170-z.
- Kumar, R. V., & Gupta, V. K., (2002). *Thrust on Neem is Need of Today*. In: Employment News. New Delhi, India.
- Kumar, S., Srivastava, K. K., & Ullah, A., (1998). New record of a fungal infection in the culture of the land slug *Laevicaulis alte* – a severe pest of *Azadirachta indica* (neem) seedlings in Rajasthan and Gujarat. *Indian Forester*, 124, 351–353.
- Kumaran, K., Surendran, C., & Palani, M., (1996). Effect of pre-sowing chemical treatment on germination and seedling growth in neem (*Azadirachta indica* A. Juss.). *Indian Journal of Forestry*, 19(1), 87–88.
- Kundu, S. K., (1999). Comparative analysis of seed morphometric and allozyme data among four populations of neem (*Azadirachta indica*). *Genetic Resources and Crop Evolution*, 46, 569–577.
- Lokanadhan, S., Muthukrishnan, P., & Jeyaraman, S., (2012). Neem products and their agricultural applications. *Journal of Biopest*, 5, 72–76.

- Madhavan, S. R., & Gopi, K. C., (1992). Seasonal drying up of the distal shoots of neem (*Azadirachta indica* A. Juss.) and important insect pests associated with it. *Myforest*, 26, 33–50.
- Maithani, A., Parcha, V., Pant, G., Dhulia, I., & Kumar, D., (2011). *Azadirachta indica* (Neem) leaf: A review. *Journal of Pharmacy Research*, 4(6), 1824–1827.
- Manikandana, P., Vidjaya, L. P., Gopalakrishnanb, M., & Naginia, S., (2008). Evaluation of *Azadirachta indica* leaf fractions for *in vitro* antioxidant potential and *in vivo* modulation of biomarkers of chemoprevention in the hamster buccal pouch carcinogenesis model. *Food Chemistry and Toxicology*, 46, 2332–2343. doi: 10.1016/j.fct.2008.03.013.
- Marz, U., (1989). *The Economics of Neem Production and its Use in Pest Control* (p. 153). Wissenschaftsverlag Vauk Kiel, Germany.
- Mehrotra, M. D., & Pandey, P. C., (1991). Some important nursery diseases of *Azadirachta indica* and their control. In: *Monograph of Neem (Azadirachta Indica)*. International Book Distributors. Dehra Dun, India.
- Mehrotra, M. D., (1989). Leaf blight of some hardwood species in Assam and Meghalaya and its control in the nursery. *The Indian Forester*, 115, 378–384.
- Mehrotra, M. D., (1990). *Rhizoctonia solani*, a potentially dangerous pathogen of Khasi pine and hardwoods in forest nurseries in India. *European Journal Forest Pathology*, 20, 329–338.
- Mishra, R. N., (1995). Neem improvement research at the Arid Forest Research Institute, Jodhpur. *Indian Forester*, 121, 997–1002.
- Mohan, J., Chaudhari, L. D., & Jha, M., (1995). A note on increasing the viability of neem seed. *Indian Forester*, 121(11), 1085, 1086.
- Mondal, D., & Mondal, T., (2012). A Review on efficacy of *Azadirachta indica* A. Juss based biopesticides: An Indian perspective. *Research Journal on Recent Sciences*, 1(3), 94–99.
- Moniz, L., & Raj, H. H., (1967). *Xanthomonas azadirachtii* sp. Nov. causing leaf spot disease in *Azadirachta indica* A. Juss. *Indian Journal of Microbiology*, 7, 159–160.
- Mordue, A. J., & Blackwell, A., (1993). Azadirachtin: An update. *Journal of Insect Physiology*, 39, 903–924.
- Morgan, E. D., & Thornton, M. D., (1973). Azadirachtin in the fruit of *Melia azedarach*. *Phytochemistry*, 12, 3–91.
- Mulla, M. S., & Su, T., (1999). Activity and biological effects of neem products against arthropods of medical and veterinary importance. *Journal of the American Mosquito Control Association*, 15(2), 133–152.
- Murty, K. S., Rao, D. N., Rao, D. K., & Murty, L. B. G., (1978). A preliminary study on hypoglycemic and anti-hyperglycemic effects of *Azadirachta indica*. *Indian Journal of Pharmacology*, 10, 247–250.
- Nagaveni, H. C., Ananthapadmanabha, H. S., & Rai, S. N., (1987). Note on the extension of viability of *Azadirachta indica*. *Myforest*, 23, 245.
- Naniwadekar, M. Y., & Jadhav, A. S., (2012). Process development of pesticide production from *Azadirachta indica* A. Juss. *International Journal of Agriculture Innovation and Research*, 1(3), 65–70.
- Narayan, P., & Jasiwal, V. S., (1985). Plantlet regeneration from leaflet callus of *Azadirachta indica* A. Juss. *Tree Science*, 4(2), 65–68.
- Niture, S. K., Rao, U. S., & Srivenugopal, K. S., (2006). Chemopreventive strategies targeting the MGMT protein: Augmented expression in human lymphocytes and tumor cells by

- ethanolic and aqueous extracts of several Indian medicinal plants. *International Journal of Oncology*, 29, 1269–1278.
- Palanisamy, K., & Kumar, P., (1997). Effect of position, size of cuttings and environmental factors on adventitious rooting in neem (*Azadirachta indica* A. Juss.). *Forest Ecology and Management*, 98(3), 277–280.
- Palanisamy, K., Ansari, S. A., Kumar, P., & Gupta, B. N., (1998). Adventitious rooting in shoot cuttings of *Azadirachta indica* and *Pongamia pinnata*. *New Forests*, 16(1), 81–88.
- Pant, N., Garg, H. S., Madhusudanan, K. P., & Bhakuni, D. S., (1986). Sulfurous compounds from *Azadirachta indica* leaves. *Fitoterapia*, 57, 302–304.
- Parotta, J. A., (2001). *Healing Plants of Peninsular India* (pp. 495, 496). CABI Publishing, New York.
- Paul, R., Prasad, M., & Sah, N. K., (2011). Anticancer biology of *Azadirachta indica* L (neem): A mini review. *Cancer Biology and Therapy*, 12(6), 467–476. doi: 10.4161/cbt.12.6.16850.
- Paul, S. C., Miah, M. Y., & Bhattacharjee, S., (2013). *Neem Oil from Neem Seeds and Its Application*. LAP Lambert Academic Publishing, ISBN: 9783659462825.
- Pillai, N. R., & Santhakumari, G., (1984). Effect of nimbidin on acute and chronic gastroduodenal ulcer models in experimental animals. *Planta Medica*, 50, 143–146.
- Plant, N., Garg, H. S., Madhusudanan, K. P., & Bhakuni, D. S., (1986). Sulfurous compounds from *Azadirachta indica* leaves. *Fitoterapia*, 57, 302–304.
- Powel, W., Morgante, M., Andre, C., Hanafey, M., Vogel, J., Tingey, S., & Rafalski, A., (1996). The utility of RFLP, RAPD, AFLP, and SSR (microsatellite) markers for germplasm analysis. *Molecular Breeding*, 2, 225–238.
- Prasad, S., Ravindran, J., & Aggarwal, B. B., (2010). NFκB and cancer: How intimate is this relationship? *Molecular Cell Biochemistry*, 336, 25–37.
- Priyadarshini, R. V., Manikandana, P., Kumar, G. H., & Nagini, S., (2009). The neem limonoids azadirachtin and nimbolide inhibit hamster cheek pouch carcinogenesis by modulating xenobiotic-metabolizing enzymes, DNA damage, antioxidants, invasion, and angiogenesis. *Free Radical Research*, 43, 492–504.
- Puri, H. S., (1999). Neem: The divine tree: *Azadirachta indica*. In: *Medicinal and Aromatic Plants – Industrial Profiles* (Vol. 5, p. 182). Harwood Academic, Amsterdam.
- Radwanski, S. A., & Wickens, G. E., (1981). Vegetative fallows and potential value of the neem tree (*Azadirachta indica*) in the tropics. *Economic Botany*, 35, 398–414.
- Raissa, R., Safitri, A., Beltran, M. A. G., & Aulanniam, A., (2019). Phytoconstituents investigation on the ethanolic extract of *Azadirachta indica* var. 'Indonesian' and 'Philippines.' *Journal of Physics: Conference Series*, 1374, 120–180. doi:10.1088/1742-6596/1374/1/012018.
- Ramesh, K., & Padhya, M. A., (1988). *In vitro* propagation of neem (*Azadirachta indica*) leaves and its callus culture. *Indian Drugs*, 25, 526, 527.
- Ramji, N., Venkatakrishnan, K., & Madyastha, K. M., (1996). I 1-EPI-azadirachtin H from *Azadirachta indica*. *Phytochemistry*, 42, 561, 562.
- Ranganathan, S. M., Thangam, B. A. M., & Raja, S. M., (1996). Antidermatophytic activities of *Azadirachta indica*: An *in vitro* and *in vivo* studies. *Indian Journal of Dermatology*, 41(4), 113–117.
- Rao, B. S. N., & Rao, M. J., (1999). Antifungal activity of gedunin. *Current Science*, 46, 714–716.
- Rao, M. V. S., Rao, Y. V., Rao, V. S., & Manga, V., (1988). Induction and growth of callus in *Azadirachta indica* A. Juss. *Crop improvement*, 5(2), 203–205.

- Rembold, H., & Garcia, E. S., (1989). Azadirachtin inhibits *Trypanosoma cruzi* infection of its triatomine insect host, *Rhodnius prolixus*. *Naturwissenschaften*, 76, 71–78.
- Rembold, H., (1996). Neem and its general development for pest control. In: Singh, R. P., Chari, M. S., Raheja, K., et al., (eds.), *Neem, and Environment* (Vol. 1). Oxford and IBH publishing Co. Pvt. Ltd., New Delhi, India.
- Rengasamy, S., & Parmar, B. S., (1994). Azadirachtin content at different states of flowering and fruiting in neem. *Pesticide Research Journal*, 6(2), 193, 194.
- Ross, I. A., (2001). *Medicinal Plants of the World: Chemical Constituents, Traditional and Modern Medicinal Uses* (Vol. 2, pp. 81–85). Totowa, New Jersey.
- Sacadé, M., Hoekstra, F. A., Van, P. J. G., & Groot, S. P. C., (1998). A multi-factorial study of conditions influencing longevity of neem (*Azadirachta indica*) seeds. *Seed Science Research*, 8, 473–482.
- Sah, N. K., Khan, Z., Khan, G. J., & Bisen, P. S., (2006). Structural, functional and therapeutic biology of survivin. *Cancer Letters*, 244, 164–171. doi: 10.1016/j.canlet.2006.03.007.
- Sanakaran, K. V., Balasundaran, M., & Sharma, J. K., (1986). Seedling diseases of *Azadirachta indica* in Kerala, India. *European Journal of Forest Pathology*, 16, 324–328.
- Sarkar, K., Bose, A., Laskar, S., Choudhuri, S. K., Dey, S., & Roychowdhury, P. K., (2007). Antibody response against neem leaf preparation recognizes carcinoembryonic antigen. *International Immunopharmacology*, 7, 306–312. doi: 10.1016/j.intimp.2006.10.014.
- Sarkar, M. S., & Datta, P. C., (1986). Age factor in biosynthesis of nimbin and sitosol in the bark and callus of *Azadirachta indica*. *Indian Drugs*, 24, 62, 63.
- Schmutterer, H., & Zebitz, C. P. W., (1984). Effect of methanolic extracts from seeds of single neem trees of African and Asian origin, on *Epilachna varivestis* and *Aedes aegypti*. In: Schmutterer, H., & Ascher, K. R. S., (eds.), *Proc. 2<sup>nd</sup> International Neem Conference* (pp. 83–90), Rauischholzhausen, Germany.
- Schmutterer, H., (1988). Potential of azadirachtin-containing pesticides for integrated pest control in developing and industrialized countries. *Journal of Insect Physiology*, 34, 713–719.
- Schmutterer, H., (1990). Properties and potential of natural pesticides from the neem tree, *Azadirachta indica*. *Annual Review of Entomology*, 35, 271–297.
- Schoonhoven, L. M., (1982). Biological aspects of antifeedants. *Entomologia Experimentalis et Applicata*, 37, 57–69.
- Serrone, P. D., Toniolo, C., & Nicoletti, M., (2015). Neem (*Azadirachta indica* A. Juss) oil to tackle enteropathogenic *Escherichia coli*. *BioMed Research* (p. 10). ID 343610. doi: <http://dx.doi.org/10.1155/2015//343610>.
- Shah, J. S., Shah, M. B., Goswami, S. S., & Santani, D. D., (2006). Mechanism of action of antiulcer activity of bark extract of *Manilkara hexandra* against experimentally induced gastric ulcer in rats. *Pharmacognosy Magazine*, 2, 40–45.
- Sharma, S., (1998). Progress and present status of the provenance trial at TFRI, Jabalpur. In: *Proceedings of a Workshop of Neem (Azadirachta indica)* (pp. 6, 7). AFRI, Jodhpur, India, (ed.) U.K. Tomar.
- Shenoi, M. M., Abdul-wajid, S. M., & Sreenivas, S. S., (1996). Evaluation of *Azadirachta indica* and *Lawsonia inennis* for antifungal activity and studies on neem products for control of damping-off in tobacco nurseries. In: Singh, R. P., Chari, M. S., Raheja, A. K., & Kraus, W., (eds.), *Neem and Environment* (Vol. 2). Oxford and IBH publishing Co. Pvt. limited. New Delhi, India.

- Shimizu, T., (1988). Suppressive effects of azadirachtin on spermiogenesis of the diapausing cabbage armyworm, *Mamestra brassicae*, *in vitro*. *Entomologia Experimentalis et Applicata*, 46, 197–199.
- Shinde, G. N., & Biswas, B., (2011). An environ-economic backbone in the economic resurgence of barren and semi-arid regions: *Azadirachta indica*. *Journal of Natural Products and Plant Resources*, 1(2), 8–13.
- Shravan, K. D., Ramakrishna, R., Santhosh, K. M., & Kannappan, N., (2011). *In vivo* Antidiabetic evaluation of Neem leaf extract in alloxan induced rats. *Journal of Applied Pharmaceutical Science*, 1(4), 100-105.
- Shrivastava, D. K., & Swarnkar, K., (2014). Antifungal activity of leaf extract of neem (*Azadirachta indica* Linn). *International Journal of Current Microbiology and Applied Sciences*, 3(5), 305–308.
- Siddiqui, S. S., Faizi, S., Mahmood, T., & Siddiqui, B. S., (1986). Two new insect growth regulator meliacins from *Azadirachta indica* A. Juss (*Meliaceae*). *Journal of Chemical Society, Perkin Transactions*, 1, 1021–1026.
- Siddiqui, S. S., Mahmood, T., Siddiqui, B. S., & Faizi, S., (1988). Nonterpenoidal constituents from *Azadirachta indica*. *Planta Medica*, 54, 457–459.
- Sidhu, O. P., & Behl, H. M., (1996). Seasonal variation in azadirachtins in seeds of *Azadirachta indica*. *Current Science*, 70, 1084–1086.
- Silver, O. A., Cabrita, P., Diniz, A., & Gomes, B., (1997). Antimicrobial activity of Guinea Bissau traditional remedies. *Journal of Ethnopharmacology*, 50, 55–59.
- Singh, B. G., Mahadevan, N. P., Shanthi, K., Geetha, S., & Manimuthu, L., (1995). Multiple seedling development in neem (*Azadirachta indica*). *Indian Forester*, 121(11), 1049–1052.
- Singh, B. G., Mahadevan, N. P., Shanthi, K., Manimuthu, L., & Geetha, S., (1997). Effect of moisture content on the viability and storability of *Azadirachta indica* A. Juss (neem) seeds. *Indian Forester*, 123(7), 631–636.
- Singh, R. P., & Raheja, A. K., (1996). Strategies in management of insect pests with neem (*Azadirachta indica* A. Juss.). In: Singh, R. P., Chari, M. S., Raheja, A. K., & Kraus, W., (eds.), *Neem and Environment* (Vol. 1.). Oxford and IBH publishing Co. Pvt. Ltd. New Delhi, India.
- Singh, R. P., & Saxena, R. C., (1999). *Azadirachta Indica* A. Juss. Oxford & IBH Publishing CO. Pvt. Ltd.
- Singh, R. P., Chavi, M. S., Raheja, A. K., & Kraus, W., (1996). *Neem and Environment*. Science Publishers, INC.
- Singh, R., & Randhawa, J., (2008). Comparative assessment of genetic diversity of Indian and exotic neem (*Azadirachta indica*) using AFLP markers. *Indian Journal of Agricultural Sciences*, 78(10), 585–861.
- Sithisarn, P., Supabphol, R., & Gritsanapan, W., (2005). Antioxidant activity of Siamese neem tree (VP 1209). *Journal of Ethnopharmacology*, 99, 109–112. doi: 10.1016/j.jep.2005.02.008.
- Sivagnanam, K., Vinaya, R. R. S., Swaminathan, C., & Surendran, C., (1989). Studies on rooting response to growth regulators in *Azadirachta indica* A. Juss. In: *Proceedings of a Seminar on Vegetative Propagation*, Coimbatore, India.
- Solanki, K. R., (1998). *A Decade of Research 1988-1998* (pp. 26–29). National Research Centre for Agroforestry, Jhansi, India.
- Sonale, R. S., Pushpa, S., Murthy, K., & Ramalakshmi, T., (2019). Efficacy of neem kernel bioactives extracted using supercritical fluid carbon dioxide on selected dermatophytes

- and foodborne pathogens. *International Journal of Innovative Technology and Exploring Engineering*, 9(1), 4034–4039. doi: 10.35940/ijitee.A4949.119119.
- Srivastava, S. K., & Patel, P. N., (1969). Epidemiology of bacterial leaf spot, blight and shot-hole disease of neem in Rajasthan. *Indian Phytopathology*, 22, 237–244.
- Stephen, J. D. A., Gurumurthi, K., & Subramanian, K., (1998). *Studies on the In Vitro Extraction of Neem (Azadirachta indica A. Juss.) Chemicals and Propagation* (p. 55). Final Report submitted to the Council of Scientific and Industrial Research, New Delhi, India.
- Subapriya, R., Bhuvanewari, V., & Nagini, S., (2005). Ethanolic neem (*Azadirachta indica*) leaf extract induces apoptosis in the hamster buccal pouch carcinogenesis model by modulation of Bcl-2, Bim, caspase 8 and caspase 3. *Asian Pacific Journal of Cancer Prevention*, 6, 515–520.
- Subapriya, R., Kumaraguruparan, R., & Nagini, S., (2006). Expression of PCNA, cytokeratin, Bcl-2 and p53 during chemoprevention of hamster buccal pouch carcinogenesis by ethanolic neem (*Azadirachta indica*) leaf extract. *Clinical Biochemistry*, 39, 1080–1087. doi: 10.1016/j.clinbiochem.2006.06.013.
- Surendran, C., Rai, R. S. V., Sivaganam, K., Kumaravelu, G., Shanmugam, M., Ragupathy, A., Preetha, S., et al., (1992). *Paper Presented at the National Workshop on Non-Wood Forest Production*, BAI, Pune.
- Tan, M. T., & Sudderuddin, K. I., (1978). Effects of neem tree (*Azadirachta indica*) extracts on diamond-back moth (*Plutellarylostella*). *Malaysian Applied Biology*, 7, 1–9.
- Tandon, P., & Sirohi, A., (2010). Assessment of larvicidal properties of aqueous extracts of four plants against *Culex quinquefasciatus* Larvae. *Jordan Journal of Biological Sciences*, 3(1), 1–6.
- Tewari, D. N., (1992). *Monograph on Neem (Azadirachta Indica A. Juss.)* (p. 279). International Book Distributors, Dehra Dun, India.
- Thakurta, P., Bhowmik, P., Mukharjee, S., Hajra, T. K., Patra, A., & Bag, P. K., (2007). Antibacterial, antisecretory and antihemorrhagic activity of *Azadirachta indica* used to treat cholera and diarrhea. *Indian Journal of Ethnopharmacology*, 111(3), 607–612.
- Thiagarajan, M., & Murali, P. M., (1993). *High Frequency Regeneration of Neem in Vitro (Azadirachta Indica A. Juss.) from Immature Embryo Explants*. World Neem Conference, Bangalore, India.
- Thomsen, A., & Souvannavong, O., (1994). *The International Neem Network*. Forest Genetic Resources 22, FAO, Rome.
- Tinghui, X., Wegener, M., OShea, M., & Deling, M., (2001). *World Distribution and Trade in Neem Products with Reference to their Potential in China*. Conference (45<sup>th</sup>) from Australian Agricultural and Resource Economics Society, Adelaide, Australia. doi: 10.22004/ag.econ.126066. Retrieved from: <https://econpapers.repec.org/paper/agsaare01/126066.htm> (accessed on 02 September 2023).
- Tiwary, M. K., & Pandey, A., (2010). Feeding neem (*Azadirachta indica*) products to small ruminants as anthelmintic. *Food Science and Technology Bioinfo Publication*, 1(1), 976–982.
- TNAU., (1999). *Neem Research* (p. 9). Forest College and Research Institute, Mettupalayam, India.
- Tomar, U. K., (1998). Macro and micropropagation of adult neem trees. In: Tomar, U. K., (ed.), *Proceedings of a workshop on neem (Azadirachta indica)* (pp. 8, 9). Arid Forest Research Institute, Jodhpur, India.



- Trease, G. E., & Evans, W. C. A., (1989). *Textbook of Pharmacognosy* (pp. 100, 101). Bailliere Tinnall Ltd, London.
- Tripathi, R. K. P., & Tripathi, R. N., (1982). Reduction in bean common mosaic virus (BCMV) infectivity vis-à-vis crude leaf extract of some higher plants. *Experimentia*, 38(3), 349.
- Tsarev, J. E., (2010). *Global Sperm DNA Methylation Comparison in Fertile and Infertile Men: Preliminary Results*. Abstract N24, 4<sup>th</sup> North eastern European Meeting (NEEM), Riga, Latvia.
- Uniyal, K., & Uniyal, D. P., (1996). Mycoflora of neem seeds. *The Indian Forester*, 122, 423–427.
- Van, D. E. S. A., (1999). *The AZTEC Project*. Paper presented at the World Neem Conference 1999, UBC, Vancouver, Canada.
- Venkateswarlu, B., Mukhopadhyay, K., Mukhopadhyay, J., & Katyal, J. C., (1999). *Selection of Plus Trees of Neem with Emphasis on Azadirachtin Content and Development of Micropropagation Protocol for Mass Propagation*. Paper presented at the World Neem Conference, UBC, Vancouver, Canada.
- Venugopalan, S. K., & Visweswaran, N., (2013). Neem (*Azadirachta indica*): Prehistory to contemporary medicinal uses to humankind. *Asian Pacific Journal of Tropical Biomedicine*, 3(7), 505–514.
- Verma, N., & Srivastava, K. K., (1993). Fungal species associated with seeds of some common desert tree species. *Proceedings of 45 Annual Meeting of Indian Phytopathological Society*. Akola, Maharashtra, India.
- Wickremasinghe, I. P., & Simons, A. J., (1994). Differentiation of jack (*Artocarpus heterophyllus* Lam.) and neem (*Azadirachta indica* A. Juss.) by polyacrylamide gel electrophoresis. In: Gunasena, H. P. M., (ed.), *Proceedings of a Review Seminar on the UP-OFI Link Project* (pp. 77–96). University of Peradeniya, Peradeniya, Sri Lanka.
- Wilps, H., (1989). The influence of neem seed kernel extracts (NSKE) from the neem tree *Azadirachta indica* on flight activity, food ingestion, reproductive rate, and carbohydrate metabolism in the *Diptera Phormiaterraenovae* (Diptera, Muscidae). *Zoologische Jahrbucher Physiology*, 93, 271–282.
- Wince, S. L., Charan, A. A., & Bind, A., (2013). Antimicrobial activity of methanolic and acetonic extracts of *Azadirachta indica*, *Saracaasoca* and *Curcuma longa*. *International Journal of Medicinal and Pharmaceutical Sciences*, 3(2), 79–86.
- Yakkundi, S. R., Thejavathi, R., & Ravindranath, B., (1995). Variation of azadirachtin content during growth and storage of neem (*Azadirachta indica*) seeds. *Journal of Agricultural and Food Chemistry*, 43(9), 2517–2519.



**Taylor & Francis**

Taylor & Francis Group

<http://taylorandfrancis.com>

## CHAPTER 3

---

# Patchouli (*Pogostemon cablin* Benth.): A Comprehensive Review on Medicinal Aromatic Plant with Industrial Utilization

SONIA SINGH,<sup>1</sup> SHILPI PATHAK,<sup>1</sup> NIDHI SHARMA,<sup>2</sup> and NITIN AGRAWAL<sup>3</sup>

<sup>1</sup>*Institute of Pharmaceutical Research, GLA University, Mathura, Uttar Pradesh, India*

<sup>2</sup>*Noida Institute of Engineering and Technology, Greater Noida, Uttar Pradesh, India*

<sup>3</sup>*Faculty of Pharmacy, Raja Balwant Singh Engineering Technical Campus, Bichpuri, Agra, Uttar Pradesh, India*

---

### ABSTRACT

Patchouli, named as *Pogostemon cablin* Benth, which is an aromatic herb with bushy appearance belongs to the mint family. The herb is generally propagated for its oil purpose, mainly used in the manufacturing of cosmetics, perfumes, beverages, foodstuffs, and in medicines. This leafy plant is known for the presence of essential oil. The oil contains patchouli alcohol, considered as major components. The Patchouli oil quality is evaluated by determining the physical characteristics and quantitative analysis of oil. The quality is measured by patchouli alcohol (PA), as found as higher content component in the patchouli plant. Another chemical component, PA-containing norpatchoulene, gives aroma which is a typical resemblance of patchouli oil.

Oil is mainly known for spicy, warm, and sensuous smell/aroma. Around 2/3 of the oil quantity is produced through Java, followed by China and Malaysia. And the total world production of patchouli oil is estimated to be 800 tons per annum. In India, the production rate has been found uplifted in the last five years, it means it has 20 tons/annum of oil in 600 hectares. The cultivation of the herb is mainly done in Tamil Nadu, Assam, Karnataka, and West Bengal. Estimated around 92% of the oil is of non-odoriferous nature and the remaining portion consists of number of sesquiterpenes, including norpatchoulanol,  $\beta$ -patchoulene and  $\gamma$ -guaissilene are major aroma components. The two essential oil components, namely patchoulol and norpatchoulanol are present as major constituents.

The demand of Patchouli oil has been raised tremendously in perfumery industry. However, the oil has no substituents which could increase its value and even the demand in perfumery industries. It is found from the survey that the utility of Patchouli oil is estimated around 2,000 tons per annum throughout the worldwide. Whereas in India, this consumption has increase up to 300 tons per annum due to heavy demand in the manufacturing of chewing tobacco and pan masala. But the production is found below 50 tons per annum. Therefore, the country mainly dependable on imports of such articles from Indonesia.

The plant oil has used in inducing relaxation. In the Chinese system of medicine, the herb is used to treat headaches, nausea, cold, and diarrhea. Even the oil has been used in aroma therapy and also as hair conditioner. The essential oil is the best fixatives for heavy perfume that impart strength, lasting, and alluring notes properties.

The main objective of writing this manuscript is to share comprehensive literature on Pharmacognosy and Pharmacology of herb based on the literature available. The collective information, shared in this review will provide an exhaustive knowledge in exploring the therapeutic utilization of secondary metabolites of plant patchouli in several different areas such as medical use.

### 3.1 INTRODUCTION

Natural or herbal product(s) manufactured from plants are widely utilized in various herbal medicines to cure and prevent several health issues. Day-by-day, the demand of consuming herbal medicines is mostly increasing through the worldwide. Many of the natural-based products formulated out from the

herbs include volatile oils, colorants, dyes, cosmetics, and pharmaceutical products (Lubbe & Verpoorte, 2011). Medicinally aromatic herbs extracting essential oils that may exhibit various therapeutic applications and therefore, utilized in food, beverages, fragrance, flavoring agent and many more pharmaceutical based industries. About 90% of essential oils get consumed by the flavor and fragrance-based industries to manufacture several brands of perfumes, cosmetics, health care products, and other medicinal products (Maheshari, Vasantha, Sharma, & Chandel, 1993).

The plant *Pogostemon cablin* Benth., is the annual herb indigenous to south part of Asia belongs to family Lamiaceae (Maheshari, Vasantha, Sharma, & Chandel, 1993). The plant leaves contain aromatic volatile oil, of high-priced value in cosmetic, perfumery-based industries and also in aromatherapy (Hasegawa, Tajima, Toi, & Sugimura, 1992). Thus, it is widely employed in various cosmetic-based industries to produce healthcare products including body lotions, creams, soaps, and perfumes (Swamy, Mohanty, & Anuradha, 2014). The oil has been broadly used in depression, and anxiety. Various bioactive compounds possess potential therapeutic activities such as antioxidant, antibacterial, insect repellent, antifungal, analgesic, antiplatelet, fibrinolytic, antiemetic, antithrombotic, and antidepressant properties (Swamy, Mohanty, & Anuradha, 2014; Chakrapani et al., 2013; Priya, Swati, & Vilasrao, 2014; Swamy, Mohanty, Sinniah, & Maniyam, 2015). Therefore, all these characteristic features would make a *P. cablin*, considered as a commercial and pharmaceutical based crop with great significance in their applications around worldwide (Vijaya, 2004; Xian et al., 2007). The plant is ranked on top 20 volatile oil yielding herbal plants that has been traded continuously in the world market (Lubbe & Verpoorte, 2011; CBI, 2009; Singh, Singh, Srinivas, Rao, & Puttanna, 2015). The largest cultivator of the plant oil is Indonesia; moreover, it also produced on large scale from several number of countries such as Malaysia, India, China, Vietnam, Africa, and Singapore (Maheshari, Vasantha, Sharma, & Chandel, 1993; Swamy, Mohanty, & Anuradha, 2014; Swamy, Balasubramanya, & Anuradha, 2010; Swamy, Sudipta, Balasubramanya, & Anuradha, 2010).

### 3.2 BOTANICAL TAXONOMICAL CLASSIFICATION

The herb, Patchouli, is a member of Lamiaceae family. The botanical nomenclature of the plant is as described as below:

- Kingdom: *Planta*.

- Division: *Magnoliophyta*.
- Class: *Magnoliopsida*.
- Order: *Lamiales*.
- Family: *Lamiaceae/Labiatae*.
- Genus: *Pogostemon*.
- Species: *Cablin*.

### 3.3 SYNONYMS AND VERNACULAR NAMES

In 1845, Patchouli was first identified by Pelletier-Sautelet. Later on, in Philippines it is commonly known as ‘cabalam.’ In India, almost twenty-five species are found present. The plant, Patchouli is to be called by vernacular names like Tamala patra, Patcholi, and so on detailed in Table 3.1. The plant is also called Patchouli, Patchouly, or Pachouli (Synonym).

**TABLE 3.1** Vernacular Names of *Pogostemon cablin* Benth

Region	Vernacular Names
India	Tamala patra (Sans); Patcholi (Hin); Marathi: Patchapan (Mar); Patchapat (Beng)
Philippines	Kabling
Malaysia	Nilam
China	Guang Hou Xiang
Indonesia	Nilam
Thailand	Phimsen
Korea	Pachuri
Vietnam	Hoac Huong

### 3.4 GEOGRAPHICAL SOURCE

Herb is indigenous to many tropical areas of Asia and also grown in India, Thailand, Malaysia, West Africa, Mauritius, Vietnam, China, Philippines, and Indonesia. The plant is cultivated for its commercial utility in many states of India, namely Karnataka, Maharashtra, Kerala, Goa, Gujarat, and Assam (Harvey, 2008). The occurrence and distribution of *Pogostemon* with its species is summarized in Table 3.2 (Bhaskar & Vasantha, 2004; Thapa, Vashist, Atal, & Gupta, 1971; Hussaini, Agarwal, Roy, Prakash, & Shoeb, 1988; Khare, 2007; Murugan, Ravi, & Livingstone, 2008; Murugan,

Ravikumar, & Livingstone, 2010; Bhuiyan, Varshney, Shiam, Varshney, & Akter, 2011; Suthar & Patel, 2014). In other words, it is concluded that the Patchouli plant is a tropical annual herb that gets well adapted in warm and humid environment (Hasegawa, Tajima, Toi, & Sugimura, 1992).

**TABLE 3.2** Occurrence and Distribution of *Pogostemon* with its Species

Plants with Species/Varieties	Synonyms	Distribution and Occurrence
<i>Pogostemon heyneanus</i>	<i>Pogostemon fleurissant</i> Benth	South India, Malaysia, and Indonesia
<i>Pogostemon paniculatus</i>	–	India
<i>Pogostemon plenranthoides</i> Desf	<i>Pogostemon benghalensis</i>	Uttar Pradesh, India
<i>Pogostemon auricularis</i>	–	Thalacauvery, Karnataka, India
<i>Pogostemon comosum</i> Miq. Var.	–	Indonesia
<i>Pogostemon tomentosus</i> Hassk		
<i>Pogostemon pubescens</i> Benth	<i>Pogostemon parviflorus</i> Benth	India
<i>Pogostemon hirsutus</i> Benth.	–	Anamalai hills (Tamil Nadu) in India
<i>Pogostemon nilagiricus</i> Gamble.	–	Nilgiri hills (Tamil Nadu) in India
<i>Pogostemon benghalensis</i>	–	Bangladesh, India, Nepal, Myanmar, Sri Lanka, China and Thailand
<i>Pogostemon parviflorus</i>	–	Gujarat, India
<i>Pogostemon purpurascens</i>	–	Gujarat, India

Note: –: Not known.

Source: Bhaskar & Vasantha (2004); Thapa, Vashist, Atal, & Gupta (1971); Hussaini, Agarwal, Roy, Prakash, & Shoeb (1988); Khare (2007); Murugan, Ravi, & Livingstone (2008); Murugan, Ravikumar, & Livingstone (2010); Bhuiyan, Varshney, Shiam, Varshney, & Akter (2011); Suthar & Patel, 2014.

### 3.5 MORPHOLOGY

The herb patchouli (Lamiaceae) is a mint family. Traditionally, it is closely resembled to the family of Verbenaceae. It is an aromatic plant, abundantly employed as culinary herbs as shown in Figure 3.1. The herb is bushy in nature with erect, straight stems of two or three feet in length containing pink-white flowers. The flowers are small in size. The plant is much branched and pubescent with minute hairy appearance on the surface. The leaves of the plant contained cuneate base with long petiole. The floral whorls are many with sub-globose form with more density and are placed separately on the inflorescences (Harvey, 2008). The flowers are completely sessile, complete,

bisexual, zygomorphic, and hypogynous. The calyx with five sepals are of gamosepalous type. The corolla consists of four petals that is gamopetalous and light violet in color. The androecium is made up of four epipetalous stamens with basifixed anthers and the gynoecium is bicarpellary and of superior type (Swamy & Sinniah, 2016).



**FIGURE 3.1** Morphological diagram of *Pogostemon cablin*.



## 3.6 PHYTOCHEMISTRY

### 3.6.1 VOLATILE CHEMICAL CONSTITUENTS

The volatile oil of *P. cablin* Benth. collected from various cultivation areas and harvesting period were generally different. However, differences in the secondary metabolites of volatile oil, the herb has been grouped into two different chemotypes i-e Pogostone and Patchouliol. The study revealed that the Pogostone-type contain pogostone (rich oxygenated components) and patchouliol (low composition of non-oxygenated components). Whereas the Patchouliol-type contained equal quantities of oxygenated and non-oxygenated compounds with higher percentage of patchouliol, delta-guaiene, and alpha-guaiene (Luo, Liu, Feng, Guo, & Cao, 2003).

The essential oil collected from the leaf of patchouli plants during daytime may produce some variations in their content percentage. Variations in the amount of phytoconstituents present with respect to different regions are summarized in Table 3.3. Using GC-MS techniques, some of chemical compounds have been isolated as essential oil, including  $\beta$ -patchoulene, 1-octen-3-ol,  $\beta$ -elemene,  $\alpha$ -guaiene, trans-caryophyllene,  $\gamma$ -patchoulene,  $\alpha\alpha$ -patchoulene, humulene, dihydroaromadendrane,  $\alpha$ -bulnesene, trans- $\beta$ -guaiene, patchoulol, and  $\beta$ -copaen-4- $\alpha$ -ol (Silva, Ehlert, Ming, & Marques, 2004). Nine more components as  $\alpha$ -guaiene, caryophyllene,  $\beta$ -patchoulene,  $\beta$ -guaiene,  $\delta$ -guaiene, seychellene, pogostone, spathulenol, and patchoulol identified using GC-MS. According to Hierarchical clustering analysis, it is observed that around 18 components have been grouped into three clusters such as pogostone, an interim and patchouliol (Hu et al., 2006). Around twenty-two compounds have been identified using GC-MS analysis, oxygenated sesquiterpenes and sesquiterpenes including  $\beta$ -patchoulene, trans-caryophyllene,  $\delta$ -elemene,  $\beta$ -elemene, cis-thujopsene,  $\alpha$ -guaiene,  $\alpha$ -humulene,  $\gamma$ -patchoulene, valencene, seychellene,  $\beta$ -selinene, germacrene D,  $\alpha$ -selinene, germacrene A, 7-epi- $\alpha$ -selinene, viridiflorene,  $\alpha$ -patchoulene,  $\alpha$ -bulnesene; longipinanol, patchoulol, globulol, 1-octen-3-ol. Out of all these, patchoulol considered as a chief constituent. Even some minor chemical constituents were seychellene,  $\alpha$ -patchoulene,  $\beta$ patchoulene,  $\gamma$ -patchoulene, and  $\delta$ -patchoulene (Tsai et al., 2007). Another study done on the essential oils obtained using steam distillation from the plants was determined using GC-MS. Approximately the technique has identified 41 components including two major biomolecules,  $\alpha$ -guaiene of 20.62% and  $\alpha$ -bulnesene of 16.18% (Bunrathep, Lockwood, Songsak, & Ruangrungsi, 2006).

From *P. cablin* plant, 1 w components from essential oil were isolated and investigated by using GC and GC/MS analysis such as  $\beta$ -patchoulene,  $\alpha$ -patchoulene, patchoulol,  $\alpha$ -guaiene, selinene, seychellene, and  $\beta$ -caryophyllene (Sundaresan, Singh, & Mishra, 2009). Patchouli volatile oils obtained from different source treatments of plant material were subjected to quantitative estimation using GC-FID technique, revealed the detection of around 36 components of which  $\alpha$ -guaiene,  $\delta$ -guaiene, pogostol,  $\alpha$ -patchoulene and seychellene considered the main ones. It is observed that patchouli alcohol as a major essential oil component was present in higher percentage in laboratory scale produced volatile oils when compared with all other commercial samples (Hussin et al., 2012). HPLC-DAD quantitative analysis was used to detect and identify the essential oil component, pogostone with flavonoids including rhamnetin, apigenin, ombuine, methoxyflavone derivatives, as tabulated in Table 3.4 and in Figure 3.2 (Li, Yin, Li, Huang, Ye, & Zhang, 2014).

### 3.6.2 NON-VOLATILE CHEMICAL CONSTITUENTS

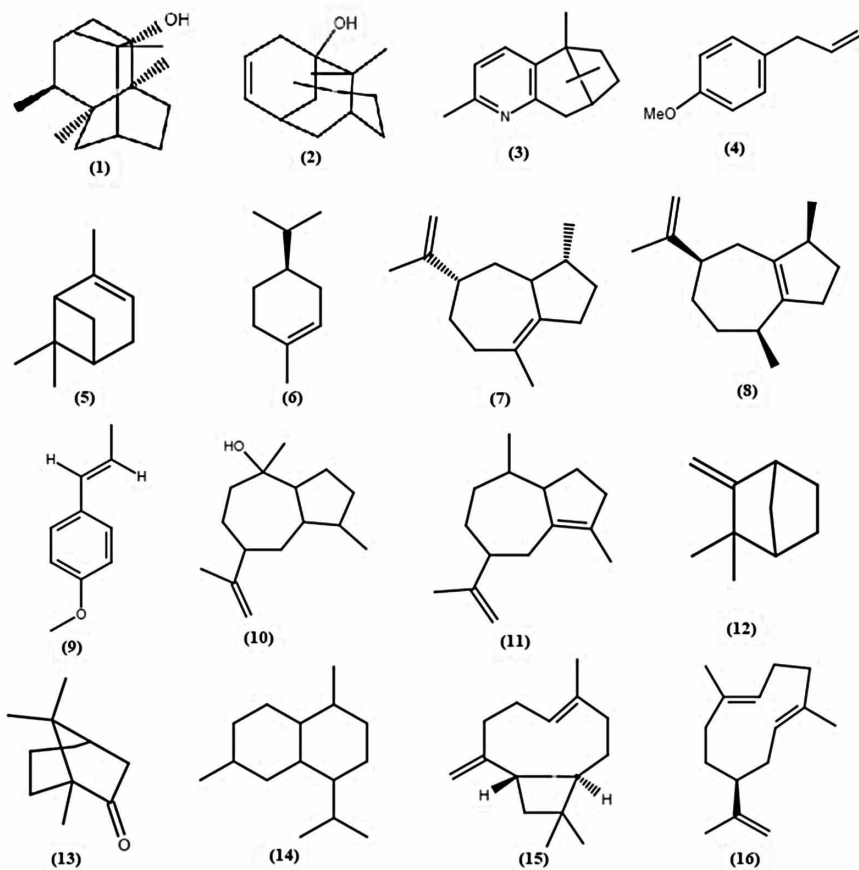
Investigators isolated three novel flavonoids, 5,7-dihydroxy-3',4'-dimethoxyflavanone, ombuin, and licochalcone A from *Pogostemon cablin* Benth. aerial parts using fractionation technique. The isolated Licochalcone A compound possessed *in-vitro* cytotoxicity as well as PI-PLC $\gamma$ 1 inhibition property (Park, Park, Lee, & Kim, 1998). The standardization of crude drug i-e "*Pogostemoni herba*" as *Pogostemon cablin* Benth., is used as an ingredient in Kampo medicines (Chinese medicines) was done by using thin layer chromatography (TLC) and high-performance liquid chromatography (HPLC) along with suitable chemical markers. Three new components belonging to phenylethanoid class named as crenatoside, acteoside, and isoacteoside extracted from the methanolic herbal extract (Amakura et al., 2008).

With the application of column chromatography and spectra data analysis, nine new compounds were identified and characterized as 5-hydroxymethyl-2-furfural, epifriedelinol, beta-sitosterol, succinic acid, daucosterol, 3'''-O-methylcrenatoside, crenatoside, apigenin-7-O-beta-D-(6''-p-coumaryl)-glucoside and isocrenatoside (Huang, Mu, Zhang, Deng, Song, & Hao, 2009). Four flavonoids named as 4',5-Dihydroxy-3',7-dimethoxyflavanone, 5-Hydroxy-7,3',4'-trimethoxyflavanone, 5,4'-Dihydroxy-3,7,3'-trimethoxyflavone, 5-Hydroxy-3,7,4'-tetramethoxyflavone from *P.*

*cablin* Benth. along with pogostone were successively separated and identified by using HSCCC, prep-HPLC, ESI-MS<sup>n</sup>, <sup>1</sup>H-NMR, and <sup>13</sup>C-NMR (Li, Zhang, Xie, Liang, Wang, & Ito, 2011). Additionally, new sesquiterpene hydroperoxide components like 10 $\alpha$ -hydroperoxyguaia-1,11-diene, 1 $\alpha$ -hydroperoxyguaia-10(15),11-diene and 15 $\alpha$ -hydroperoxyguaia-1(10),11-diene were fractionated out using chromatographic techniques from acetone extract of dried patchouli (Kongkathip et al., 2009). Furthermore, the hexane fraction was separated and then it has been purified to result in obtaining patchouli alcohol, a mixture of  $\beta$ -sitosterol and stigmasterol, and 7,3',4-tri-O-methylerydiol (Wang, Yin, Zhang, Ye, Zhang, & Zhang, 2010). Around 12 non-volatile compounds were isolated and identified from the ethanolic stem extract of the plant as tilianin; diosmetin-7-O-beta-D-glucopyranoside; uracil; 3''-O-methylcrenatoside; apigenin-7-O-(3'',6''-di-(E)-p-coumaroyl)-beta-D-galactopyranoside; agastachoside; 4,5-dihydroxy-3, 3,7-trimethoxyflavone; soya-cerebroside I and II; 5-hydroxy-3, 3,4,7-tetramethoxy flavone; crenatoside; isocrenatoside and acacetin. The isolation of these components was done by using silica gel and Sephadex LH-20 CC (Column chromatography) and with the application of spectroscopic analysis, the structural elucidations of such compounds were obtained (Ding, Lin, Liu, & Wei, 2011).

Using spectroscopic analysis of 15-hydroxypatchoulol 15-O- $\beta$ -D-glucopyranoside and 3 $\alpha$ -hydroxypatchoulol 3-O- $\beta$ -D-glucopyranoside with rubusoside, as diterpene glycoside, identified from the *Pogostemon cablin* Benth. ethanolic extract (Zhou et al., 2011).

Four novel patchoulol derivatives i.e 6 $\alpha$ -hydroxypatchoulol, 2 $\beta$ ,12-dihydroxypatchoulol, 8 $\alpha$ ,9 $\alpha$ -dihydroxypatchoulol and 3 $\alpha$ ,8 $\alpha$ -dihydroxypatchoulol, and together with sesquiterpenoids and flavonoids were obtained from *Pogostemon cablin* Benth. aerial parts and even their structure elucidation were done with the help of 1D- and 2D-NMR (Kiuchi, Matsuo, Ito, Qui, & Honda, 2004). Sesquiterpenes such as 2-keto-1(5)- $\beta$ -patchoulene-4 $\beta$ -ol; 8-keto-9(10)- $\alpha$ -patchoulene-4 $\alpha$ -ol; 2-keto-4 $\beta$ -hydroxyguaia-1,11-diene and 2-keto-1(5)- $\beta$ -patchoulene-4 $\alpha$ -ol obtained from *P. cablin* Benth. stems (Zhou, Peng, Li, Guo, Xiong, & Lin, 2013). Around 13 target compounds were isolated and elucidated as patchoulol; friedelin; pogostone; epifriedelinol; methyl oleanolate; oleanolic acid; 5- $\alpha$ -stigmast-3,6-dione; beta-sitosterol; stigmast-4-ene-3-one; retusin; pachypodol; dibutyl phthalate; (-)-guaiaicylglycerol (Swamy & Sinniah, 2015). Using HPLC-DAD method, both volatile and non-volatile compounds quantified and identified as pogostone and flavonoids including rhamnetin; apigenin; ombuine from patchouli (Kocevski et al., 2013).



**FIGURE 3.2** Chemical structure of volatile and non-volatile constituents of *Pogostemon cablin*. Structure: (1) patchouli alcohol; (2) nor-patchoulinol; (3) Patchouli pyridine; (4) methyl chavicol; (5) pinene; (6) limonene; (7) bulnescene; (8) guaiene; (9) anethole; (10) pogostol; (11) aciphyllene; (12) camphene; (13) camphor; (14) cardinine; (15) caryophyllene; and (16) germacrene.

## 3.7 PHARMACOLOGICAL ACTIVITIES

### 3.7.1 ANTIFUNGAL ACTIVITY

The bioactive compound, Patchoulol present in the essential oil exhibited suppression action on the growth of *Aspergillus flavus* and *A. oryzae* observed in the colony form (Li et al., 2012). Li *et al.* demonstrated both *in vitro* as

**TABLE 3.3** Distribution of Chemical Constituents of *Pogostemon cablin* Along with Their Percentage in Different Regions of Countries

Geographical Source	Active Constituents	Part of Plant with Percentage	Analytical Methods	References
Wanning City, Hainan	Patchouli alcohol	Stem (36.06%); leaf (37.74%)	GC/MS	Pullagummi et al. (2014)
	Pogostone $\beta$ -patchoulene, $\beta$ -elemene, transcaryophyllene, $\delta$ -guaiene, seychellene, $\alpha$ -patchoulene, aciphyllene, $\alpha$ -guaiene, patchouli alcohol and pogostone.	Stem (17.08%); leaf (0.85%) 1%		
Vietnam	$\beta$ -patchoulene, $\alpha$ -patchoulene, $\delta$ -patchoulene, $\beta$ -elemene, $\alpha$ -guaiene, seychellene, $\delta$ -guaiene, pogostol, $\delta$ -cardinene, $\alpha$ -bulnesene, $\beta$ -caryophyllene.	–	GC, GC/MS, NMR	Dung, Leclercq, Thai, & Moi (1989)
Philippines	Patchoulol	32%–37%		
	Germacrene-B	–	–	Hasegawa, Tajima, Toi, & Sugimura (1992); Rakotonirainy, Gaydou, Faure, & Bombarda (1997)
Gaoyao County, Guangdong Province	Pogostone	Stems (30.99%); leaf (21.31%).	GC/MS	Luo, Feng, Guo, & Li (1999)
	Patchoulol	Stems (10.26%); leaf (37.53%)		
	<i>Trans</i> -caryophyllene	Stems (4.92%); leaf (6.75%)		
	$\alpha$ -guaiene	Stems (2.27%); leaf (6.18%)		
Leizhou county	Seychellene	Stems (1.56%); leaf (1.99%)		
	Alpha-guaiene, delta-guaiene, alpha-patchoulene, trans-caryophyllene, seychellene, patchouli alcohol, aciphyllene	Stem leaves	GC-MS	Feng, Guo, & Luo (1999)

**TABLE 3.3** (Continued)

Geographical Source	Active Constituents	Part of Plant with Percentage	Analytical Methods	References
Indonesia	Aciphyllene, $\gamma$ -gurjunene, 7-epi- $\alpha$ selinene, germacrene D  $\alpha$ -guaiene, $\delta$ -patchoulene, $\alpha$ -pinene, $\beta$ -pinene, limonene, $\alpha$ -copaene, aciphyllene, $\delta$ -guaiene, 7-epi- $\alpha$ -selinene, caryophyllene oxide, $\delta$ -elemene, $\alpha$ -patchoulene, norpatchoulol, 1,10-epoxi-11-bulnesene, $\beta$ -elemene, nortetrapatchoulol, patchoulol, $\beta$ -caryophyllene, seychellene, patchoulenone, oxopatchoulol, pogostol, cycloseychellene, $\alpha$ -humulene, germacrene-D, $\gamma$ -gurjunene, isopatchoulenone, $\alpha$ -patchoulene.	–  –	GC (FID) and GC/MS	Guan, Quan, Xu, & Cong (1998); Kang, Kim, Chi, & Won (1998)

**TABLE 3.4** Distribution of Chemical Constituents in Different Parts of the Plant, *Pogostemon cablin* Benth

Chemical Class	Part Used	Chemical Constituents	References
Volatile oil	Root	Pogostone (71%); d nerolidol (88%); hexadecanoic acid (21%); patchouli alcohol (98%); trimethyl dodecatrienol acetate in the root oil; pogostone (45%); d nerolidol (17%); hexadecanoic acid (15%); patchouli alcohol (15%); geranyl acetate (93%); trans farnesol (63%); trans-farnesal (40%).	Luo, Feng, & Guo (2000)
–	–	Patchouli oil; patchouli alcohol	Su et al. (2014)
Whole herb	–	Patchouli; friedelin; pogostone; epifriedelinol; retusine; pachypodol; oleanolic acid; daucosterol; $\beta$ -sitosterol.	Guan, Quan, Xu, & Cong (1994)
Leaves, aerial-parts	–	Patchouli (42.2–57.7%); $\alpha$ -guaiene (6.4–17.9%); pogostol (0.3–5.0%); ( <i>E</i> )-caryophyllene (2.1–3.6%); $\alpha$ -bulnesene (9.0–15.2%); seychellene (3.4–6.9%)	Ram, Rajendra, Amit, & Ved (2019)
–	Root	Norpatchoulenol (5.3%); $\beta$ -pinene (4.5%); pogostone (70.2%)	Ram, Rajendra, Amit, & Ved (2019)
–	Leaf; cell cultures.	Patchouli alcohol (60.30%)	Bunrathep, Lockwood, Songsak, & Ruangrunsi (2006)
–	Leaf	$\alpha$ -Pinene; $\beta$ -pinene; sabinene; isodene; $\beta$ -patchoulene; $\alpha$ -copaene; $\beta$ -caryophyllene; $\alpha$ -guaiene; seychellene; $\alpha$ -humulene; $\alpha$ -patchoulene; Dselinene; germacrene; calamenene; cadina-1,4-diene; ledene; patchouli.	Sundaresan, Singh, & Mishra (2009)
–	–	$\alpha$ -Pinene; $\beta$ -pinene; limonene; pentadecane; $\alpha$ -humulene; germacrene D; $\beta$ -elemene; $\delta$ -elemene; $\alpha$ -selinene; selina-4,11-diene; selina-4,6-diene; 7-epi- $\alpha$ -selinene; $\beta$ -selinene; selina-4(15),7(11)-diene; $\alpha$ -bulnesene; $\alpha$ -guaiene; aciphyllene; ( <i>E</i> )- $\beta$ -caryophyllene; ( <i>E</i> )-7-epi- $\beta$ -caryophyllene; ( <i>Z</i> )- $\beta$ -caryophyllene; $\beta$ -patchoulene; $\delta$ -patchoulene; $\gamma$ -patchoulene; $\alpha$ -patchoulene; $\alpha$ -copaene; seychellene; cycloseychellene; 1 $\alpha$ ,5 $\alpha$ -epoxyguai-11-ene; caryophyllene oxide; ( <i>Z</i> )-nerolidol; patchouli; norpatchoulenol; nortetracyclopatchouli; 6-hydroxy patchouli; pogostol; $\beta$ -patchoulenone; rotundone; 2 $\beta$ -methoxy-14-nor- $\beta$ -patchoul-1(5)-ene-4-one; 14-nor- $\beta$ -patchoul-1(5),2-diene-4-one; pocahemiketal A; pocahemiketal B; 4-hydroxy-6-methyl-3-(1-oxobutyl)-2H-pyran-2-one; pocahemiketal B; dhelwangan; pogostone; nonyl acetate; 2-methylbutyric acid; pentanoic 4-methylpentanoic acid; 2-methylpentanoic acid; heptanoic acid; nonanoic acid; cis-2-pentylcyclopropanecarboxylic acid; trans-2-pentylcyclopropanecarboxylic acid; pheno, o-cresol; dimethylphenol; 4-vinylphenol; 14-nor- $\beta$ -patchoul-1(5)-ene-4-one; guaiacol; eugenol; patchouli pyridine; guaipyridine; ( <i>Z</i> )-3-(but-1-enyl)-4-propylpyridine; ( <i>E</i> )-3-(but-1-enyl)pyridine; 2-ethylfuran; $\eta$ -selinene; hotrienol; geosmin; 2-methoxy-3-isopropylpyrazine; quinoxaline; methyl N-methylanthranilate; 14-nor- $\beta$ -patchoul-1(5)-ene-2,4-dione; pentanoic acid.	Swamy & Sinniah (2015)

TABLE 3.4 (Continued)

Chemical Class	Part Used	Chemical Constituents	References
Sesquiterpenes	Leaves, stems, and roots.	Isocaryophyllene; caryophyllene; $\alpha$ -guaiene; seychellene; patchoulene; $\alpha$ -bulnesene; caryophyllene oxide; $\beta$ -guaiene; (-)-globulol; $\beta$ -humulene; patchouli alcohol; trans-farnesol.	Teris & Daniel (2017)
	–	Patchoulol; $\alpha$ -guaiene; $\alpha$ -patchoulene; $\delta$ -guaiene; seychellene.	Ying et al. (2014)
	–	$\alpha$ -guaiene; $\alpha$ -patchoulene; $\alpha$ -patchoulene; patchoulol; $\alpha$ -bulnesene.	Yuliani & Sri Haryani (2012); Gokulakrishnan et al. (2013)
	–	2 $\beta$ ,12-Dihydroxypatchoulol; 3 $\alpha$ ,8 $\alpha$ -Dihydroxypatchoulol; 8 $\alpha$ ,9 $\alpha$ -Dihydroxypatchoulol; 6-Hydroxypatchoulol.	Zhou et al. (2011)
	–	1 $\alpha$ -Hydroperoxyguaia-10(15),11-diene; 10 $\alpha$ -Hydroperoxyguaia-1,11-diene; 15 $\alpha$ -Hydroperoxyguaia-1(10),11-diene; 1 $\alpha$ -Hydroperoxyguaia-10(15),11-diene; 15 $\alpha$ -Hydroperoxyguaia-1(10),11-diene.	Kiuchi, Matsuo, Ito, Qui, & Honda (2004)
	–	4-Hydroxy-10-epi-rotundone; 2-Keto-4 $\beta$ -hydroxyguaia-1,11-diene.	Li et al. (2013)
Phytosterols	–	Daucosterol; $\beta$ -sitosterol; stigmasterol; stigmast-4-ene-3-one; 5 $\alpha$ -Stigmast-3,6-dione.	Swamy & Sinniah (2015)
Triterpenoids	–	Methyl oleanolate; friedelin; epifriedelinol; oleanolic acid.	Swamy & Sinniah (2015)
Phenyl propene	–	Methyl chavicol; anethole.	Swamy & Sinniah (2015)
Fatty acids	–	2-methyl-haxanoic acid; 2-methyl-butyric acid; nonanoic-acid; 4-methyl-pentanoic acid; octanoic acid; heptanoic acid; pentanoic acid.	Swamy & Sinniah (2015)
Glycosides	–	Acteoside; agastachoside; 3 $\alpha$ -hydroxypatchoulol 3-O- $\beta$ -D-glucopyranoside; apigenin-7-O-(3'',6''-di-(E)-p-coumaroyl)- $\beta$ -D-galacto-pyranoside; 15-Hydroxypatchoulol 15-O- $\beta$ -D-glucopyranoside; 3''-O-methylcrenatoside; soya-cerebroside I and II; isocrenatoside; tilianin; rubusoside.	Li, Zhang, Xie, Liang, Wang, & Ito (2011); Wang, Yin, Zhang, Ye, Zhang, & Zhang (2010); Ding, Lin, Liu, & Wei (2011)
	–	Acacetin; diosmetin-7-O- $\beta$ -D-gluco-pyranoside; 4',5-dihydroxy-3,3',7-trimethoxyflavone; 5-hydroxy-3,3',4',7-tetramethoxyflavone.	Swamy & Sinniah (2015)
	–	Apigenin; 5,4'-dihydroxy-3,3',7-trimethoxyflavanone; rhamnetin; 4',5-dihydroxy-3,3',7-trimethoxyflavone; ombuin; 3,5-dihydroxy-7,4'-dimethoxyflavanone; 5-hydroxy-3,7,3',4'-tetramethoxyflavanone; 5-Hydroxy-7,3',4'-trimethoxyflavanone.	Swamy & Sinniah (2015)
	–	Licochalcone A; 4',5-Dihydroxy-3',7-dimethoxyflavanone; 5,7-Dihydroxy-3',4'-dimethoxyflavanone.	Swamy & Sinniah (2015)
	–	Retusine	Swamy & Sinniah (2015)



**TABLE 3.4** (Continued)

Chemical Class	Part Used	Chemical Constituents	References
Miscellaneous	–	p-Vinyl-phenol; phenol; trans-2-pentylcyclopropyl carboxylic-acid; dibutyl phthalate; succinic acid; tschimganical A; uracil; p-methoxycinnamaldehyde; anisaldehyde; benzaldehyde; dehydracetic-acid; dimethylphenol; eugenol; eugenol cinnamic aldehyde; o-cresol.	Li, Zhang, Xie, Liang, Wang, & Ito (2011); Kongkathip et al. (2009); Wang et al. (2010); Ding, Lin, Liu, & Wei (2011)

*Note:* –: not known.

well *asin vivo* antifungal properties of pogostone, considered as the most promising component extracted from *P. cablin* Benth and found efficacious in *Candida* infections, especially against vulvovaginal candidiasis (Yi et al., 2013). Another study demonstrated the effective action of pogostone, along with its semi-synthesized analogs against *Candida albican* infections. From this experimental work it is suggested that with some structure alteration in pogostone analogs would result in representing them as the most promising antifungal compounds (Liu et al., 2012). Hexane, acetone, and even ethanol extracts of plant showed *in-vitro* anti-candida activity, by inhibited the fungal growth up to 50% (Xie & Tang, 2009).

### **3.7.2 GASTRO-PROTECTIVE ACTIVITY**

*P. cablin* Benth. aqueous extract found effective in protecting the intestinal barrier by regulating the serum nitric oxide (NO) levels, TNF-alpha, and maintaining the membrane fluidity of IMC in Wistar rats. This research investigation would give the evidence bases of gastroprotective action of the plant extract against surgical or trauma operation (Yang et al., 1999).

### **3.7.3 ANTIEMETIC ACTIVITY**

Five chemical compounds namely, stigmast-4-en-3-one, pogostol, patchouli alcohol, pachypodol, retusin, and extracted from n-hexane plant extract demonstrated antiemetic property against copper sulfate induced-emesis in young chick model (Miyazawa, Okuno, Nakamura, & Kosaka, 2000).

### **3.7.4 ANTI-MUTAGENIC ACTIVITY**

Miyazawa *et al.* explained the suppressive action of plant methanolic extract on UMU gene expression by producing SOS response in bacterial strain, *Salmonella typhimuium* TA1535/pSK1002 against furylfuramide as mutagen. Furthermore, the different fractions such as hexane, butanol, dichloromethane, and water were obtained from the methanol extract, where it has been concluded that some effective compounds of flavonoid group, kumatakenin, pachypodol, ombuine were extracted and characterized from dichloromethane fraction with the aid of silicon-di-oxide column chromatography (Jing et al., 2013).

### **3.7.5 ANTI-NOCICEPTIVE ACTIVITY**

Patchouli oil at 20 mg/kg, 40 mg/kg, and 80 mg/kg possessed a significant anti-nociceptive action; this activity was proved against the writhing test and the hot-plate test. It is observed that all respective doses of patchouli oil significantly extended the writhing latent period and even potentially reduced the writhing frequency. Additionally, all different doses of oil significantly attenuated the latency duration at a time interval of 30, 60, and 90 minutes in hot plate test (Xuan et al., 2019).

### **3.7.6 ANTI-ALLERGIC ACTIVITY**

Anti-allergic property of patchouli oil was evaluated by using delayed-type hypersensitivity, passive cutaneous anaphylaxis test and Schultz–Dale reaction induced in the serum anti-ovalbumin and 2,4-dinitrochlorobenzene model in Sprague Dawley rat. However, it is resulted that all doses (20, 40, and 80 mg/kg) of oil considerably suppressed the delayed-type hypersensitivity and the passive cutaneous anaphylaxis test (Manglani, Deshmukh, & Kashyap, 2011).

The patchouli oil significantly decreased the intracellular calcium ion level and up-regulation of cyclooxygenase 2 along with reduction in the mu-opioid receptor expression; this would play a crucial role as an anti-nociceptive effect of oil. Furthermore, the component markedly reduced the latency duration of writhing and visceral pain after the induction of intra-plantar administration of formalin in mice model (Cahyono, Rimawati, & Kusuma, 2019).

### **3.7.7 ANTI-DEPRESSANT**

Alcoholic extract markedly decreased the immobility duration in tail suspension and forced swimming test which direct towards its potential antidepressant activity (Kiyohara et al., 2012). Encapsulation of patchouli alcohol was done by freeze drying technique using maltodextrin, and gum Arabic along with tween 80 catalysts as an emulsifier. Such essential oil encapsulation was then tested for antidepressant activity in mice. The method of encapsulation would help in resolving the oxidative damage of essential oil as these oils are very much sensitive and even susceptible towards the increased temperature,

oxidation, humidity which ultimately causes degradation of the components (Wu, Li, Wang, Jin, & Wang, 2011).

### **3.7.8 ANTI-VIRAL ACTIVITY**

The essential oil component, patchouli alcohol possessed anti-viral activity against influenza virus H1N1 having  $IC_{50}$  of 2.635  $\mu$ M in a dose dependent fashion, collectively obtained from methanolic leaf extract of *Pogostemon cablin* Benth. The activity was investigated using the plaque forming assay, in which active ingredients declined the increased plaque numbers via showing 75% and 89% at concentration of 2  $\mu$ g/mL and 10  $\mu$ g/mL, respectively (Lu, Liao, Huang, Lin, Liu, Chiu, & Peng, 2011). Similarly, the patchouli alcohol also tested against H<sub>2</sub>N<sub>2</sub> influenza A virus (Kim, Cho, Kim, Cho, & Kim, 2010).

### **3.7.9 ANTIOXIDANT ACTIVITY**

Patchouli alcohol (28.8%) showed efficient free radical scavenging activity in patchouli (Feng et al., 2014). In Korea, the herb is effectively possessed antioxidant activity against free radical induced human brain cell injury. It potentially protected necrotic as well as apoptotic cell death produced via H<sub>2</sub>O<sub>2</sub> radical in human neuroglioma cell line A172. It mainly acted as a dose dependent manner at 0.2 to 5 mg/ml of concentrations. It markedly inhibited the cellular ATP depletion and PARPs activation induced by Hydrogen peroxide radical (Li et al., 2014). Ultraviolet irradiation produces ROS in excess amount, followed by generating inflammatory response, by which it is known as an efficient skin photoaging inducer. Excess production of ROS along with inflammation causes over stimulation of matrix metalloproteinases, which ultimately produces extracellular matrix degradation. This may lead to cause dryness, wrinkling effect, and skin laxity. Patchouli alcohol, an active ingredient considerably urged the speedy retrieval in UV-induced skin lesions, either via anti-inflammatory mechanism or through free radical scavenger properties which may cause down-regulation in MMP-1 and MMP-3 expression (Lin et al., 2014). Patchouli alcohol inhibited the phosphorylation of NF- $\kappa$ B and I $\kappa$ B which attenuate inflammation caused by lipopolysaccharide in mice (Ichikawa, Kinoshita, & Sankawa, 1989).

### 3.7.10 SKIN DISEASES

The herb is well known in Chinese traditional medicine for curing various skin disorders. Protective effect of patchouli oil against UV induced skin photoaging effect in mice through antioxidant property, followed by suppression in the MDA content and effectively up regulation mechanism in SOD, CAT, and GSH-Px (Pattnaik, Subramanyam, & Kole, 1996).

### 3.7.11 ANTIBACTERIAL ACTIVITY

Hot aqueous extract of *P. cablin* Benth. were screened to possess inhibitory action against K<sup>+</sup> contracture of guinea pig taenia coli (Edwards, Buck, Shawcross, Dawson, & Dunn, 2004). Additionally, it is found that the patchouli oil was satisfactorily efficacious in inhibiting bacterial strains (around 20) and fungi (12) (Yang, Zhang, Yang, & Liu, 2013). Apart from this, the plant contained antibacterial action against *Staphylococcus aureus* strains, namely, methicillin-resistant *S. aureus*, MRSA, and *S. aureus* NCTC 6571 (Pullagummi et al., 2014). Though, pogostone and patchouli alcohol proved to possess strong antimicrobial effects. Such activities were determined using antimicrobial *in vitro* assay and molecular docking technology (Vázquez-Sánchez, Cabo, & Rodríguez-Herrera, 2014). Hexane extract of the plant showed maximum zone of inhibition against *S. aureus* using disc diffusion assay (Singh, Singh, Ebibeni, & Singh, 2013). The volatile oils were found effective against foodborne pathogen, *S. aureus* (Yu et al., 2015). Even the ethanol extract of patchouli oil with 5.4% found effective against enteric micro-organisms from the fecal droppings of Gecko (*Hemidactylus frenatus*), a common house lizard (Karimi, 2014). The patchouli alcohol was employed in the prevention of *H. pylori* infection and contained urease inhibitory action potential (Park, Park, Lee, & Kim, 1998). With this, the bioactive component, patchouli alcohol was evaluated for antibacterial activity and urease inhibitory action, through it is proved to be used in the treatment of GIT disorders (Hsu, Yang, Tsai, Chen, Huang, & Tsai, 2006).

### 3.7.12 ANTI-CANCER ACTIVITY

Using cytotoxicity-guided fractionation, Licochalcone A isolated from *P. cablin* Benth. showed effective recovery in curing of promyelocytic leukemia cells (HL-60). The compound contained effective *in vitro* cytotoxicity and

PI-PLC $\gamma$ 1 inhibition property; and was capable of generating terminal differentiation along with monocyte by using non-specific acid esterase assay (Luo, Feng, & Guo, 2000). Patchouli alcohol contained anticancer property via declining the growth of cell and even enhances the apoptosis in case of human colorectal cancer cells. It exhibited HDAC enzyme inhibition activity and HDAC2 expression as described in Table 3.5 (Su et al., 2014).

### **3.8 MARKET TRADE AND ITS APPLICATION**

Patchouli oil is well known for pleasant aroma and extensively used in beverage, soap, incense stick, perfume, and food product based industries that have increased its market demand (Vijaya, 2004). In recent years, India is nearby importing about 175–250 tons patchouli oil from various sources such as Malaysia, Singapore, and Indonesia. Though it is mixed with different levels of grades. A small volume of 10 tons is produced by the India. Though, the international rate of oil has fluctuating from US\$ 25 to 150/kg. But India has the potential to meet continuous supply of oil. From the survey; it is observed the worldwide demand of *P. cablin* Benth. is around 1,600 tons of oil per yearly, whereas the India has 10–20 tons/annum. Some of the patent formulations are tabulated in Table 3.6.

#### **3.8.1 PERFUME INDUSTRY**

Patchouli is mainly used in fragrances like particularly in camphor, cedarwood, vetiver, calamus, oakmoss, and orris. An old-fashioned form of patchouli perfume, popular in Europe many years ago. It remained however a common export item to South America for a long time. Before World War II Germans innovated alcohol-free perfumes. Dissolved the perfume oils in diethyl phthalate, castor oil, or other solvents.

#### **3.8.2 BIOTECHNOLOGY ASPECTS**

The herb has considered as industrially valued medicinal aromatic plant that currently gained its demand because of the presence of essential oils. It is mainly employed in flavoring, fragrance, and pharmaceutical based industries. Thus, clonal propagation technique is quite necessary to have homogeneous *P. cablin* Benth. to recover the increased worldwide demand. The

**TABLE 3.5** Phytochemical Constituents of *Pogostemon cablin* Benth. and Their Pharmacological actions

Part Used/Extract Used	Mode of Study	Active Constituents	Mechanism of Action	Pharmacological Action	References
Patchouli oil	–	Pogostone, patchouli alcohol	–	Antimicrobial	Ding, Lin, Liu, & Wei (2011)
–	Bacteria strains screened using <i>in-vitro</i> agar double dilution; <i>In vivo</i> study using white mice (Kunming strain).	Patchouli alcohol	–	Antibacterial	Xian, Xue, Shui-Ping, & Wei-Qi (2013)
–	Human bacteria (10) and fungi (06) using agar well diffusion as well as macro-broth dilution method.	Essential oil	–	Antibacterial, antifungal	Wan et al. (2016)
–	Strains of skin bacteria (16) <i>in vivo</i> .	Patchouli alcohol, alpha-bulnesene, patchoulene	–	Antibacterial	Puspa, Shoma, Jaripa, & Md Nural (2013)
Patchouli oil, obtained through the hydro-distillation of fresh leaves and young shoots of <i>P. cablin</i>	Gram-positive micro-organisms using disk diffusion method.	Patchouli oil	–	Antibacterial	Yang, Chaumont, & Millet (1998)
–	<i>Aspergillus flavus</i> and <i>Aspergillus oryzae</i> .	Patchouli alcohol	–	Antifungal	Karimi (2014)
Leaves	Dermatophytes and fungi	Patchouli alcohol, $\alpha$ -bulnesene, patchoulene	–	Antifungal	Kocevski et al. (2013); Depo, Jean-Pierre, & Joëue (2000)

TABLE 3.5 (Continued)

Part Used/Extract Used	Mode of Study	Active Constituents	Mechanism of Action	Pharmacological Action	References
–	<i>Candida albican</i> , <i>Candida tropicalis</i> , <i>Candida krusei</i>	Pogostemon oil	–	Antifungal	Gang-Sheng, Jie-Hua, Yao-Hui, Min, & Bo (2012)
<i>P. cablin</i> Benth. methanol extract	Paw licking, writhing response model (analgesic activity); paw edema (anti-inflammatory)	–	↓ed MDA (malondialdehyde) level, ↑sed antioxidant enzymes activities, ↓sed the tumor necrosis factor- $\alpha$ and cyclooxygenase-2 activities.	Analgesic, anti-inflammatory	Lu Tsung, Jung-Chun, Tai-Hung, & Ying-Chih (2011)
Patchouli oil	Xylene-induced ear edema, acetic acid-induced vascular permeability, carrageenan-induced paw edema.	$\beta$ -patchoulene	↓sed the cellular infiltration in paw tissue, MDA level, MPO activity.	Anti-inflammatory	Zhang et al. (2016)

Note: –: not known;

↓ed: decreased;

↑sed: increased



**TABLE 3.6** Patent Formulations of *Pogostemon cablin* Benth

Sl. No.	Formulations	Models Used	Applications	References
1.	Transdermal patch of indomethacin using patchouli oil.	Modified Keshary-chein diffusion cells ( <i>in vitro</i> ).	Transdermal patch	Das & Ahmed (2017)
2.	Gel dosage form using patchouli oil.	Skin irritation tests on human volunteers.	Burn wound	Febriyenti, Rizki, & Netty (2019)
3.	Lotion formulation combination of Cananga and patchouli oil.	Against <i>Aedes aegypti</i> mosquitoes.	Natural repellent lotion.	Uswatun & Dian (2019)
4.	Pellet formation with patchouli alcohol and poloxamers.	<i>In-vitro</i> testing	Immediate release pellets formulation.	Jin-Bin et al. (2015)
5.	Novel herbal oil formulation using oils of patchouli, eucalyptus, rosemary, citronella, and neem leaves.	Against mosquito larvae.	Natural mosquito and house fly repellent oil.	Das, Vasudeva, & Dang (2016)
6.	Modified gel using Piper betel and patchouli oil.	Against nulliparous (3–5 days old) female <i>Aedes aegypti</i> .	Natural repellants.	Mutiara & Umar (2015)
7.	Anti-acne serum formulation (essential oil and patchouli oil).	Antibacterial property against <i>Propioni bacterium acnes</i> .	Antibacterial	Noor, Ifat, Lutfi, & Febi (2017)
8.	Anti-acne emulgel preparation using patchouli leaves aromatic oil.	Agar diffusion method against <i>Propioni bacterium acnes</i> .	Anti-acne	Dra Rr Sulistiyarningsih, & Dra Emma, & Puti (2015)
9.	Anti-adherence and anti-biofilm using volatile oils of patchouli, vanilla, ylang ylang stabilized with metal nanoparticles (iron oxide).	Against <i>Klebsiella pneumoniae</i> and <i>Staphylococcus aureus</i> .	Anti-adherence, anti-biofilm.	Maxim et al. (2014)
10.	Montmorillonite (MMT) nanoparticles as patchouli oil bleaching.	–	Bleaching material to reduce colors in oil.	Tisna, Yulida, & Teuku (2019)
11.	Biocompatible coating containing iron oxide nanoparticles incorporated with patchouli essential oil.	Biocompatibility and bio-distribution assays ( <i>in vitro</i> and <i>in vivo</i> ).	Antimicrobial, as wound dressing.	Marius et al. (2016)

**TABLE 3.6** (Continued)

Sl. No.	Formulations	Models Used	Applications	References
12.	Silver nanoparticles using methanol leaf extract of Patchouli.	<i>Staphylococcus aureus</i> , <i>Bacillus subtilis</i> , <i>Pseudomonas aeruginosa</i> , <i>Escherichia coli</i> .	Antibacterial, antioxidant, anticancer.	Qing et al. (2019)
13.	Microcapsules containing patchouli oil with chitosan and Arabic gum.	–	–	Guang et al. (2013)
14.	Silver nanoparticles bio-fabricated using an essential oil of <i>Aquilaria sinensis</i> and <i>Pogostemon cablin</i> .	Larvicidal and pupicidal toxicity tested against larvae and pupae of the dengue and Zika virus vector, <i>Aedes albopictus</i> .	Natural biopesticide for mosquito control.	Hassan, Hatem, Guofeng, Jiabin, & Mo (2018)

Note: –: not known.

information regarding plant genetics, their chemistry, and other applicable technologies provide more resources to produce commercial crop.

### **3.8.3 INSECTS REPELLENT**

Its oil is also used in all-purpose insect repellent and mainly against the Formosan subterranean termite.

### **3.8.4 NUTRITIVE**

Herbal tea is composed of Patchouli leaves. In most of the places of India, it is used as a vegetable (Swamy & Sinniah, 2016).

## **3.9 CONCLUSION**

The herb, *P. cablin* Benth. is explored worldwide as a key bioactive component for the discovery of new entities with advanced therapeutic potential. This chapter summarizes all the latest updated experimental and research work with respect to the chemistry and pharmacological effectiveness of the plant.

## **KEYWORDS**

- **antifungal activity**
- **anti-mutagenic activity**
- **antioxidant activity**
- **biotechnology**
- **essential oils**
- **non-volatile chemical constituents**
- **patchouli oil**
- **phytochemistry**
- ***Pogostemon cablin* Benth**

## REFERENCES

- Amakura, Y., Yoshimura, M., Mouri, C., Mikage, M., Kawahara, N., Goda, Y., Yoshida, T., & Yakugaku, Z., (2008). Convenient TLC-based identification test for the crude drug “*Pogostemon herba*.” *Yakugaku Zasshi.*, 128, 1833–1837.
- Bhaskar, S., & Vasantha, K. T., (2004). Agronomic bottlenecks, genetic barriers, and marketing impediments in patchouli production. *J. Med. Aromat. Plant Sci.*, 22, 396–403.
- Bhuiyan, M. N. I., Varshney, V. K., Shiam, C., Varshney, T. A., & Akter, F., (2011). Composition of essential oil of the leaf and inflorescence of *Pogostemon benghalensis* (Burm.f.) Kuntze. *Int. Res. J. Plant Sci.*, 2, 271–275.
- Bunrathep, S., Lockwood, G. B., Songsak, T., & Ruangrunsi, N., (2006). Chemical constituents from leaves and cell cultures of *Pogostemon cablin* and use of precursor feeding to improve patchouli alcohol level. *Sci. Asia*, 32, 293–296.
- Cahyono, E., Rimawati, B. C., & Kusuma, E., (2019). Antidepressant activity of patchouli alcohol microcapsule. *Journal of Physics: Conference Series.*, 1321.
- CBI, (2009). *Natural Ingredients for Cosmetics: The EU Market for Essential Oils for Cosmetics*. CBI.
- Chakrapani, P., Venkatesh, K., Singh, B. C. S., Jyothi, B. A., Kumar, P., Amareshwari, P. A., & Rani, R., (2013). Phytochemical, pharmacological importance of patchouli [*Pogostemon cablin* (Blanco) Benth.] an aromatic medicinal plant. *Int. J. Pharm. Sci. Rev. Res.*, 21, 7–15.
- Das, A., & Ahmed, A. B., (2017). Formulation and evaluation of transdermal patch of indomethacin containing patchouli oil as natural penetration enhancer. *Asian Journal of Pharmaceutical and Clinical Research.*, 10, 320–325.
- Das, K., Vasudeva, C., & Dang, R., (2016). Economical novel formulation and evaluation of herbal oils for mosquito and house fly repellent activities. *Annals of Phytomedicine.*, 5, 91–96.
- Depo, Y., Jean-Pierre, C., & Joëue, M., (2000). Antifungal activity of the essential oils from *Agastache rugosa* and *Pogostemon cablin* against dermatophytes and opportunistic fungi. *Journal of Chinese Pharmaceutical Sciences.*, 35, 9–11.
- Ding, W. B., Lin, L. D., Liu, M. F., & Wei, X. Y., (2011). Two new sesquiterpene glycosides from *Pogostemon cablin*. *J. Asian Nat. Prod. Res.*, 13, 599–603.
- Dra Rr Sulistiyarningsih, M. K., & Dra Emma, S. M. S., & Puti, L., (2015). Anti-acne (*Acne vulgaris*) emulgel formulation of aromatic oil from patchouli leaves (*Pogostemon cablin* Benth) and *in vitro* antibacterial activity test against *Propionibacterium acnes*. *International Journal of Medicine and Pharmacy*, 3, 57–64.
- Dung, N. X., Leclercq, P. A., Thai, T. H., & Moi, L. D., (1989). Chemical composition of patchouli oil of Vietnam. *Proceedings of the International Congress of Essential Oils, Fragrances, and Flavors*. New Delhi, India.
- Edwards, J. V., Buck, R., Shawcross, S. G., Dawson, M. M., & Dunn, K., (2004). The effect of essential oils on methicillin-resistant *Staphylococcus aureus* using a dressing model. *Burns.*, 30, 772–777.
- Febriyenti, F., Rizki, F. P., & Netty, S., (2019). Formulation and evaluation of patchouli oil gel for burn wound. *J. Sains. Farm. Klin.*, 6, 191–194.
- Feng, X. X., Yu, X. T., Li, W. J., Kong, S. Z., Liu, Y. H., Zhang, X., Xian, Y. F., et al., (2014). Effects of topical application of patchouli alcohol on the UV-induced skin photoaging in mice. *Eur. J. Pharm. Sci.*, 63, 113–123.

- Feng, Y., Guo, F., & Luo, J., (1999). GC–MS analysis of volatile oil of *Herba Pogostemonis* collected from Leizhou county. *Zhong Yao Cai.*, 22, 241–243.
- Gang-Sheng, W., Jie-Hua, D., Yao-Hui, M., Min, S., & Bo, L., (2012). Mechanisms, clinically curative effects, and antifungal activities of cinnamon oil and pogostemon oil complex against three species of candida. *Journal of Traditional Chinese Medicine.*, 32, 19–24.
- Gokulakrishnan, J., Elumalai, K., Dhanasekaran, S., Anandan, A., & Krishnappa, K., (2013). Pupicidal and repellent activities of *Pogostemon cablin* essential oil chemical compounds against medically important human vector mosquitoes. *Asian Pacific Journal of Tropical Disease.*, 3, 26–31.
- Guan, L., Quan, L. H., Xu, L. Z., & Cong, P. Z., (1994). Chemical constituents of *Pogostemon cablin* (Blanco) Benth]. *Zhongguo Zhong Yao Za Zhi.*, 19, 355, 356.
- Guan, L., Quan, L. H., Xu, L. Z., & Cong, P. Z., (1998). Chemical constituents of *Pogostemon cablin* (Blanco) Benth. *Planta Med.*, 64, 464–466.
- Guang, T. H., Zi, M. Y., Zheng, P., Guang, W., Min, Z., Yu, X. P., & Pu, W. L., (2013). Preparation, and properties analysis of slow-release microcapsules containing patchouli oil. *Advanced Materials Research*, 641, 642, 935–938.
- Harvey, A. L., (2008). Natural products in drug discovery. *Drug Discov. Today.*, 13, 894–901.
- Hasegawa, Y., Tajima, K., Toi, N., & Sugimura, Y., (1992). An additional constituent occurring in the oil from a patchouli cultivar. *Flavor Fragrance J.*, 7, 333–335.
- Hasegawa, Y., Tajima, K., Toi, N., & Sugimura, Y., (1992). An additional constituent occurring in the oil from a Patchouli cultivar. *Flavor Fragr. J.*, 7, 333–335.
- Hassan, G., Hatem, F., Guofeng, M., Jiaxin, T., & Mo, J., (2018). Larvicidal and pupicidal evaluation of silver nanoparticles synthesized using *Aquilaria sinensis* and *Pogostemon cablin* essential oils against dengue and zika viruses vector *Aedes albopictus* mosquito and its histopathological analysis. *Journal Artificial Cells, Nanomedicine, and Biotechnology*, 46.
- Hsu, H. C., Yang, W. C., Tsai, W. J., Chen, C. C., Huang, H. U., & Tsai, Y. C., (2006). Alpha-bulnesene, a novel PAF receptor antagonist isolated from *Pogostemon cablin*. *Biochem. Biophys. Res. Commun.*, 345, 1033–1038.
- Hu, L. F., Li, S. P., Cao, H., Liu, J. J., Gao, J. L., Yang, F. Q., & Wang, Y. T., (2006). GC–MS fingerprint of *Pogostemon cablin* in China. *J. Pharm. Biomed. Anal.*, 42, 200–206.
- Huang, L., Mu, S., Zhang, J., Deng, B., Song, Z., & Hao, X., (2009). Chemical constituents from involatile moiety of *Pogostemon cablin*. *Zhongguo Zhong Yao Za Zhi.*, 34, 410–413.
- Hussaini, F. A., Agarwal, S., Roy, R., Prakash, O., & Shoeb, A., (1988). Novel cleistanthane diterpenoids from *Pogostemon auricularis*. *J. Nat. Prod.*, 51, 212–216.
- Hussin, N., Mondello, L., Costa, R., Dugo, P., Yusoff, N. I., Yarmo, M. A., Abwahab, A., & Said, M., (2012). Quantitative and physical evaluation of patchouli essential oils obtained from different sources of *Pogostemon cablin*. *Nat. Prod. Commun.*, 7, 927–930.
- Ichikawa, K. T., Kinoshita, T., & Sankawa, U., (1989). The screening of Chinese crude drugs for calcium antagonist activity: Identification of active principles from the aerial part of *Pogostemon cablin* and the fruits of *Prunus mume*. *Chem. Pharm. Bull.*, 37, 345–348.
- Jin-Bin, L., Yong-Zhuo, L., Yun-Long, C., Jian-Hui, X., Wei-Hai, L., Jian, N. C., Xiao-Ping, L., & Zi-Ren, S., (2015). Novel patchouli alcohol ternary solid dispersion pellets prepared by poloxamers. *Iran J. Pharm. Res.*, 14, 15–26.
- Jing, J. H., Hai, M. C., Chu-Wan, L., Dian-Wei, W., Xiao-Li, W., & Shu-Jiang, S., (2013). Experimental study on antinociceptive and anti-allergy effects of patchouli oil. *Journal of Essential Oil Research.*, 25, 488–496.

- Kang, S. S., Kim, J. S., Chi, H. J., & Won, D. H., (1998). Isolation and quantitative determination of patchouli alcohol from *Pogostemon cablin* Benth. *Korean J. Pharmacogn.*, 29, 18–21.
- Karimi, A., (2014). Characterization and antimicrobial activity of patchouli essential oil extracted from *Pogostemon. cablin* [Blanco] Benth [*Lamiaceae*]. *Adv. Env. Biol.*, 8, 2301–2309.
- Karimi, A., (2014). Characterization and antimicrobial activity of patchouli essential oil extracted from *Pogostemon cablin* (Blanco) Benth. (*Lamiaceae*). *Advances in Environmental Biology.*, 8, 2301–2309.
- Khare, C. P., (2007). *Indian Medicinal Plants: An Illustrated Dictionary*. Springer Science & Business Media, New York, USA.
- Kim, H. W., Cho, S. J., Kim, B. Y., Cho, S. I., & Kim, Y. K., (2010). *Pogostemon cablin* as ROS scavenger in oxidant-induced cell death of human neuroglioma cells. *Evid. Based Complement. Alternat. Med.*, 7, 239–247.
- Kiuchi, F., Matsuo, K., Ito, M., Qui, T. K., & Honda, G., (2004). New sesquiterpene hydroperoxides with trypanocidal activity from *Pogostemon cablin*. *Chem. Pharm. Bull.*, 52, 1495–1496.
- Kiyohara, H., Ichino, C., Kawamura, Y., Nagai, T., Sato, N., & Yamada, H., (2012). Patchouli alcohol: *In vitro* direct anti-influenza virus sesquiterpene in *Pogostemon cablin* Benth. *J. Nat. Med.*, 66, 55–61.
- Kocevski, D., Du, M., Kan, J., Jing, C., Lačanin, I., & Pavlović, H., (2013). Antifungal effect of *Allium tuberosum*, *Cinnamomum cassia*, and *Pogostemon cablin* essential oils and their components against population of *Aspergillus* species. *J. Food Sci.*, 78, M731–M737.
- Kongkathip, N., Sam-ang, P., Kongkathip, B., Pankaew, Y., Tanasombat, M., & Udomkusionsri, P., (2009). Development of Patchouli extraction with quality control and isolation of active compounds with antibacterial activity. *Kasetsart. J. (Nat. Sci.)*, 43, 519–525.
- Li, F., Li, C. J., Ma, J., Yang, J. Z., Chen, H., Liu, X. M., Li, Y., & Zhang, D. M., (2013). Four new sesquiterpenes from the stems of *Pogostemon cablin*. *Fitoterapia.*, 86, 183–187.
- Li, K., Zhang, H., Xie, H., Liang, Y., Wang, X., & Ito, Y., (2011). Preparative isolation and purification of five flavonoids from *Pogostemon cablin* Benth by high-speed countercurrent chromatography and preparative high-performance liquid chromatography. *J. Liquid Chromatogr. Relat. Technol.*, 34, 1617–1629.
- Li, P., Yin, Z. Q., Li, S. L., Huang, X. J., Ye, W. C., & Zhang, Q. W., (2014). Simultaneous determination of eight flavonoids and pogostone in *Pogostemon cablin* by high performance liquid chromatography. *J. Liquid Chromatogr. Relat. Technol.*, 37, 1771–1784.
- Li, Y. C., Liang, H. C., Chen, H. M., Tan, L. R., Yi, Y. Y., Qin, Z., Zhang, W. M., et al., (2012). Anti-candida albicans activity and pharmacokinetics of pogostone isolated from *Pogostemonis Herba*. *Phytomedicine.*, 20, 77–83.
- Li, Y. P., Yuan, S. F., Cai, G. H., Wang, H., Wang, L., Yu, L., Ling, R., & Yun, J., (2014). Patchouli alcohol dampens lipopolysaccharide induced mastitis in mice. *Inflammation.*, 37, 1757–1762.
- Lin, R. F., Feng, X. X., Li, C. W., Zhang, X. J., Yu, X. T., Zhou, J. Y., Zhang, X., et al., (2014). Prevention of UV radiation-induced cutaneous photoaging in mice by topical administration of patchouli oil. *J. Ethnopharmacol.*, 154, 408–418.
- Liu, Q., Luyten, W., Pellens, K., Wang, Y., Wang, W., Thevissen, K., Liang, Q., et al., (2012). Antifungal activity in plants from Chinese traditional and folk medicine. *J. Ethnopharmacol.*, 143, 772–778.

- Lu Tsung, C., Jung-Chun, L., Tai-Hung, H., & Ying-Chih, L., (2011). Analgesic and anti-inflammatory activities of the methanol extract from *Pogostemon cablin*. *Evidence-based Complementary and Alternative Medicine.*, 9, 671741.
- Lu, T. C., Liao, J. C., Huang, T. H., Lin, Y. C., Liu, C. Y., Chiu, Y. J., & Peng, W. H., (2011). Analgesic and anti-inflammatory activities of the methanol extract from *Pogostemon cablin*. *Evid. Based Complement. Alternat. Med.*, 2011, 671–674.
- Lubbe, A., & Verpoorte, R., (2011). Cultivation of medicinal and aromatic plants for specialty industrial materials. *Ind. Crop Prod.*, 34, 785–801.
- Luo, J. P., Liu, Y. P., Feng, Y. F., Guo, X. L., & Cao, H., (2003). Two chemotypes of *Pogostemon cablin* and influence of region of cultivation and harvesting time on volatile oil composition. *Acta Pharmacol. Sin.*, 38, 307–310.
- Luo, J., Feng, Y., & Guo, X., (2000). Studies on volatile oil of root and rhizome of herba *pogostemonis*. *Natural Product Research and Development.*, 12, 66–70.
- Luo, J., Feng, Y., Guo, X., & Li, X., (1999). GC-MS analysis of volatile oil of *Herba Pogostemonis*. collected from Gaoyao county. *Zhong Yao Cai.*, 22, 25–28.
- Maheshari, M. L., Vasantha, K. T., Sharma, N., & Chandel, K. P. S., (1993). Patchouli an Indian perspective. *Indian Perfumer*, 37, 9–11.
- Manglani, N., Deshmukh, V. S., & Kashyap, P., (2011). Evaluation of anti-depressant activity of *Pogostemon cablin* (Labiatae). *International Journal of Pharmtech Research.*, 3.
- Marius, R., Ecaterina, A., Alina, M. H., Bogdan, S. V., Florin, I., Laurentiu, M., George, D. M., et al., (2016). Antimicrobial nanostructured bioactive coating based on Fe<sub>3</sub>O<sub>4</sub> and patchouli oil for wound dressing. *Metals*, 6, 103.
- Maxim, B., Alexandru, M. G., Alexandra, E. O., Roxana, C. P., George, D. M., Radu, H., George, A. S., et al., (2014). Efficiency of vanilla, patchouli, and ylang ylang essential oils stabilized by iron oxide@C14 nanostructures against bacterial adherence and biofilms formed by *Staphylococcus aureus* and *Klebsiella pneumoniae* clinical strains. *Molecules.*, 19, 17943–17956.
- Miyazawa, M., Okuno, Y., Nakamura, S. I., & Kosaka, H., (2000). Antimutagenic activity of flavonoids from *Pogostemon cablin*. *J. Agric. Food Chem.*, 48, 642–647.
- Murugan, R., Ravi, K. K., & Livingstone, C., (2008). Addition of a wild aromatic plant *Pogostemon hirsutus* Benth. (*Lamiaceae*) to the flora of India. *Curr. Sci.*, 95, 835.
- Murugan, R., Ravikumar, K., & Livingstone, C., (2010). Rediscovery of *Pogostemon nilagiricus* (*Lamiaceae*), a steno-endemic and critically endangered aromatic species. *Rheedia.*, 20, 50–52.
- Mutiara, W., & Umar, R. M., (2015). Study of herbal topical repellent made of betel leaves (*Piper betle*) and patchouli oil (*Pogostemon cablin*) mixture against yellow fever mosquito (*Aedes aegypti*) formulation of anti-acne serum based. *Biotropia.*, 22, 45–51.
- Noor, F., Ifat, F., Lutfi, C., & Febi, I. F., (2017). Formulation of antiacne serum based on lime peel essential oil and *in vitro* antibacterial activity test against *Propionibacterium acnes*. *AIP Conference Proceedings.*, 1823.
- Park, E. J., Park, H. R., Lee, J. S., & Kim, J. W., (1998). Licochalcone A: An inducer of cell differentiation and cytotoxic agent from *Pogostemon cablin*. *Planta Med.*, 64, 464–466.
- Pattnaik, S., Subramanyam, V. R., & Kole, C., (1996). Antibacterial and antifungal activity of 10 essential oils *in vitro*. *Microbios.*, 86, 237–246.
- Priya, D., Swati, D., & Vilasrao, D. K., (2014). A review on *Pogostemon patchouli*. *Res. J. Pharmacogn. Phytochem.*, 691, 41–47.

- Pullagummi, C., Rao, N. B., Singh, B. C. S., Bheemagani, A. J., Kumar, P., Venkatesh, K., & Rani, A. R., (2014). Comparative studies on antibacterial activity of patchouli [*Pogostemon cablin* (Blanco) Benth] and geranium (*Pelargonium graveolens*) aromatic medicinal plants. *Afr. J. Biotechnol.*, *13*, 2379–2384.
- Puspa, D., Shoma, D., Jaripa, B., & Md Nural, A., (2013). Antibacterial and antifungal activity analysis of essential oil of *Pogostemon cablin* (Blanco) Benth. *Bangladesh J. Microbiol.*, *30*, 7–10.
- Qing, S., Shoutian, Q., Hongyan, G., Ming, Y., Swamy, M. K., Sinniah, U. R., Umar, A., & Akhtar, M. S., (2019). Biosynthesis, characterization, and biological activities of silver nanoparticles from *Pogostemon cablin* Benth. methanolic leaf extract. *Journal of Nanoscience and Nanotechnology*, *19*, 4109–4115.
- Rakotonirainy, O., Gaydou, E. M., Faure, R., & Bombarda, I., (1997). Sesquiterpenes from Patchouli (*Pogostemon cablin*) essential oil. Assignment of the proton and carbon-13 NMR spectra. *J. Essent. Oil Res.*, *9*, 321–327.
- Ram, S. V., Rajendra, C. P., Amit, C., & Ved, R. S., (2019). Chemical composition of leaves, inflorescence, whole aerial-parts and root essential oils of patchouli {*Pogostemon cablin* (Blanco) Benth.}. *Journal of Essential Oil Research.*, *31*, 319–325.
- Silva, M. A. S., Ehler, P. A. D., Ming, L. C., & Marques, M. O. M., (2004). Composition and chemical variation during daytime of constituents of the essential oil of *Pogostemon patchouli* pellet leaves. *Acta Hort.*, *629*, 145–147.
- Singh, B. R., Singh, V., Ebibeni, N., & Singh, R. K., (2013). Antimicrobial and herbal drug resistance in enteric bacteria isolated from faecal droppings of common house Lizard/ Gecko (*Hemidactylus frenatus*). *Int. J. Microbiol.*
- Singh, R., Singh, M., Srinivas, A., Rao, E. P., & Puttanna, K., (2015). Assessment of organic and inorganic fertilizers for growth, yield, and essential oil quality of industrially important plant patchouli (*Pogostemon cablin*) (Blanco) Benth. *J. Essent. Oil Bear. Pl.*, *18*, 1–10.
- Su, Z. Q., Wu, X. L., Bao, M. J., Li, C. W., Kong, S. Z., Su, Z. R., Lai, X. P., et al., (2014). Isolation of (–) patchouli alcohol from patchouli oil by fractional distillation and crystallization. *Trop. J. Pharm. Res.*, *13*, 359–363.
- Sundaresan, V., Singh, S. P., & Mishra, A. N., (2009). Composition and comparison of essential oils of *Pogostemon cablin* (Blanco) Benth. (Patchouli) and *Pogostemon travancoricus* Bedd var *travancoricus*. *J. Essent. Oil Res.*, *21*, 220–222.
- Suthar, B. A., & Patel, R. S., (2014). A taxonomic study of *Lamiaceae* (Mint family) in Rajpipla (Gujarat, India). *World Appl. Sci. J.*, *32*, 766–768.
- Swamy, M. K., & Sinniah, U. R., (2015). A comprehensive review on the phytochemical constituents and pharmacological activities of *Pogostemon cablin* Benth.: An aromatic medicinal plant of industrial importance. *Molecules.*, *20*, 8521–8547.
- Swamy, M. K., & Sinniah, U. R., (2016). Patchouli (*Pogostemon cablin* Benth.): Botany, agrotechnology, and biotechnological aspects. *Industrial Crops and Products.*, *87*, 161–176.
- Swamy, M. K., Balasubramanya, S., & Anuradha, M., (2010). *In vitro* multiplication of *Pogostemon cablin* Benth. through direct regeneration. *Afr. J. Biotechnol.*, *9*, 2069–2075.
- Swamy, M. K., Mohanty, S. K., & Anuradha, M., (2014). The effect of plant growth regulators and natural supplements on *in vitro* propagation of *Pogostemon cablin* Benth. *J. Crop Sci. Biotechnol.*, *17*, 71–78.
- Swamy, M. K., Mohanty, S. K., Sinniah, U. R., & Maniyam, A., (2015). Evaluation of patchouli (*Pogostemon cablin* Benth.) cultivars for growth, yield, and quality parameters. *J. Essent. Oil Bear. Pl.*, *18*, 826–832.



- Swamy, M. K., Sudipta, K. M., Balasubramanya, S., & Anuradha, M., (2010). Effect of different carbon sources on *in vitro* morphogenetic response of patchouli (*Pogostemon cablin* Benth). *J. Phytol.*, 2, 11–17.
- Teris, A. B., & Daniel, J., (2017). The essential oil of patchouli, *Pogostemon cablin*: A review. *Flavor Fragr J.*, 1–45.
- Thapa, R. K., Vashist, V. N., Atal, C. K., & Gupta, R., (1971). The essential oil of *Pogostemon plectranthoides*. *Planta Med.*, 20, 57–60.
- Tisna, H., Yulida, A., & Teuku, A. F., (2019). Isolation, and characterization montmorillonite nanoparticles of Aceh tamiang bentonite as patchouli oil (*Pogostemon cablin*) bleaching. *Orient. J. Chem.*, 35, 1535–1538.
- Tsai, Y. C., Hsu, H. C., Yang, W. C., Tsai, W. J., Chen, C. C., & Watanabe, T., (2007). Alpha-bulnesene a PAF inhibitor isolated from the essential oil of *Pogostemon cablin*. *Fitoterapia.*, 78, 7–11.
- Uswatun, C., & Dian, E., (2019). Lotion formulation combination of *Cananga* and patchouli oil as a repellent. *AIP Conference Proceedings.*, 2108.
- Vázquez-Sánchez, D., Cabo, M. L., & Rodríguez-Herrera, J. J., (2014). Antimicrobial activity of essential oils against *Staphylococcus aureus* biofilms. *Food Sci. Technol. Int.*, 3.
- Vijaya, K. K., (2004). Patchouli and India—A great leap forward. In: *National Seminar of Prospectus and Potentials of Medicinal and Aromatic Crops* (pp. 106, 107). Bangalore, India.
- Wan, F., Peng, F., Xiong, L., Jian-ping, C., Cheng, P., & Min, D., (2016). *In vitro* and *in vivo* antibacterial activity of patchouli alcohol from *Pogostemon cablin*. *Chin. J. Integr. Med.*
- Wang, D., Yin, Z., Zhang, Q., Ye, W., Zhang, X., & Zhang, J., (2010). Non-volatile chemical constituents from *Pogostemon cablin*. *Zhongguo Zhong Yao Za Zhi*, 35, 704–707.
- Wu, H., Li, B., Wang, X., Jin, M., & Wang, G., (2011). Inhibitory effect and possible mechanism of action of patchouli alcohol against influenza A (H2N2) virus. *Molecules*, 16, 6489–6501.
- Xian, Y. F., Suo, J., Huang, X. D., Hou, S. Z., Chen, J. N., Ye, M. R., & Su, Z. R., (2007). A pharmacological study on anti-inflammatory effects of refined Huodan recipe. *Chin. J. Exp. Tradit. Med. Formulae*, 13, 54–56.
- Xie, Y. C., & Tang, F., (2009). Protective effect of *Pogostemon cablin* on membrane fluidity of intestinal epithelia cell in ischemia/reperfusion rats after ischemia/reperfusion. *Chin. J. Integr. Traditional West. Med.*, 29, 639–641.
- Xuan, Y., Xin-Pei, W., Xiao-Jin, Y., Jing-Fei, J., Fan, L., Dong-Ming, X., Yue-Ying, G., & Li-Jun, D., (2019). Anti-nociceptive effect of patchouli alcohol: Involving attenuation of cyclooxygenase 2 and modulation of mu-opioid receptor. *Chinese Journal of Integrative Medicine.*, 25, 454–461.
- Yang, D., Chaumont, J. P., & Millet, J., (1998). Antibacterial activity on skin and chemical composition of the volatile oils from *Agastache rugosa* and *Pogostemon cablin*. *Wei Sheng Wu Xue za Zhi.*, 18, 1–4.
- Yang, X., Zhang, X., Yang, S. P., & Liu, W. Q., (2013). Evaluation of the antibacterial activity of patchouli oil. *Iran. J. Pharm. Res.*, 12, 307–316.
- Yang, Y., Kinoshita, K., Koyama, K., Takahashi, K., Tai, T., Nunoura, Y., & Watanabe, K., (1999). Anti-emetic principles of *Pogostemon cablin* (Blanco) Benth. *Phytomedicine.*, 6, 89–93.

- Yi, Y. Y., He, J. J., Su, J. Q., Kong, S. Z., Su, J. Y., Li, Y. C., Huang, S. H., et al., (2013). Synthesis and antimicrobial evaluation of pogostone and its analogues. *Fitoterapia.*, 84, 135–139.
- Ying, C., You-Gen, W., Yan, X., Jun-Feng, Z., Xi-Qiang, S., Guo-Peng, Z., & Xin-Wen, H., (2014). Dynamic accumulation of sesquiterpenes in essential oil of *Pogostemon cablin*. *Rev. bras. farmacogn.*, 24.
- Yu, X. D., Xie, J. H., Wang, Y. H., Li, Y. C., Mo, Z. Z., Zheng, Y. F., Su, J. Y., et al., (2015). Selective antibacterial activity of patchouli alcohol against *Helicobacter pylori* based on inhibition of urease. *Phytother. Res.*, 29, 67–72.
- Yuliani, A., & Sri Haryani, A., (2012). Physico-chemical properties of patchouli oils (*Pogostemon cablin*) separated by fractional distillation method. *Proceedings of the 2<sup>nd</sup> Annual International Conference Syiah Kuala University 2012 & The 8th IMT-GT Uninet Biosciences Conference Banda Aceh*.
- Zhang, Z., Chen, X., Chen, H., Wang, L., Liang, J., Luo, D., Liu, Y., et al., (2016). Anti-inflammatory activity of  $\beta$ -patchoulene isolated from patchouli oil in mice. *Eur. J. Pharmacol.*, 781, 229–238.
- Zhou, L., Xu, M., Yang, C. R., Wang, Y. F., Wang, Y. F., & Zhang, Y. J., (2011). New patchoulol-type sesquiterpenoids from *Pogostemon cablin*. *Helv. Chim. Acta*, 94, 218–223.
- Zhou, Q. M., Peng, C., Li, X. H., Guo, L., Xiong, L., & Lin, D. S., (2013). Study on constituents of the aerial parts of *Pogostemon cablin*. *J. Chin. Med. Mater.*, 36, 915–918.

## CHAPTER 4

---

# Pippali (*Piper longum* L.): A Plant with Versatile Pharmaceutical Uses

RICHA SHARMA,<sup>1</sup> ANKITA MAURYA,<sup>2</sup> HIMANSHU YADAV,<sup>2</sup>  
AMRITESH C. SHUKLA,<sup>2</sup> and SUMPAM TANGJANG<sup>1</sup>

<sup>1</sup>Rajiv Gandhi University, Rono Hills, Doimukh, Arunachal Pradesh, India

<sup>2</sup>Department of Botany, University of Lucknow, Lucknow,  
Uttar Pradesh, India

---

### ABSTRACT

Traditionally several ethno-medicinal plants are using to treatment of so many diseases. Along with them, several species of *Piper* genus are significantly ethno-medicinal plants used in different organizations of medicine. *Piper longum* Linn. is a originally from Indo-Malaya areas, and that is belongs to the family Piperaceae as well as commonly well-known as ‘Pippali.’ The tribal people traditionally use the different plant parts for painkiller, various heart problems, cough, fever, anti-inflammatory activity, antivenin, and also like a spice. Essential oil, lignans alkaloids and flavonoids are identifieds in this plant such as piperlongumine, piperine, sesamin, pipermonaline, piperundecalidine, and sylvatin. Fruits extract of *P. longum* showing to various actions like carminative, anti-diarrhoeic, Anti-ulcer, Bioavailability enhancers, Cardioprotective activity, Coronary vasodilation, Hepatoprotective activity, Immunomodulatory activity, treatment of asthma, Larvicidal activity, dementia, sleeplessness, fever, both diabetic types, hansen’s disease, rheumatic diseases and spleen chaos, etc. All ethno-medicinal plants have revealed marvelous probability for the development of the several novel drug molecules for diverse life threatening diseases. A lots of plant imitative

products have reported to play an significant role in different disease and other health circumstances.

In the present chapter we are focusing on the different aspects of *P. longum* traditionally use for pharmacological as well as hytochemistry profile, safety profile and it have expects for exploration on this plant.

## 4.1 INTRODUCTION

Approximately 20,000 different plant species are exploited in diverse traditional medicine organizations around the world, furthermore are measured as possible agents for the exposure of novel medications. Ethno-medicinal plants have revealed marvelous probability for the development of the novel drug/fresh compounds for various life threatening diseases and to cure and prevent various health issues. Numerous ethno-medicinal plants derived novel products have reported to play a significant role in different disease circumstances. While, present time medicines are accessible and herbal medicines contain frequently reserved fame for historical, traditional, and civilizing reasons. Practice of these herbal medicines has augmented throughout the worldwide; the issues concerning their protection, usefulness, and quality in mechanized and growing countries are occurred up (Anonymous, 1999). Medicinally aromatic shrubs extracting essential oil that, may exhibit several therapeutic applications and therefore, utilized in beverages, food, flavoring agent, fragrance, and various pharmaceutical based industries. About 90% of essential oils get consumed by the fragrance and flavor based industries to manufacture numerous brands of cosmetics, perfumes, health care products, and several medicinal products (Maheshari et al., 1993).

*P. longum* Linn. belongs to the genus Piper in the family Piperaceae, is one of the oldest spices known to the worldwide. *P. longum* is commonly known as “long pepper,” is native to India. Piperine is generally famous for important alkaloid present in the fruit of *P. longum* and numerous other species member of the Piperaceae family.

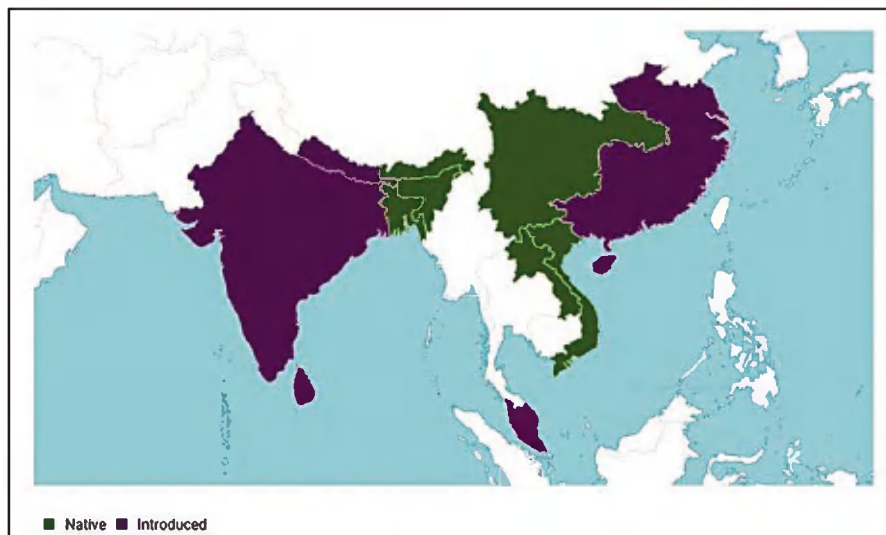
The uses of *piper* are recommended in the Ayurvedic medicinal organization as well as accessible literature has suggested that, immature fruit of *P. longum* used for stomach disorder, analgesic, respiratory problems, inequity of metabolic disorders, emmenagogue, and circulatory manure (Evans, 2009). *P. longum* and *P. nigrum* are recognized to have an alkaloid mentioned as piperine, which provides spiciness to this aromatic plant. *P.*

*longum* species are well-known component in the formulation of ‘Trikatu’ (meaning three components) and it is also famous to be an important bio-enhancer (Johri & Zutshi, 1992). Several biological activities of piperine have been recognized (Kanaki, Dave, Padh, & Rajani, 2008; Rahman & Rahmatullah, 2010) and fruit of *P. longum* was reported numerous piperic amides such as piperine, piperlonguminine, and pipernonaline (Jin et al., 2009). The nutritional piperine is recognized for its bioavailability and digestion improving qualities. Moreover, it is identified to use as an antitumor agent, antidiarrheic, anti-mutagenic, and antidysenteric qualities of this spice improve its medicinal significance (Srinivasan et al., 2001). Therapeutic qualities of this plant also comprise radioprotective, antifungal, antioxidant, hepatoprotective, cardioprotective, antimicrobial, immunomodulatory, anti-depressant, antiinflammatory, antihyperlipidemic, antiplatelet, antiamebic, antiobesity analgesic and also antidiabetic (Kumar, Kamboj, & Sharma, 2011; Sunila & Kuttan, 2004; Sharma, Kumar, Chashoo, Saxena, & Pandey, 2014; Jalalpura, Patil, Prakash, Hemalata, & Manvi, 2003; Clark, Arnold, Lasserson, & Wu, 2010; Nabi et al., 2013); which is commonly used as a significant ingredient in different Ayurvedic medicines to treatment of various diseases, including cure of dyspnea, cough-cold, spleen disorders, chronic fever, gout leprosy and tuberculosis, etc. (Khushbu, Roshni, Anar, Carol, & Mayuree, 2011).

We believed that, the present chapter resolving better and appreciative of *P. longum* and its properties. This information may be precious in preparation potential inspections particularly in growing new pharmaceuticals industries and clinical preliminaries, or active constituent. *P. longum*.

## 4.2 OCCURRENCE AND GEOGRAPHICAL DISTRIBUTION

Long pepper is a inhabitant of the India and Malaya area. This is growing very wildly in the tropical rain-forests of India, Generally, Indian Long pepper is mainly occurred from the wild plants. Besides, plant also found in tropical areas of India, Khasi, Mikir hills, Himalayas to Assam, Konkan to Kerala part from Western Ghats, lower hills of West Bengal as well as occurred from Andaman Nicobar Islands (Satyavati, Gupta, Ashok, & Tandon, 1987). While various part of world such as Bangladesh, China Southeast, Hainan, Malaya, Nepal, Sri Lanka, Vietnam Figure 4.1 (<http://www.plantsoftheworldonline.org/taxon/urn:lsid:ipni.org:names:682031-1>).



**FIGURE 4.1** Geographical locations of *P. longum* Linn. and its occurrence.

### 4.3 BOTANICAL TAXONOMICAL CLASSIFICATION

The shrub, *P. longum* Linn. is belongs to the Piperaceae family. The taxonomic classification of the plant is as described as below (Kirtikar & Basu, 1980):

- Kingdom: Plantae.
- Division: Magnoliophyta.
- Class: Magnoliopsida.
- Order: Piperales.
- Family: Piperaceae.
- Genus: Piper.
- Species: Longum.
- Botanical Name: Piper longum.

### 4.4 ANTONYMS AND VERNACULAR NAMES

In India, the plant, *P. longum* is to be called by vernacular names like Krishna pippali, Magadhi, Pippali, Tikshnatanduli (Sanskrit), Piplamul (Hindi), Hippali, Lippali, Thippili (Kannada), and the plant is also called Pippal, pippar (<http://www.plantnames.unimelb.edu.au/Sorting/Piper.html>). Synonyms and vernacular names are showing in Table 4.1.

**TABLE 4.1** Synonyms and Vernacular Names of *Piper longum* in Different Languages

Language	Vernacular Names
Indian	Arabic: Dâr fulful Bengali: Piplamor and Pipul, Gujarati: Pipli and Lindi Hindi: Piplamul, Pippal, and pippar Kannada: Thippili Hippali and Lippali, Malaya: Thippili, Pippali, Magadhi, and Tippili Marathi: Pippal and Pimpli Sanskrit: Krishnapippali, Magadhi, Pippali, Tikshnatanduli Tamil: Tippili, thippili, and sirumulam Urd.: Filfil daraz,
Chinese	Bi ba gen and Bi bo
Dutch	Langwerpige peper
Nepalese	Saano pipla and Gaj pipla
German	Langer Pfeffer and Jaborandi-Pfeffer
Hungarian	Bengáli bors
Swedish	Långpeppar
Turkish	Dar biberi
Portuguese	Pimenta-longa
English	long pepper, Indian long pepper and jaborandi pepper

#### 4.5 DESCRIPTION OF THE PLANT

*P. longum* Linn is a tiny shrub along with bulky woody, stems are thickened and jointed at the nodes climbing, creeping rooting below and several creeping. Morphological explanation of ethno-medicinal plant of *P. longum* L. showing in Figure 4.2 and Table 4.2.

#### 4.6 CULTIVATION

*Piper longum* is mostly originated from the uncultivated plants, the mainly reported from Uttar Pradesh and North East part of Assam and West Bengal. Few quantities of long pepper are also collected from Kerala, some parts of Andhra Pradesh, hills of Annamalai and generally in the Cherrapunji of Assam (The Wealth of India: A Dictionary of Indian Raw Materials and

**TABLE 4.2** Description of *Piper longum* Plant

Sl. No.	Plant Part	Description	References
1.	Leaves	Branches are epiphytic have oval or terse blade. Leaves are present on creeping branch. Leaf blades are dark green and membranous. Leaf apex is fine; base is oblique and sometimes cordate.	Chaveerach, Mokkamul, Sudmoon, & Tanee (2006); Wiart (2013)
2.	Stem	Stems having aromatic aura, slim, and slender in shape. The color is reddish brown to gray and aromatic aroma with strong taste. These are accessible in cut pieces, having separate internodes and with bump nodes, small root scare, rootlets, and solid and cylindrical.	Chaveerach, Mokkamul, Sudmoon, & Tanee (2006); Wiart (2013)
3.	Root	Creeping rooting below and several creeping.	Kapoor (2000)
4.	Fruit	Dark greenish-black to black in color, round in shape. Fruit surface is rough and combined. When broken the fruit, its outside showed a middle axis with 5–13 fruit lets roughly organized an axis. Tastes fruit is strong producing deadness on the tongue and aromatic aroma.	Chaveerach, Mokkamul, Sudmoon, & Tanee (2006); Wiart (2013)
5.	Male part of spikes.	Stalked with 2 stamens and orbicular bract.	Evans (2009); Wiart (2013)
6.	Female part of spikes.	Female spike part is vertical, circular bract and peltates are along with three stigmas.	

Industrial Products Raw Materials Series, 1969). These plants are also extremely obtained from its natural source and the species of this plant has now become extremely unusual in the Kerala's forests (Nair, 2000).

*P. longum* is naturally found in tropical moist type of environment and prefers dappled humid areas, sandy soil of pH range between (5.6 to 8.4) with well-off humus. Lateritic soils along with organic matter substances and excellent water holding ability are suitable. Rainy areas and prominent humidity are excellent for its good quality growth. It is a darkness loving plants however, for improved fruiting quality reported from 50% shaded areas (Sumy, Ved, & Krishnan, 2000).





**FIGURE 4.2** Morphological diagram of *Piper longum* Linn.

#### **4.6.1 VEGETATIVE PROPAGATION**

*P. longum* grown as a bushy runner and spread by vegetatively, similar to fully grown branches or by suckers of plant at the get going of the rainy season:

- 1. Through Cuttings:** Semi-hard stem cuttings, 12 to 14 cm long with at least 2–4 nodes are reported in the shaded nursery and mainly upper bud uncovered. A spacing of 10 to 15 cm should be provided between each pair of cuttings. The cuttings root in 12 to 15 days and success is 60 to 70%.
- 2. Through Tillers:** The tillers growing from the lower part of fully grown plant could be split and planted individually. The sprouted trimmings can be grown in the ground at a distancing of two-by-two meter. These florals are prone to numerous plant diseases (Sumy, Ved, & Krishnan, 2000).

## 4.7 IDENTIFICATION OF PHYTOCHEMICAL COMPOUNDS

Plants generate a various type of metabolites and new products, the main primary metabolic products are used as the resource of energy and the subordinate (secondary) metabolites are stored and working for exacting functions like plant defense. Those secondary metabolites occupy broad collections of chemical components grouping from glycoside, alkaloids, flavonoids, fatty acid, terpenoids, and steroids. Piperine alkaloids are standard constituent in *P. longum* L. which are present in the plant 3–5%. Content of piperine is accountable for strong and burning flavor of the plant.

*P. longum* also have spectacles the amount of alkaloids, arbutin, sour principle, coumarins, essential oil, various steroids and sterols from the extract of *P. longum* (Saraf & Saraf, 2014). Medicinal performances of *P. longum* L. are contemplated to be recognized mainly to its alkaloid substance.

The major phytochemicals were summarizes in Table 4.3, which were isolated and categorized from *P. longum*. Moreover, the medicinal activities of *P. longum* are accepted to be recognized mostly to its alkaloid components. Overall 159 phytochemicals were secluded and identified from *P. longum* and all the phytochemicals were allotted a individual ID, name, and their reference in Table 4.4. A range of chemical structures of major secondary metabolites were secluded and identified from *P. longum* are shown in Table 4.5.

## 4.8 PHARMACOLOGICAL PROFILE

*P. longum* L. have a great amount of biological activities, which has been assessed throughout various *in vivo* and *in vitro* investigations. It have been reported that amides, the popular researcher reports the different activity of *P. longum* L are associated to its activity on neurological problems. Along with, mainly of the researches connecting to *P. longum* were managed by scientists sited in China and India. Moreover, it is may be connected to the geographical allocation of *P. longum*, while a huge amount of species have been reported in China and India. The fruit of *P. longum* have alkaloids, 1% resin, waxy alkaloid N-isobutyl deca-trans-2-trans-4-dienamide, volatile oil, piperlonguminine, terpenoid, and Piperin substances. The roots have piperlonguminine, dihydro-stigmasterol, piperine, and piperlonguminine, which have been the cause that it is widely used in practice to encourage breathing health. Moreover, *P. longum* carry the approximately 6% alkaloid piperine, which is faintly advanced than in black pepper. Piperines have various

**TABLE 4.3** Phytoconstituents of *Piper longum* Linn.

Sl. No.	Active Components	Plant Part	References
Alkaloids	Piperlongumine, Piperlonguminine, and Piperine	Root	Bao, Bai, & Borijihan (2012)
	Dehydropiperonaline	Fruit	Shoji et al. (1986)
	2-hydroxy-1-methoxy-4H-dibenzode, Cephadione A, Aristolactam AII, piperolactam B 2-hydroxy-1-methoxy-6-methyl-4Hdibenzode and glumoline-4,5(6H)-dione, glumolone-4,5(6H)-dione Cepharonone B, norcephadione A, piperolactam A	Root	Desai, Prabhu, & Mulchandani (1988)
	Betasitosterol, Desmethoxyplartine, Piperine, Z-12-octadecenalalpha-glycerol monoester and Daucosterol	Fruit	Zhang, Chen, Wang, & Wu (1996)
	Tetrahydropiperine	Fruit	Madhusudhan & Vandana (2001)
	1-[1-oxo-5 (3,4 methylenedioxyphenyl)-2E, Coumaperine, Piperolactam A, Bisdemethoxycurcumin, methylenealpha-(1-methylethyl)-1H-indene-1-methanol, Aphanamol, Demethoxycurcumin, 4E-pentadienyl]-pyrrolidine, N-5-(4-hydroxy-3-methoxyphenyl)-2E-pentenoyl piperidine, 8Enonadienyl]-pyrrolidine, octahydro-4-hydroxy-3alpha-methyl-7, Turmerone, and 1-[1-oxo-5 (3,4-methylenedioxyphenyl)-2E-pentenyl]-pyrrolidine	Entire plant	Liu et al. (2009)
	Piperloein B, Pellitorin, Guineesine, Pipericide, Dehydropiperonaline, P(2E,4Z,8E)-piperonaline, Retrofractamide C and Dehydroretrofractamide C.	Fruits	Lee et al. (2010)
	GB-N	Fruits	Bao, Bai, & Borijihan (2012)
	Pipyahyine	Fruits	Madhu, Vijayan, & Shaikath (2011)
	Piperchabamide B and Piperlongumamides A-C	Fruits	Yang et al. (2013)
Ethyl 3',4',5'-trimethoxycinnamate	Fruits	Kumar et al. (2005)	
4 $\alpha$ -dihydroxy-1-(3-phenylpropanoyl) piperidine-2-one and (2E, 4E,14Z)-6-hydroxy-1-N-isobutyleicosa-2,4,14-trienamide and 3 $\beta$	Fruits	Jiang et al. (2013a, b)	

**TABLE 4.3** (Continued)

Sl. No.	Active Components	Plant Part	References
Lignans	Diaaedesmin, Sesamin, and Sylvatin	Seed	Dutta, Banerjee, & Roy (1975)
Essential oils	Caryophyllene oxide, p Selinene, a-Copaene, $\alpha$ -Pinene, Sabinene, $\delta$ -3-Carene, 0-Elemene, 6-Elemene, Myrcene, p-Caryophyllene, 9-Octadecene, a-Selinene, 6-Cadinene and Limonene.	Fruits	Tewtrakul et al. (2000)
–	$\alpha$ -Pinene, Dodecanal, $\beta$ -Elemene, $\beta$ -Pinene, Linalool, Limonene, Bornyl acetate, Elemol, $\beta$ -Cubebene, $\gamma$ -Elemene, 9-Eicosyne, Caryophyllene, Humulene (Z)- $\alpha$ -Farnesene, 2-Undecanone, Copaene, Gurjunene, Cadinene, Guaiene, $\alpha$ -Muuroleone, $\beta$ -Patchoulene, Nerolidol, Caryophyllene oxide, $\alpha$ -Cadinol, $\delta$ -Cadinol, $\beta$ -Eudesmol, $\alpha$ -Eudesmol, 1-Methylhexyl acetate Decanal, and $\gamma$ Muuroleone.	Leaves	Varughese et al. (2016)
–	Camphene, $\alpha$ -Pinene, $\beta$ -Pinene, $\beta$ -Phellandrene, Bisabolene, Caryophyllene, $\beta$ -Myrcene, cis-Ocimene, Limonene, Terpinolene, Linalool, 2-Nonanone, Terpineol, 2-Undecanone, 2-Tridecanone, Nerolidol, and 1-Methylhexyl acetate.	Fruits	Varughese et al. (2016)
–	Camphene, $\beta$ -Pinene, $\beta$ -Pinene, $\alpha$ -Phellandrene, Limonene, $\beta$ -Phellandrene, $\beta$ -Myrcene, Eucalyptol, Bornyl acetate, trans-Ocimene, cis-Ocimene, Tridecane, $\delta$ -Cadinol, 2-Undecanone, Caryophyllene oxide, $\delta$ -Elemene, $\beta$ -Elemene, Nerolidol, Humulene, 1-Pentadecene, Caryophyllene, Terpinyl acetate, $\beta$ -Patchoulene, Pentadecane, and Heptadecane.	Roots	Varughese et al. (2016)
–	Terpinyl acetate, Bornyl acetate, Nerolidol, Tridecane, 2-Undecanone, Caryophyllene oxide, Pentadecane, $\delta$ -Elemene, Caryophyllene, Humulene, Gurjunene, and $\beta$ -Patchoulene.	Stems	Varughese et al. (2016)
Flavonoids	Apigenin Epicatechin, Kaempferol, Myricetin, Naringenin Catechin, Quercetin, and Luteolin	Fruits	Mustafa, Hamid, Mohamed, & Bakar (2010)
Amide	Sarmentine	Fruits	Huang, Morgan, Asolkar, Koivunen, & Marrone (2010)

**TABLE 4.4** List of Identified Phytochemicals with ID from *P. longum*

Sl. No.	Phytochemical ID	Names of Phytochemical	ChEMBL and PubChem ID	References
1.	PL1	3 $\beta$ ,4 $\alpha$ -dihydroxy-1-(3-phenylpropanoyl)-piperidine-2-one	NA	Jiang et al. (2013b)
2.	PL2	(2E, 4E, 14Z)-6-hydroxyl-N-isobutyleicosa-2,4,14-trienamide	NA	
3.	PL3	Coumaperine	10131321	Liu et al. (2009)
4.	PL4	N-5-(4-hydroxy-3-methoxyphenyl)-2E-pentenoyl piperidine	NA	
5.	PL5	Piperolactam A	3081016	
6.	PL6	1-[1-oxo-5 (3,4-methylenedioxyphenyl)-2E,4E-pentadienyl]-piperidine	NA	
7.	PL7	(R)-(-)-turmerone	558221	
8.	PL8	Octahydro-4-hydroxy-3 $\alpha$ -methyl-7-methylene- $\alpha$ -(1-methylethyl)-1H-indene-1-methanol	NA	
9.	PL9	(+)-aphanamol I	11031884	
10.	PL10	Bisdemethoxycurcumin	5315472	
11.	PL11	Demethoxycurcumin	5469424	
12.	PL12	Longumosides A	NA	Jiang et al. (2013a)
13.	PL13	Longumosides B	71579641	
14.	PL14	Erythro-1-[1-oxo-9(3,4-methylenedioxyphenyl)-8,9-dihydroxy-2E-nonenyl]-piperidine	NA	
15.	PL15	9-dihydroxy-2E-nonenyl]-piperidine, Threo-1-[1-oxo-9(3,4-Methylenedioxyphenyl)-8	NA	
16.	PL16	3 $\beta$ ,4 $\alpha$ -dihydroxy-2-piperidinone	NA	
17.	PL17	5,6-dihydro-2(1H)-pyridinone	NA	
18.	PL18	Piperlongumide (1) [N-isobutyl-19-(3',4'-methylenedioxyphenyl)-2E,4E nonadecadienamide]	NA	Sahi, Tewatia, & Ghosal (2012)
19.	PL19	1-(3,4-methylenedioxyphenyl)-1E tetradecene	NA	

**TABLE 4.4** (Continued)

Sl. No.	Phytochemical ID	Names of Phytochemical	ChEMBL and PubChem ID	References
20.	PL20	Piperlongimin A [2E-N-isobutyl-hexadecenamide]	NA	
21.	PL21	2E,4E-N-isobutyl-octadecenamide	NA	
22.	PL22	Piperlongimin B [2E-octadecenoylpiperidine]	NA	
23.	PL23	2E,4E-N-isobutyl-dodecenamide	NA	
24.	PL24	2E,4E,12E,13-(3,4-methylenedioxyphenyl)-trideca-trienoic acid isobutyl amide	NA	
25.	PL25	Piperine	638024	
26.	PL26	Pellitorine	5318516	Li et al. (2013)
27.	PL27	N-[(2E,4E)-Decadienoyl]-piperidine	11118018	
28.	PL28	N-Isobutyl-2E,4E-undecadienamide	20157325	
29.	PL29	Piperlonguminine	5320621	
30.	PL30	Piperanine	5320618	
31.	PL31	N-[(2E,4E)-Tetradecadienoyl]piperidine	11130083	
32.	PL32	N-Isobutyl-2E,4E-hexadecadienamide	6442402	
33.	PL33	Pipercollosine	5372201	
34.	PL34	(2E,4E,12Z)-N-Isobutyl-octadeca-2,4,12-trienamide	NA	
35.	PL35	N-Isobutyl-2E,E-octadecadienamide	9974234	
36.	PL36	Dehydropiperonaline	6439947	
37.	PL37	Piperonatinine	9974595	
38.	PL38	(E)-9-(Benzo[d][1,3]dioxol-5-yl)-1-(piperidin-1-yl)non-2-en-1-one	NA	
39.	PL39	1-(2E,4E,12E)-Octadecatriinoylpiperidine	NA	
40.	PL40	Retrofractamide B	5372162	
41.	PL41	(2E,4E,14Z)-N-Isobutyleicosa-2,4,14-trienamide	NA	

TABLE 4.4 (Continued)

Sl. No.	Phytochemical ID	Names of Phytochemical	ChEMBL and PubChem ID	References
42.	PL42	N-isobutyl-2E,4E-decyldecadienamide	NA	
43.	PL43	(2E,4E,10E)-N-11-(3,4-Methylenedioxyphenyl)hmdecatrienoylpiperidine	NA	
44.	PL44	1-[(2E,4E,14Z)-1-Oxo-2,4,14-eicosatrienyl]-piperidine	NA	
45.	PL45	Guineensine	6442405	
46.	PL46	(2E,4E,14Z)-N-Isobutyldocosa-2,4,14-trienamide	NA	
47.	PL47	(2E,4E,12E)-13-(Benzo[d][1,3]dioxol-6-yl)-1-(piperidin-1-yl)trideca-2,4,12-trien-1-one	NA	
48.	PL48	(2E,4E,13E)-14-(Benzo[d][1,3]dioxol-6-yl)-N-isobutyltetradeca-2,4,13-trienamide	NA	
49.	PL49	Brachyamide B	14162526	
50.	PL50	Dihydropiperlonguminine	12682184	
51.	PL51	Piperdardine	10086948	
52.	PL52	Retrofractamide A	11012859	
53.	PL53	Piperchabamide D	16041827	
54.	PL54	N-isobutyl-2E,4E-dodecadienamide	6443006	
55.	PL55	Piperchabamide B	44453655	
56.	PL56	13-(1,3-Benzodioxol-5-yl)-N-(2-methylpropyl)-(2E,4E)-tridecadienamide	NA	
57.	PL57	Piperchabamide C	44454018	
58.	PL58	1-[(2E,4E)-1-oxo-2,4-hexadecadienyl]-piperidine	10980124	
59.	PL59	2,2-Dimethoxybutane (C <sub>6</sub> H <sub>14</sub> O <sub>2</sub> )	137941	Das et al. (2012)
60.	PL60	2-Hydroxy myristic acid (C <sub>14</sub> H <sub>28</sub> O <sub>3</sub> )	1563	
61.	PL61	β-Myrcene (C <sub>10</sub> H <sub>16</sub> )	31253	
62.	PL62	N-methyl-1-octadecanamine (C <sub>19</sub> H <sub>41</sub> N)	75539	

**TABLE 4.4** (Continued)

Sl. No.	Phytochemical ID	Names of Phytochemical	ChEMBL and PubChem ID	References
63.	PL63	Piperazine adipate (C <sub>10</sub> H <sub>20</sub> N <sub>2</sub> O <sub>4</sub> )	8905	
64.	PL64	2-Nonynoic acid (C <sub>9</sub> H <sub>14</sub> O <sub>2</sub> )	61451	
65.	PL65	Dodecanal (CH <sub>3</sub> (CH <sub>2</sub> ) <sub>10</sub> CHO)	8194	
66.	PL66	1,2-Benzenedicarboxylic acid, bis(2-ethylhexyl] ester (C <sub>24</sub> H <sub>38</sub> O <sub>4</sub> )	8343	
67.	PL67	2-Amino-4-hydroxypteridine-6-carboxylic acid (C <sub>7</sub> H <sub>5</sub> N <sub>5</sub> O <sub>3</sub> )	70361	
68.	PL68	Piperlongumine	637858	Chatterjee & Dutta (1967)
69.	PL69	Hydrochloric acid (HCl)	107	Ru et al. (2014)
70.	PL70	Palmitic acid	985	
71.	PL71	1,8-cineole	2758	
72.	PL72	Lawsone	6755	
73.	PL73	Cis-Decahydronaphthalene	7044	
74.	PL74	Piperonylic acid	7196	
75.	PL75	Hypnon	7410	
76.	PL76	Moslene	7461	
77.	PL77	Cymol	7463	
78.	PL78	Methyl hydrocinnamate	7643	
79.	PL79	Hexahydropyridine (PIP)	8082	
80.	PL80	Pisol	8193	
81.	PL81	Piperonal	8438	
82.	PL82	Isobutylisovalerate	11514	
83.	PL83	Tridecane (TRD)	12388	



**TABLE 4.4** (Continued)

Sl. No.	Phytochemical ID	Names of Phytochemical	ChEMBL and PubChem ID	References
84.	PL84	Pentadecane (MYS)	12391	
85.	PL85	N-Heptadecane	12398	
86.	PL86	N-Nonadecane (UPL)	12401	
87.	PL87	Tridecylene	17095	
88.	PL88	Heptadecene	23217	
89.	PL89	Pentadecene	25913	
90.	PL90	Nonadecene	29075	
91.	PL91	Tetradecadiene-1,13	30875	
92.	PL92	Linalool (D)	67179	
93.	PL93	Cyclopentadecane	67525	
94.	PL94	Beta-Bisabolene	68128	
95.	PL95	Sesamol	68289	
96.	PL96	Sesamin	72307	
97.	PL97	p-Amino-o-cresol	76081	
98.	PL98	2,4-Dimethoxytoluene	96403	
99.	PL99	D-Camphor (CAM)	159055	
100.	PL100	Cis-2-Decalone	246289	
101.	PL101	Piperitenone	381152	
102.	PL102	(-)-Nopinene	440967	
103.	PL103	(-)-Alpha-Pinene	440968	
104.	PL104	Isodiprene (CHEBI:7)	443156	
105.	PL105	(R)-linalool	443158	

**TABLE 4.4** (Continued)

Sl. No.	Phytochemical ID	Names of Phytochemical	ChEMBL and PubChem ID	References
106.	PL106	N-(2,5-dimethoxyphenyl)-4-methoxybenzamide	532276	
107.	PL107	Anethole	637563	
108.	PL108	Isoeugenol	853433	
109.	PL109	(3S)-3,7-dimethylocta-1,6-dien-3-yl] propanoate	1616358	
110.	PL110	Terpinen-4-ol	2724161	
111.	PL111	Alpha-Farnesene	5281516	
112.	PL112	Farnesene	5281517	
113.	PL113	alpha-humulene	5281520	
114.	PL114	Isocaryophyllene	5281522	
115.	PL115	p-Ocimene	5281553	
116.	PL116	8-Heptadecene	5364555	
117.	PL117	9,17-OCTADECADIENAL (Z)	5365667	
118.	PL118	Cyclodecene, 1-methyl-	5367581	
119.	PL119	1,4,7,-Cycloundecatriene, 1,5,9,9-tetramethyl-, Z,Z,Z-	5368784	
120.	PL120	(+/-)-Isoborneol	6321405	
121.	PL121	(Z)-caryophyllene	6429301	
122.	PL122	-cis-.beta.-Elemene diastereomer	6431152	
123.	PL123	N-Isobutyl-2,4-icosadienamido	6441067	
124.	PL124	(E,E,E)-11-(1,3-Benzodioxol-5-yl)-N-(2-methylpropyl)-2,4,10-undecatrienenamide	6453083	
125.	PL125	Epicudesmin (ZINC03996196)	7299790	
126.	PL126	Valencene	9855795	

**TABLE 4.4** (Continued)

Sl. No.	Phytochemical ID	Names of Phytochemical	ChEMBL and PubChem ID	References
127.	PL127	(1S,5S)-1-isopropyl-4-methylenebicyclo[3.1.0]hexane	11051711	
128.	PL128	(5S)-5-[(1R)-1,5-dimethylhex-4-enyl]-2-methylcyclohexa-1,3-diene	11127403	
129.	PL129	(E)-5-(4-hydroxy-3-methoxy-phenyl)-1-piperidino-pent-2-en-1-one	11630663	
130.	PL130	(3R,8S,9S,10R,13R,14R,17R)-17-[(2R,5S)-5-ethyl-6-methylheptan-2-yl]-10,13-dimethyl-2,3,4,7,8,9,11,12,14,15,16,17-dodecahydro-1H-cyclopenta[a]phenanthren-3-ol (ZINC03982454)	11870467	
131.	PL131	Delta-elemene	12309449	
132.	PL132	(2R,4aR,8aR)-2-methyldecalin	12816526	
133.	PL133	(1R,5R,7S)-4,7-dimethyl-7-(4-methylpent-3-enyl)bicyclo[3.1.1]hept-3-ene	13889654	
134.	PL134	Calarene	15560279	
135.	PL135	Bisdemethoxycurcumin	45934475	
136.	PL136	1,4-cadinadiene	50986185	
137.	PL137	Tricyclene	55250308	
138.	PL138	Alpha-Cubebene	42608159	
139.	PL139	Piperundecalidine	44453654	
140.	PL140	3-phenylundecane	20655	
141.	PL141	4-[(1-Carboxy-2 methylbutyl)amino]-2(1H)-pyrimidinone	591989	
142.	PL142	Bicyclo[3,2,2]non-6-en-3-one	NA	
143.	PL143	Cedryl acetate	9838172	
144.	PL144	Isolongifolene epoxide	107035	
145.	PL145	N-isobutyleicosa-2(E),4(E),8(Z)-trienamide	NA	
146.	PL146	Pisatin	101689	

**TABLE 4.4** (Continued)

Sl. No.	Phytochemical ID	Names of Phytochemical	ChEMBL and PubChem ID	References
147.	PL147	Tetradecahydro-1-methylphenanthrene	609802	
148.	PL148	Undulatone	5281311	
149.	PL149	Copaene	25245021	
150.	PL150	Linalool	6549	
151.	PL151	Sylvatine	NA	
152.	PL152	beta-Cubebene	93081	
153.	PL153	(-)-Caryophyllene oxide	1742210	
154.	PL154	(-)-alpha-cedrene	6431015	
155.	PL155	(+)-Fargesin	CHEMBL 462822	http://www.genome.jp/db/pcidb
156.	PL156	Piperolactam A	CHEMBL 387864	
157.	PL157	(+)-Sesamin	CHEMBL 252915	
158.	PL158	2-Phenylethanol	CHEMBL 448500	
159.	PL159	l-Zingiberene	CHEMBL 479020	

**TABLE 4.5** Chemical Structures of the Main Phytochemicals Isolated from *P. longum* Linn

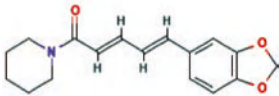
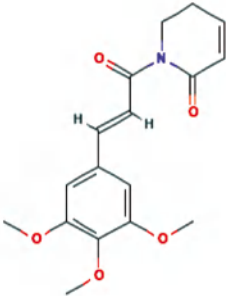
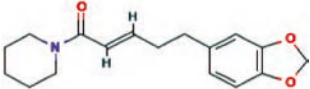
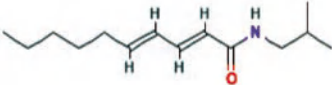
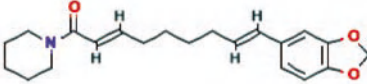
SL. No.	Isolated Major Phytochemical	Chemical Formula	Chemical Structure	References
1.	Piperine	$C_{17}H_{19}NO_3$		<a href="https://pubchem.ncbi.nlm.nih.gov/">https://pubchem.ncbi.nlm.nih.gov/</a>
2.	Piperlongumine	$C_{17}H_{19}NO_5$		<a href="https://pubchem.ncbi.nlm.nih.gov/">https://pubchem.ncbi.nlm.nih.gov/</a>
3.	Piperanine	$C_{17}H_{21}NO_3$		<a href="https://pubchem.ncbi.nlm.nih.gov/">https://pubchem.ncbi.nlm.nih.gov/</a>
4.	Pellitorine	$C_{14}H_{25}NO$		<a href="https://pubchem.ncbi.nlm.nih.gov/">https://pubchem.ncbi.nlm.nih.gov/</a>
5.	Pipernonaline	$C_{21}H_{27}NO_3$		<a href="https://pubchem.ncbi.nlm.nih.gov/">https://pubchem.ncbi.nlm.nih.gov/</a>

TABLE 4.5 (Continued)

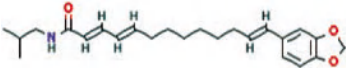
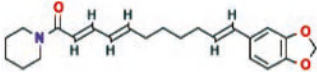
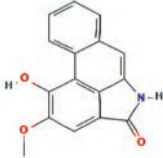
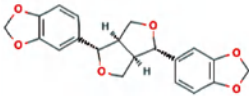
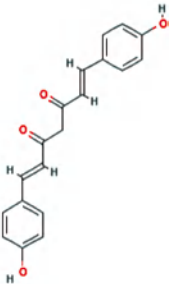
SL. No.	Isolated Major Phytochemical	Chemical Formula	Chemical Structure	References
6.	Guineensine	$C_{24}H_{33}NO_3$		<a href="https://pubchem.ncbi.nlm.nih.gov/">https://pubchem.ncbi.nlm.nih.gov/</a>
7.	Piperundecalidine	$C_{23}H_{29}NO_3$		<a href="https://pubchem.ncbi.nlm.nih.gov/">https://pubchem.ncbi.nlm.nih.gov/</a>
8.	Piperolactam A	$C_{16}H_{11}NO_3$		<a href="https://pubchem.ncbi.nlm.nih.gov/">https://pubchem.ncbi.nlm.nih.gov/</a>
9.	Sesamin	$C_{20}H_{18}O_6$		<a href="https://pubchem.ncbi.nlm.nih.gov/">https://pubchem.ncbi.nlm.nih.gov/</a>
10.	Bisdemethoxycurcumin	$C_{19}H_{16}O_4$		<a href="https://pubchem.ncbi.nlm.nih.gov/">https://pubchem.ncbi.nlm.nih.gov/</a>

TABLE 4.5 (Continued)

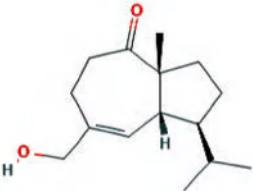
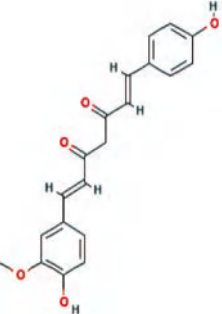
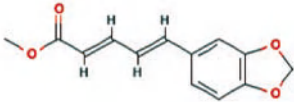
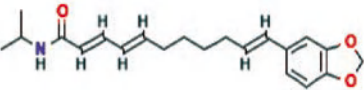
SL. No.	Isolated Major Phytochemical	Chemical Formula	Chemical Structure	References
11.	Aphanamol I	$C_{15}H_{24}O_2$		<a href="https://pubchem.ncbi.nlm.nih.gov/">https://pubchem.ncbi.nlm.nih.gov/</a>
12.	Demethoxycurcumin	$C_{20}H_{18}O_5$		<a href="https://pubchem.ncbi.nlm.nih.gov/">https://pubchem.ncbi.nlm.nih.gov/</a>
13.	Methyl piperate	$C_{13}H_{12}O_4$		<a href="https://pubchem.ncbi.nlm.nih.gov/">https://pubchem.ncbi.nlm.nih.gov/</a>
14.	Pipericide	$C_{21}H_{27}NO_4$		<a href="https://pubchem.ncbi.nlm.nih.gov/">https://pubchem.ncbi.nlm.nih.gov/</a>

TABLE 4.5 (Continued)

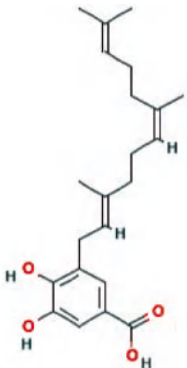
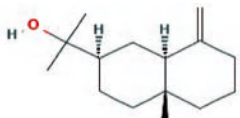
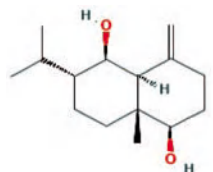
SL. No.	Isolated Major Phytochemical	Chemical Formula	Chemical Structure	References
15.	Piperolic acid	$C_{22}H_{30}NO_4$		<a href="https://pubchem.ncbi.nlm.nih.gov/">https://pubchem.ncbi.nlm.nih.gov/</a>
16.	$\beta$ -Eudesm	$C_{15}H_{26}NO$		<a href="https://pubchem.ncbi.nlm.nih.gov/">https://pubchem.ncbi.nlm.nih.gov/</a>
17.	7-epi-eudesm-4	$C_{15}H_{26}O_2$		<a href="https://pubchem.ncbi.nlm.nih.gov/">https://pubchem.ncbi.nlm.nih.gov/</a>



TABLE 4.5 (Continued)

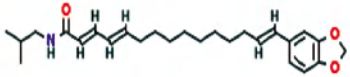
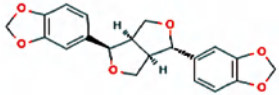
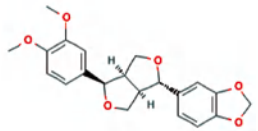
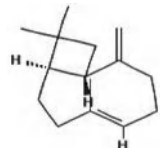
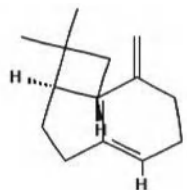
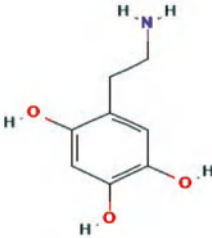
SL. No.	Isolated Major Phytochemical	Chemical Formula	Chemical Structure	References
18.	Brachystamide B	$C_{26}H_{37}NO_3$		<a href="https://pubchem.ncbi.nlm.nih.gov/">https://pubchem.ncbi.nlm.nih.gov/</a>
19.	Asarinine	$C_{20}H_{18}O_6$		<a href="https://pubchem.ncbi.nlm.nih.gov/">https://pubchem.ncbi.nlm.nih.gov/</a>
20.	Fargesin	$C_{21}H_{22}O_6$		<a href="https://pubchem.ncbi.nlm.nih.gov/">https://pubchem.ncbi.nlm.nih.gov/</a>
21.	Caryophyllene	$C_{15}H_{24}$		<a href="https://pubchem.ncbi.nlm.nih.gov/">https://pubchem.ncbi.nlm.nih.gov/</a>
22.	$\beta$ -caryophyllene	$C_{15}H_{24}$		<a href="https://pubchem.ncbi.nlm.nih.gov/">https://pubchem.ncbi.nlm.nih.gov/</a>

TABLE 4.5 (Continued)

SL. No.	Isolated Major Phytochemical	Chemical Formula	Chemical Structure	References
23.	6-Hydroxydopamine	$C_8H_{11}NO_3$	 The chemical structure of 6-Hydroxydopamine is shown. It consists of a benzene ring with three hydroxyl groups (-OH) at the 2, 3, and 4 positions. A 2-aminoethyl side chain (-CH2-CH2-NH2) is attached to the benzene ring at the 6 position.	<a href="https://pubchem.ncbi.nlm.nih.gov/">https://pubchem.ncbi.nlm.nih.gov/</a>

pharmacological performances, chemo-shock seizures. Furthermore, it contains 1% essential oils, which shows antibacterial activity. Commonly fruits of *P. longum* L. are in the avoidance of recurring attacks of bronchial asthma as well as in malaria.

The reported pharmacological activities of *P. longum* show a broad series of performance including following: Anti-inflammatory activity, Antifungal activity, Antidepressant activity, Adulticidal activity, Antiamoebic activity, Anticancer activity, Antihyperlipidemic activity, Antifertility activity, Analgesic activity, Antimicrobial activity, Antiobesity activity, Antioxidant activity, Antiplatelet activity, Anti-snake venom, Anti-ulcer, Bioavailability enhancers, Cardioprotective activity, Coronary vasodilation, Hepatoprotective activity, Immunomodulatory activity, Larvicidal activity, Melanin-inhibiting activity and Radioprotective activity

#### **4.8.1 ADULTICIDAL ACTIVITY**

The ethanol extract from *P. longum* was appeared the dose-dependent adulticidal consequence and observed aligned with *Stegomyia aegypti*, a major vector of dengue hemorrhagic and dengue fever. While, extracts of *P. longum* also established remarkable adulticidal action, while experienced on female mosquitoes by relevant reason (Choochote et al., 2006).

#### **4.8.2 ANALGESIC ACTIVITY**

Root of the *P. longum* for opioid type analgesia via NSAID type analgesia utilizing acetic-acid writhing technique and rat tail-flick method for by utilizing ibuprofen along with pentazocine as drug standard. The aqueous deferment of *P. longum* roots powder was taken orally to rat and mice to assess its analgesic effects. This desired that the plant root causes a weak opioid-type, other than powerful non-steroidal antiinflammatory drug-type of pain reliever (Vedhanayaki, Shastri, & Kuruvilla, 2003).

#### **4.8.3 ANTIAMOEBIC ACTIVITY**

Different part of *P. longum* such as fruit and root was tested for its efficiency alongside investigational amebiasis *in vivo* and aligned with *Entamoeba histolytica in vitro*. Isolated piperine and ethanol extract enhanced cecum amebiasis by 40%–90% in rats respectively (Ghoshal & Lakshmi, 2002). Moreover, *n*-butanol soluble fraction, ethanolic extract and hexane fraction

applied *in vitro* amoebicidal activity and the chloroform fraction showed the same action (Sawangjaroen, Sawangjaroen, & Poonpanang, 2004).

#### **4.8.4 ANTICANCER ACTIVITY**

Being the presence of several phytochemical components in the plant, they supply defense in case of cancer throughout different method. *P. longum* was reported to reveal major anti-tubercular activity (Gupta, Nath, Gupta, & Shrivastava, 1980). Piperine, an alkaloid exhibited in *P. longum* revealed considerable antimetastasis activity (Pradee & Kuttan, 2002). Chemopreventive property showing by piperine, where treated vocally on lung cancer manner animals, beside this, Piperlonguminine revealed an avoidance result on  $\alpha$ -MSH-induced tyrosinase synthesis (Selvendiran & Sakthisekaran, 2004; Min et al., 2004). The two active ideology piperine and ethyl 3', 4', 5'-trimethoxycinnamate were recognized and considered from the collective chloroform and hexane extracts of *P. longum*. The extracts extensively clogged-up the sticking of neutrophils to endothelium in a instance and concentration-dependent manner (Kumar et al., 2005). Piplartine and piperine alkaloidal along with were remote from *P. longum* and revealed the cytotoxic activity near numerous tumor cell lines (Bezerra et al., 2006). Benzene extract of *P. longum* was established 63% cell cycle inhibitory activity at subG1 phase and hexane extract of *P. longum* was generally effective alongside all cell line through 90% cytotoxicity (Sharma, Kumar, Chashoo, Saxena, & Pandey, 2014). The research evidently established that piperine have the antiapoptotic, antioxidative, and curative skill besides the cell blooming mutagenic reply and phenotypic modifications by piperine (Pathak & Khandelwal, 2006). Owing the ethno-pharmacological significance of *P. longum* like anticancer herb, the exceeding-reported studies have been capable to winning clarify the performance of *P. longum* extract beside diverse cancer cell lines and its act over normal cells.

#### **4.8.5 ANTI-DEPRESSANT ACTIVITY**

The ethanolic fruit extraction of *P. longum* yields a renowned piperine and piperidine alkaloids having effective anti-depressant-like qualities, which are arbitrate in part throughout hang-up of monoamine oxidase. Consequently *P. longum* fruits were representing a hopeful pharmacotherapeutic applicant against melancholy (Lee et al., 2008).

#### **4.8.6 ANT-FERTILITY ACTIVITY**

Various fractions, basic extract and the purified compound remoted from the fruits powder of *P. longum* were studied used for anti-fertility belongings in female rats, while the simple extract of its hexane portion revealed the effectiveness. Beside this, 1-butanol insoluble, 1-butanol soluble and chloroform portions were shown inactiveness. The benzene extract of *P. longum* fruits and methanol extract of the *Embelia ribes* berries the repressed pregnancy in rats (Lakshmi, Kumar, Agarwal, & Dhar, 2006; Sarwar et al., 2014).

#### **4.8.7 ANTIFUNGAL ACTIVITY**

Fruit derived essential oil exhibited fungicidal action of *P. longum*. Fruit-derived resources were tested to 6 phytopathogenic fungi such as *Botrytis cineria*, *Erysiphe graminis*, *Puccinia recondita*, *Rhizoctonia solani* and *Phytophthora infestans* utilizing a entire plant *in vivo* process (Kokate, D'cruz, & Nimbker, 1980). Piperonaline and piperidine alkaloids were isolated from *P. longum* its hexane fraction were exhibited the fungicidal action along with *P. recondita* (Lee et al., 2001).

#### **4.8.8 ANTI-HYPERLIPIDEMIC ACTIVITY**

Ethanol extract of *P. longum* fruit yields piperonaline, piperine, and piperlonguminine as the major anti-hyperlipidemic components. They showed significant anti-hyperlipidemic action *in vivo*, which were equivalent to with the purpose of the industrial anti-hyperlipidemic drug simvastatin (Jin et al., 2009). However, the experiments led to verify the activity of *P. longum* implies evaluation of lipid marker of blood signifying, it is a valuable result in case of hyperlipidemia (Kumar, Anilakumar, & Naveen, 2015; Kumar, Sharma, & Vasudeva, 2013).

#### **4.8.9 ANTI-INFLAMMATORY ACTIVITY**

Indian origin textbooks for the basic extract of herbs have described the use of *P. longum* fruits as painkiller as well as anti-inflammatory, exclusively worned locally for muscular pain (Khare, 2008) furthermore; another study reported that the *P. longum* extract provides relief in pain (Vedhanayaki, Shastri, & Kuruvilla, 2003). Anti-inflammatory actions of *P. longum* fruits decoction have been declared using carrageenaninduced rat edema (Choudhary, 2006). Moreover, eight species of *Piper*, together with *P. longum*

were presented for antiinflammatory activity throughout *in vivo* methods and the reaction was advanced due to cyclooxygenase-2 (COX) repression and anti-histaminic activity exclusive of substantiating the processor during experimental work (Vaghasiya, Nair, & Chanda, 2007).

#### **4.8.10 ANTIMICROBIAL ACTIVITY**

Petroleum ether and ethyl acetate extract isolated from *P. longum* were originated to wield antimicrobial effects next to diverse microorganisms (Ali et al., 2007). The extracts of *P. longum* were revealed effectual efficiency against *Salmonella typhi*, *Staphylococcus albus*, *S. epidermidis*, *S. typhrium*, *S. aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Bacillus cerus*, *B. megaterium*, *B. subtilis*, *Micrococcus flavus*, *Klebsiella aerogenes*, *Pseudomonas aeruginosa*, *Citrobacter freundii*, *Aspergillus niger* and two other species of *Proteus* such as *Proteus mirabilis* and *P. vulgaris* (Vaghasiya, Nair, & Chanda, 2007; Khan & Siddiqui, 2007). Again, extract of *P. longum* in specify opposing 13 pathogenic bacteria (five gram-positive and eight gram negative) and six fungi. It was also reported that, extracts of various solvents were susceptible towards particular bacterial strains and the activity were less significant towards fungal strains (Ali et al., 2007). Moreover, *P. longum* was additionally imperative to care for oral fungal infection particularly beside of *C. albicans* (Aneja, Joshi, Sharma, & Aneja, 2010).

#### **4.8.11 ANTI OBESITY ACTIVITY**

Pharmacological reticence of acyl CoA diacylglycerol acyltransferase have appeared as a possible treatment for the obesity. Piperidine substances are measured possible acyl CoA diacylglycerol acyltransferase interception (Lee et al., 2005).

#### **4.8.12 ANTIOXIDANT ACTIVITY**

The happening of terpenes, flavonoids, and phenols in the plants create them improved antioxidant negotiator that is not simply financial excluding varied and produces action activity exclusive of harm reaction (Barua, Singh, Sen, Barua, & Barua, 2014; Nile, Keum, Nile, Jalde, & Patel, 2018). *P. longum*

shows potential antioxidant probability alongside of free radical induced oxidative harm. Furthermore, petroleum ether and piperine extract of the roots from *P. longum* reduce lipid peroxide quantity and uphold glutathione content, representative antioxidant action (Natarajan, Narasimhan, Shanmugasundaram, & Shanmugasundaram, 2006). However, extract of *P. longum* has been established for utilization isoproterenol enhanced oxidative stress, monosodium glutamate induced stress and adriamycin induced oxidative stress (Jagdale et al., 2009; Wakade, Shah, Kulkarni, & Juvekar, 2008; Thomas, Sujatha, & George, 2009).

#### **4.8.13 ANTIPLATELET ACTIVITY**

Inhibitory effects were showed by four acid amides such as piperoctadecaldine, piperlongumine piperine, and pipernonaline obtained from the fruits of *P. longum* was assessed on washed rabbit platelet aggregation. However, they were not that enhanced by thrombin (Iwashita, Saito, Yamaguchi, Takagaki, & Nakahata, 2007).

#### **4.8.14 ANTI-SNAKE VENOM**

Fruits extract of *P. longum* were examined in case of snake venom in embryonated fertile, rat, mice, and also chicken eggs. Inhibition of venom lethal activity, necrotizing activity, paw edema, hemorrhagic activity, catalase activity, creatine kinase assay mast cell degranulation and defibrinogenating action were examined This research gives the confirmation that, plant extract can be utilized to decrease mortality and can be accepted in rural regions where traditional medications are available (Shenoy et al., 2013).

#### **4.8.15 ANTI-ULCER**

The extract of *P. longum* was reported significantly fair the offensive activities of ulcer even though no important action were observed on mucin and gastric mucosal glycoproteins discharge (Agrawal, Rao, Sairam, Joshi, & Goel, 2000). Moreover, extract of *P. longum* to foot shock persuaded stress animals and given the defense in ulcer harshness as related with doxycycline (Yadav, Chatterjee, Majeed, & Kumar, 2015).

#### **4.8.16 BIOAVAILABILITY ENHANCERS**

Piperine alkaloid isolated from *P. longum* were reported to improve the bioavailability of therapeutically as well as structurally diverse drugs, perhaps by modulating layer kinetics, considering its simple dividing along with increasing permeability. Moreover, diverse procedure have as well place presumptuous to examine the bio-amplifier activity of piperine, which contains of DNA receptor compulsory, inhibiting enzymes engaging in biotransformation of drugs and inflection of cell signal transduction and obstruction of drug effluence pump, (Pattanaik, Hota, Prabhakar, Kharbanda, & Pandhi, 2006; Singh, Varshneya, Telang, & Srivastava, 2005). However, the most important mechanism exposed by *P. longum* demonstrate bio enhancer action is due to of inhibition of P-gp effluence carrier found in gastro-intestinal wall along with major metabolizing enzyme CYP3A4 (Harwansh et al., 2014).

#### **4.8.17 CARDIO PROTECTIVE ACTIVITY**

Methanol extract of *P. longum* were examined on adriamycin-lured cardiotoxicity, in other words tissue peroxidation injure. Studies of the heart tissues, exposed degraded variations and cellular penetration in rats cured with adriamycin, on the other hand, pre-treatment with *P. longum* condensed the potency of certain lesions. The results identify that *P. longum* provides important safety aligned with adriamycin-lured oxidative tension and decreed cardiotoxicity by good quality of its antioxidant action (Wakade, Shah, Kulkarni, & Juvekar, 2008).

#### **4.8.18 CORONARY VASODILATION**

Inaccessible amide dehydropiperonaline from the fruits of *P. longum* has established the capability to support coronary vasodilation (Shoji et al., 1986; <http://www.ayushveda.com/herbs/piper-longum.htm>).

#### **4.8.19 HEPATOPROTECTIVE ACTIVITY**

Various flavonoids were reported from *P. longum*. It appears to be accountable in support of hepatoprotective activity. Fruit extract of *P. longum*



were evaluated in rabbit intended for its hepatoprotective activity aligned with chronic reversible, tempting harm operata morphological, carbon tetrachloride-persuade acute, biochemical as well as histopathological limitations. While, the pull out induced renewal by limiting fibrosis, excluding provides no protection against acute/cirrhosis harm. Piperines were creating to defend aligned with carbon tetrachloride-persuade in addition tertiary butyl hydroperoxide-persuade hepatotoxicity via dropping lipid peroxidation *in vivo* along with *in vitro* (Christina et al., 2006). Thus the *in vivo* hepatoprotective activities of *P. longum* have also been confirmed by making  $AlCl_3$  enhanced liver toxicity. Even, that metal enhanced toxicity was overturned by *P. longum* extract and the activity were having to be appropriate to antioxidant result (Sharma, Kumar, Chashoo, Saxena, & Pandey, 2014).

#### **4.8.20 IMMUNOMODULATORY ACTIVITY**

A famous Ayurvedic mixture having long pepper were analyzed in mice tainted with *Giardia lamblia* furthermore, reported to get going macrophages, as revealed by an improved macrophage phagocytic catalog in addition to immigration catalog and representing immunostimulatory action (Tripathi, Gupta, Lakshmi, Saxena, & Agrawal, 1999). Moreover, alcoholic extract of *P. longum* were observed the immuno-modulatory achievement of while assessed in mice, resulted in increase of bone marrow cellularity, leukocyte quantity, entire antibody making and  $\alpha$ -esterase positive cells. While, these results recommended that Immune achievement of *P. longum* (Sunila & Kuttan, 2004).

#### **4.8.21 LARVICIDAL ACTIVITY**

Ethanol extracts *P. longum* was analyzed, 100% mortality coverage against *Aedes aegypti* mosquito's larva utilizing a larvicidal bio-assay (Chaithong et al., 2006). Moreover, isolated piperonaline act as a bio-active factors from *P. longum*. Which were answerable in favor of larvicidal activity, whereas piperlongumine, piperettine, and also piperine did not demonstrate any activity alongside the larva (Yang, Lee, Lee, Kim, Lee, & Lee, 2002). However, confirmation can be begin by means of the oil portion of *P. longum* confirmed that, erstwhile larvae similar to *Culex quinquefasciatus*, as well requirements to be assessed.

#### **4.8.22 MELANIN-INHIBITING ACTIVITY**

Isolated Piperlonguminine from *P. longum* which, prohibit melanin assembly in melanoma B16 cells and enthused by means of alpha-melanocyte-enhancing hormone, 3-isobutyl-1-methylxanthine or protoporphyrin IX, where the complex showed powerfull de-pigmenting efficiency. These outcomes have be recognized to the inhibitory action of piperlonguminine on alpha melanocyte stimulating hormones signaling throughout the C-AMP to the C-AMP-respective component holding protein and also turned ianimator of tyrosinase appearance. Like this the enzyme is repressed inside, in that method abolishing the creation of melanin (Kim, Kim, Eom, Lee, Min, & Kim, 2006).

#### **4.8.23 RADIOPROTECTIVE ACTIVITY**

The ethanol extract of *P. longum* fruits was reported the radioprotective property in Swiss rats. The extract reduced the prominent quantity of alkaline phosphatase, lipid peroxidation as along with glutathione pyruvate transaminase in the liver in addition to serum of radiation-applied animals. Besides, the extract renewed glutathione manufacturing to offer radio fortification (Sunila & Kuttan, 2005).

### **4.9 PHARMACOLOGICAL REPORT**

*P. longum* carry a huge quantity of biological activities which have been assessed in the course of different *in vivo* and *in vitro* researches. This chapter presents hug quantity of publications observing different pharmacological properties of *P. longum* shows in Figure 4.3. It have been reported that diverse actions of amidst. So many research articles are associated to its activity on central nervous system. Moreover, the popular studies relating to *P. longum* were regulated by researceher groups situated in China and India. This is possibly connected to the geographic portion of *P. longum*, because a huge amount of different species have been reported in China and India. However, the below-cited text determines the pharmacological activity of *P. longum* Linn. extract. The diverse performance are accessible in Table 4.6.

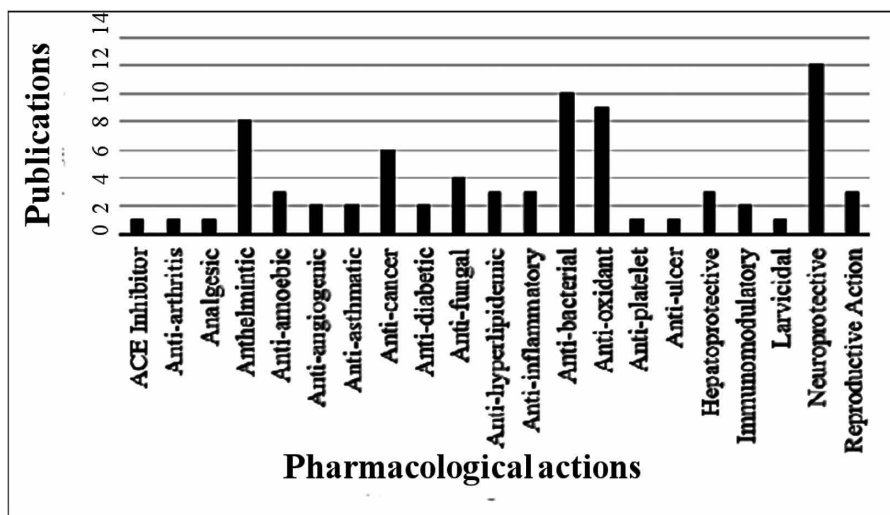


FIGURE 4.3 Most important pharmacological effects of *Piper longum* Linn.

#### 4.10 MEDICINAL USES OF *P. LONGUM* IN AYURVEDIC MEDICINE SYSTEM

Generally in Ayurveda, Unani, and Siddha systems of medicines are used *P. longum*, mainly in favor of different respiratory tract diseases. The dehydrated female spikes varieties are utilized in the Ayurvedic requirements such as Pipplayasava, Panchakola Pipalarishta, Pippalaya-diluha, and Lavanabhaskar churnam. This is the most important ingredient of an Ayurvedic concoction 'Triaktu' either is taken frequently for diverse health related issues. Generally roots are intended for stomachache, bronchitis, tumors, and various spleen diseases. It enhances hunger too. The mixtures of roots are given later than parturition to encourage the placenta expulsion. Moreover, the roots and spikes are taken in gout and lumbago problems. In the Ayurveda, the combination is used as a carminative, antidepressant, aphrodisiac, and agent as well as superficially works as medications. Mixture of honey and long pepper powdered used with cold, cough, asthma gruffness and glitch. Long pepper fruits, roots, and gingers combination powder having in equal parts which is called "*Chaturushana churnam*" is helpful in cough, flatulence, and colic as well coryza. A combine powder of five peppery named *Panchakola churna* having, roots, and fruit of long pepper, arid ginger and stalk of pepper plant along with chitraka is an excellent first course. The *Astakatvara taila* of chakradatta having of mustard, ginger, butter, long pepper, curd, milk, boiled

**TABLE 4.6** Pharmacological Performance of *Piper longum* Linn.

Activity	Animal, Dose, Duration, Route of Administration	Extract	Part	Models	Various Evaluating Parameters	Foremost Findings	References
Analgesics	Rats, 200, 400, and 800 mg/kg, p.o.	Aqueous	Roots	Acetic acid Induced and writhing test Rat tail flick method	Reduction in number of writhes and Reaction time for thermal stimulus.	Stoppage in response time to thermal spur was 6% even as 50% defense was accessible alongside.	Vedhanayaki, Shastri, & Kuruvilla (2003)
Anti-inflammatory	2.5 to 17.5 µg/ml	Chloroform	Fruits	<i>In vitro</i> , human Endothelial cells from umbilical vein	TNF- $\alpha$ -induced appearance of CAM	Adhesion of neutrophils inhibits to endothelial monolayer, chunk the TNF- $\alpha$ -induced expression of CAM, peroxidation.	Singh, Kumar, & Tandan (2008)
	Rats – 300 mg/kg, p.o.	Methanol	Leaves	Edima in rat paw induce by carrageenan, edema in rat paw induce by Dextran paw, granuloma in rat induced by cotton pellet-induced.	Percentage reticence in inflammation.	Even as 66.51% reticence in dextran induce paw edema was examined with cure, 38.89% inhibition in carrageenan induced edema.	Vaghasiya, Nair, & Chanda (2007)
	Rats – 0.5 to 1 ml/kg, p.o.	Oil	Fruits	Carrageenan-induced right posterior paw edema replica.	Decrease in paw edema.	72% reduction of edema prompted by carrageenan.	Kumar et al. (2009)
–	Rats – 200 mg/kg, p.o.	Ethanol	Fruits	Carrageenan-prompted paw edema and formaldehyde prompted paw edema.	Reduction in paw edema.	28.1% reticence in inflammation of paw prompted by carrageenan, 46.1% inhibition in formaldehyde prompted paw edema.	Kumari, Ashok, Ravishankar, Pandya, & Acharya (2012)

TABLE 4.6 (Continued)

Activity	Animal, Dose, Duration, Route of Administration	Extract	Part	Models	Various Evaluating Parameters	Foremost Findings	References
Antimicrobial	MIC = 25 mg/mL 400 µg	Methanol Acetone and ethanol.	Fruits	Agar well dispersal process.	Zone of inhibition	Curing was especially useful for <i>C. albicans</i> (Standard drug – Amphotericin-B and Ciprofloxacin.	Aneja, Joshi, Sharma, & Aneja (2010)
	400 µg	Methanol petroleum ether, chloroform, and ethyl acetate	Entire plant	Agar well dispersal process	Zone of inhibition	Treatment was effectual (Standard drug Kanamycin and Clotrimazole).	Ali, Alam, Yeasmin, Khan, Sayeed, & Rao (2007)
	1, 5, 25, 50, and 100 µg/ml	Methanol	Leaves	Agar well dispersal	Zone of inhibition	Treatment was effectual alongside these bacterial strains (standard drug-cefotaxime).	Vaghasiya, Nair, & Chanda (2007)
	1, 5, 25 to 100 µg/ml	Benzene, CCl <sub>4</sub> , ethyl acetate, chloroform acetone, ethanol, aqueous	Fruit	Agar well dispersal	Zone of inhibition	Treatment was efficient as antibacterial.	Khan & Siddiqui (2007)
	MIC = 41.60 and 83.90 mg/ml	Ethanol	Pods	Agar well dispersal	Zone of inhibition	Treatment was effective (standard drug-gentamicin).	Arambewela & Wijesundera (1999)
Anti-arthritis	Rats, 200 and 400 mg/kg, p.o.	Aqueous	Seed	Freund's entire adjuvant induced arthritis rat.	Decrease in paw edema by plethysmometer also radiographic image.	Abridged paw inflam- mation (standard drug – diclofenac).	Yende, Sannapuri, Vyawahare, & Harle (2010)
Antioxidant	Rats, 300.0 mg/ kg, p.o., 20 days	Ethanol	Fruits	Monosodiumglutamate induced toxicity.	AST, ALT, GSH, TG, CH, urea, histological experiments	Offered defense to liver also kidney from oxida- tive stress of monosodium glutamate.	Thomas, Sujatha, & George (2009)

**TABLE 4.6** (Continued)

Activity	Animal, Dose, Duration, Route of Administration	Extract	Part	Models	Various Evaluating Parameters	Foremost Findings	References
	Rats, 250, 500 mg/kg, p.o. 21 days	Ethanol	Fruits	Adriamycin induced cardiotoxicity.	Alanine and aspartate transaminase, GSH, lactate dehydrogenase, CAT, creatine kinase and SOD.	Defensed alongside ADR prompted oxidative pressure and decrease the cardiotoxicity because of anti-oxidant potential.	Wakade, Shah, Kulkarni, & Juvekar (2008)
	Rats, 100.0 mg/kg, p.o., 7 days	Petroleum ether	Roots	Myocardium ischemia induced by isoproterenol	DPPH, glutathione lipid and peroxide.	Probable anti-oxidant activity with defense in myocardial ischemic.	Jagdale et al. (2009)
	Rats, 50.0 mg/kg p.o., 14 days	Ethanol	Seed	Carbontetra chloride induced hepatotoxicity.	Whole antioxidant action, inhibitory effects against protein oxidation, ALP, ACP, SGOT SGPT and LDH.	Hepatoprotective cause is probably connected to its marked antioxidant action (standard drug-silymarin).	Samudram, Vasuki, Rajeshwari, Geetha, & Moorthi (2009)
	50, 100, 250, and 500 µg/ml.	Acetate, ethyl hydro and alcoholic butanol	Fruits	–	DPPH action	Antioxidant action was assessed.	Chaudhary, Mukherjee, Maiti, De, Bhadra, & Saha (2013)
–	10, 20, 40, and 50 µg/ml	Methanol, hexane, and ethanol	Fruits	3T3L1 (Mouse pre-adipocytes) and L6 (mouse myoblast)	Flavonoid content, DPPH, TPC, scavenging action, hydroxyl radical scavenging action, α-glucosidase analyze and α-amylase analyze.	Treatment gives a natural source of antioxidants amid antidiabetic and antiobesity prospective.	Krishna, Joy, & Sundaresan (2015)
Antidiabetic	Abino rat, Male Wisters 200 mg/kg, 30 days.	Aqueous	Root	Diabetes induced by streptozotocin	Fasting blood glucose and glycosylated hemoglobin.	Treatment helps in stopping hyperglycemia.	Nabi, Kasetti, Sirasanagandla, Tilak, Kumar, & Rao (2013)

TABLE 4.6 (Continued)

Activity	Animal, Dose, Duration, Route of Administration	Extract	Part	Models	Various Evaluating Parameters	Foremost Findings	References
	Albino rats, 100.0 and 200.0 mg/kg, 27 days	Essential oil	Fruit	Diabetes induced by streptozotocin	Insulin level, glycogen content in liver Glycosylated hemoglobin and blood glucose level.	Treatment results in anti-diabetic activity.	Kumar, Sharma, & Vasudeva (2013)
Anthelmintic	0.1, 0.2, 0.3, 1.0–3.0 mg/ml	Oil	Fruits	Baseline, amplitude, tension, and occurrence of unstructured muscular activity.	Helminthic species – <i>Fasciola gigantica</i>	Permanent paralytic outcome was reported.	Singh, Kumar, Tandan, & Mishra (2009)
	1:1,000 v/v dilutions of oil.	Oil	Fruits	Baseline tension, amplitude, and regularity of impulsive muscular action.	Helminthic species – <i>Ascaris lumbricoides</i>	Repressed rhythmic activities of ascaris (standard drug tetramisole).	Kokate, Chaudhari, & Nimbkar (1980)
	100, 300, 1,000, and 3,000 µg/ml	Alcohol	Fruits	Glucose uptake and motility	Helminthic species – <i>F. gigantica</i> along with <i>G. explanatum</i> .	Paralyzing outcome was reported (standard drug-oxytoclozanide).	Singh, Kumar, Gupta, & Tandan (2007)
	100.0, 300.0, 1000.0, and 3000.0 µg/ml	Alcohol	Fruits	Baseline tension, amplitude, and regularity of impulsive muscular activity of the amphistome.	Helminthic species – <i>Gigantocotyle explanatum</i>	Paralytic reason was reported	Singh, Kumar, Singh, Raj, Prasad, Parmar, & Ghosh, (2008)
	90.0, 120.0, 150.0, 200.0 mg/ml	Chloroform, ether, acetone, ethanol	Fruits	Anti-larvicidal	<i>I. exustus</i>	Molluscicides against the snail <i>I. exustus</i>	Pandey & Singh (2009)

**TABLE 4.6** (Continued)

Activity	Animal, Dose, Duration, Route of Administration	Extract	Part	Models	Various Evaluating Parameters	Foremost Findings	References
	1.95, 3.91, 7.81, 15.63, 500, 250, 125, 62.5, 31.25 mg/mL	Methanol, fraction, hexane, chloroform fraction	Fruits	Egg hatch analyze, larval motility assess, adulticidal assay on amphistomes larval migration nhhibition assay.	Mature Amphistomes	Portion of chloroform from <i>P. longum</i> obsessed utmost broad-spectrum anthelmintic action analogous to controls (standard drug-ivermectin and thiabendazole).	Koorse et al. (2018)
Hepatoprotective	Rats, 50 and 100 mg/kg, p.o.	Ethanol	Fruits	CCl <sub>4</sub> enhanced liver fibrosis.	ALT, ALP, liver hydroxyl proline, serum AST, body weight, TBL	Anti fibrotic activity was pragmatic due to the flavonoid pleased of <i>Pipper</i> .	Christina et al. (2006)
	Rats, 200 mg/kg, 21 days	Aqueous	Fruits	AlCl <sub>3</sub> enhanced hepatotoxicity	SGPT, SGOT, ALP, bilirubin, and creatinine.	Reduce levels of serum biochemical markers.	Sharma, Kumar, Chashoo, Saxena, & Pandey (2014)
Anti-asthmatic	Rats, 200.0 mg/kg, p.o., For 14 days	Ethanol	Fruits	–	Mast cell establishing, histopathology, mast cell staining	Antiasthmatic activity was noticed (standard drug-prednisolone)	Choudhary (2006)
Antiulcer	Rats, 50.0 mg/kg, 1 hour prior to testing p.o.	Ethanol	Fruits	Cold restraint stress, pyloric ligation induced ulcer, aspirin induced gastric ulcer, gastric secretion study.	Severity per stomach, ulcer per stomach, ulcer index, DNA, pepsin, total hexose, protein, hexamine, fucose, sialic acid, amount of acid, total carbohydrate.	Stability linking violent and suspicious factors of ulcer creation was achieved by action.	Agrawal, Rao, Sairam, Joshi, & Goel (2000)



TABLE 4.6 (Continued)

Activity	Animal, Dose, Duration, Route of Administration	Extract	Part	Models	Various Evaluating Parameters	Foremost Findings	References
Antifertility	Female rat, 200 mg/kg from days 1–7 post coital, p.o	Ethanol	Fruits	Antifertility bioassay process	% Anti-implantation activity	Infertility was examined	Lakshmi, Kumar, Agarwal, & Dhar (2006)
	Rats, 150.0 and 250.0 mg/kg, p.o. for 30 days.	Hexane	Fruits	–	Histological variations in ovary and uterus estrous cycle, hormonal level in the blood serum, antioxidant enzymes, quantity of cytokines, 2 expression, anti-implantation, and antifertility action.	Treatment reduced LH, FSH, COX-2 IL-1 $\beta$ , expression, actions of CAT, GPx, SOD, GST, and GR levels, TNF- $\alpha$ level was improved.	Sarwar, Sharma, Arif, Thakur, Athar, Khillare, & Thakur (2014)
	20 mg/ml	Hexane	Fruits	–	Hypo-osmotic swelling, sperm immobilization.	<i>In vitro</i> activity of contraceptive spermicidal by the treatment demonstrate.	Sarwar, Nirala, Arif, Khillare, & Thakur (2015)
Anti-amoebic	Mice, 125.0, 250.0, 500.0, 1000.0 mg/kg, five days, p.o	Ethanol	Fruits	Experimental production of caecal amoebiasis in rat.	Percent caecal amoebiasis of rats cleared, average caecal store in wall.	Harshness of caecal walls were condensed in mice which inward the extract.	Sawangjaroen, Sawangjaroen, & Poonpanang (2004)
	1,000 $\mu$ g/ml <i>in vitro</i> , 900 mg/kg for Rats, 5 days, p.o.	Ethanol	Fruits	<i>In vitro</i> screening, investigational invention of amoebiasis in rat caecal.	Percent caecal amoebiasis of rats cleared and average caecal store in wall and contents.	Plants may have assured compounds erstwhile piperine, that have accountable for improved efficiency.	Ghoshal, Prasad, & Lakshmi (1996)

**TABLE 4.6** (Continued)

Activity	Animal, Dose, Duration, Route of Administration	Extract	Part	Models	Various Evaluating Parameters	Foremost Findings	References
	1000.0 µg/ml <i>in vitro</i> , 900.0 mg/kg for five days <i>in vivo</i> .	Ethanol	Root	Production of caecal amoebiasis in rats <i>in vitro</i> .	Percent caecal amoebiasis of rats cleared and average caecal store in wall and contents.	Treatment have low <i>in vitro</i> activity, exhibited demonstrable <i>in vivo</i> .	Ghoshal & Lakshmi (2002)
Antiplatelet	1, 5, 25, 50 g/ml	Butanol and aqueous ethanol	Fruits	Rabbit platelet aggregation	Measurement of inositol phosphates, reason of platelet aggregation, receptor binding analyze.	Plant have a ingredient that reduced aggregation of platelets.	Iwashita, Saito, Yamaguchi, Takagaki, & Nakahata (2007)
Antiparkinsonian	Rat, 50.0 and 75.0 mg/kg, p.o.	Ethanol	Fruits	Dopaminergic neuronal damage rat induced by lipopolysacch aride	Dopamine, open-field test, rotational behavior, IL-1β, IL-6, TNF-α, ROS, and NO action were resolved	Over activated microglial cells were dormant, IL-1β, IL-6, ROS TNF-α, and no levels were decreased, enhanced behavioral dysfunction improved the levels of DOPAC and DA	He, Guo, Xu, Chen, Zhang, Wu, & Wang (2016)
	30.0, 60.0 and 120.0 mg/kg for 1 week in C57BL/6 mice	Ethanol	Seeds	MPTP induced mouses	Dopaminergic neurons, Antioxidant enzymatic level tyrosine and hydroxylase immuno-histoc hemistry analyze	Treatment demonstrate ameliorative properties in dopaminergic neurons.	Bi et al. (2015)
	Mice, 45 days, 50.0 mg/kg, p.o	Ethanol	Fruits	6-OHDA-induced Parkinson's disease	Rotary rod tests, apomorphine, TH, induced rotation, SOD, GSH-Px, MDA, CAT, GSH, NO, and NOS level were determined.	Treatment enhanced behavioral defect, enhance the figure of TH-cells, regulate the actions of SOD, GSH-Px, CAT, GSH, reduce the content of NOS, NO.	Zheng et al. (2014)

TABLE 4.6 (Continued)

Activity	Animal, Dose, Duration, Route of Administration	Extract	Part	Models	Various Evaluating Parameters	Foremost Findings	References
	Rats, 100 and 200 mg/kg, p.o. anti-hyperlipidemia	Oil	Fruits	Streptozotocin-induced diabetic	Insulin level, glucose level, liver glycogen content, glycosylated hemoglobin, entirety plasma cholesterol, triglyceride, and anti-oxidant parameter.	Liver glycogen content, cure show raise in weight, plasma insulin, and high-density lipoprotein, triglyceride, and entire plasma cholesterol (standard drug-glibenclamide).	Kumar, Sharma, & Vasudeva (2013)
ACE-inhibitor	0.5, 1.0, 1.5, 2.0, 2.5 mg/ml	Butanol, ethyl acetate	Fruits	–	Hippuric-L-histidyl-L-leucine as a substrates	Antihypertensive activity was examined.	Chaudhary, Mukherjee, Maiti, De, Bhadra, & Saha (2013)
Mosquito larvicidal	25 mg/L	Methanol	Fruits	Bioassay was performed for larvicidal action for <i>Aedes aegypti</i>	Death rate	Replant towards insects can provide by <i>P. longum</i> .	Yang, Lee, Lee, Kim, Lee, & Lee (2002)
Antistress	Rats, 100, 200 and 300 mg/kg, p.o.	Alcoholic	Fruits	Strained swimming stress	5-HIAA, HVA, and urinary VMA	The levels of VMA and 5HIAA were reduced while HVA levels show increase in mice urine.	Kilari, Rao, Sreemanthula, & Kola (2015)
	Rats, 250.0 mg/kg and 500.0 mg/kg, p.o., 20 days	Aqueous	Fruits	Chronic cold self-control stress	Total proteins, plasma levels of glucose, corticosterone, triglycerides, and cholesterol	Adaptogenic activity was observed.	Juvekar, Kulkarni, & Juvekar (2008)

**TABLE 4.6** (Continued)

Activity	Animal, Dose, Duration, Route of Administration	Extract	Part	Models	Various Evaluating Parameters	Foremost Findings	References
Anti angiogenic	C57BL/6 mice at 10 mg/animals	Ethanol	Fruits	B16F-16 melanoma cell-induced capillary preparation in mice and VEGF-induced vessel sprouting in ratarotic ring analyze.	Appraisal of tumor-directed capillaries, measurement of IL-6, IL-2IL-1 $\beta$ , TNF- $\alpha$ , VEGF, GM-CSF, TIMP-1, VEGF-induced capillary-like tube, proliferation.	The number of tumor-directed capillaries has been reduced. enhanced IL-1, IL-6, IL-2, GM- CSF, TNF-, VEG, TIMP-1 levels VEGF-induced vascular sprouting, propagation, cell migration, and capillary-like tube formation were all inhibited.	Sunila & Kuttan (2006)
Anticonvulsant	Mices, 7 days 250.0 mg/kg and 500.0 mg/kg, p.o.	Aqueous	Fruits	Seizures induced by strychnine. PTZ and 4-aminopyridine.	Accessible protection against 4 aminopyridine along with convulsion and PTZ.	Anticonvulsant activity validated in this study.	Juvekar, Kulkarni, & Juvekar (2008)
Anticancer	<i>In vitro</i>	Benzene, hexane, chloroform, alcohol, ethyl acetate, aqueous	Fruits	Lung (A549), Prostate (DU 145), ovary (IGR-OVI-1) leukemia (THP-1), breast (MCF-7) and cancer cell line	Cell cycle investigation, cytotoxic assay, purpose of lipid and flavonoid peroxidation reticence analyze	Cytotoxicity with effect on sub G1 phase	Sharma, Kumar, Chashoo, Saxena, & Pandey (2014)
Nootropic	Mice, 100, 200 and 300 mg/kg, p.o.	Alcoholic	Fruits	Scopolamine-induced memory impairment, Y-maze model	Reduce scopolamine-induced memory.  Interruption and raise cognitive activity and effective remembrance in the Y-maze.	<i>P. longum</i> may serve as good nootropic cause.	Kilari, Rao, Sreemanthula, & Kola (2015)

**TABLE 4.6** (Continued)

Activity	Animal, Dose, Duration, Route of Administration	Extract	Part	Models	Various Evaluating Parameters	Foremost Findings	References
	Mice, 250 mg/kg And 500 mg/kg, 7 days, p.o.	Aqueous	Fruits	Elevated plus maze model and passive evasion model	Improved step-down-latency and summarized the shift latency.	It may be provide as a excellent nootropic mediator.	Juvekar, Kulkarni, & Juvekar (2008)

*Abbreviations:* Alanine transaminase (ALT); Adriamycin (ADR); Alkaline phosphatase (ALP); Aspartate aminotransferase (AST); Cholesterol (CH); Cyclooxygenase (COX-2); Catalase (CAT); 3,4-Dihydroxyphenylacetic acid (DOPAC); Dopamine (DA); Dalton's lymphoma ascites (DLA); Granulocyte-macrophage colony-stimulating factor (GM-CSF); Glutathione peroxidase (GSH-Px); Glutathione (GSH); 5-hydroxyindoleacetic acid (5-HIAA); Ehrlich aascites carcinoma (EAC) cell line, High density lipoproteins (HDL); Homo vanillic acid (HVA); Interleukin-2 (IL-2); Interleukin-6 (IL-6); Interleukin-1 $\beta$  (IL-1 $\beta$ ); Lactate dehydrogenase (LDH); Low density lipoproteins (LDL); Minimum inhibitory concentration (MIC); Methylendioxyamphetamine (MDA); Serum glutamic oxaloacetic transaminase (SGOT); Nitric oxide (NO); 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP); 3,4-Nitric oxide synthases (NOS); Nicotinamide adenine dinucleotide phosphate (NADPH); Pentylentetrazol (PTZ); Serum glutamic-pyruvic transaminase (SGPT); Superoxide dismutase (SOD); Total protein content (TPC); Tissue inhibitor of metalloproteinases (TIMP-1); Tumor necrosis factor alpha (TNF- $\alpha$ ); Triglyceride (TG); Tyrosine hydroxylase (TH); Vascular endothelial growth factor (VEGF); and Vanillyl mandelic acid (VMA).

collectively in the common method, which is useful in paraplegia and also sciatica. A brief uses of *P. longum* known as Ayurvedic medicine.

#### **4.10.1 USES OF DRY FRUIT OF *P. LONGUM* IN AYURVEDIC MEDICINE**

- Amanut: Useful in indigestion
- Anushna: Not very hot
- Arshahara: Useful in piles
- Deepani: Improves digestion strength
- Gulmahara: Useful in abdominal tumor
- Kapha Vataghni: Balance kapha and vata dosha
- Kasahara: Relives cough, cold
- Katu: Pungent taste
- Kshayapaha: Relieves chronic lung disorders
- Kushtahara: Useful in skin diseases
- Pitta Avirodhini: Dose not increase Pitta to a large extent
- Pramehahara: Useful in diabetes
- Rasayani: Antiaging, rejuvenative
- Rechani: Causes purgation
- Shwasahara: Useful in asthma,
- Snigdha: Unctuous, oily
- Udarahara: Useful in ascites
- Ushna: Hot
- Vrushya: Aphrodisiac

#### **4.10.2 PREPARATIONS OF *P. LONGUM* FOR MARKET USE**

1. **Ayurvedic Articulation:** Trikattu Churna (Shailajan, Sayed, Joshi, & Tiwary, 2011; Vyas et al., 2011), Pippli Churna (Gupta & Jain, 2011), Sitopaladichurna (STPLC) (Gupta & Jain, 2011), Ajmodadichurna (AJC) (Gupta & Jain, 2011; Sarkar, Tiwari, Patel, & Dubey, 2011), Triphalaguggulu (Patel, Patel, & Patel, 2012), Eladi Gutika (Rode, Bhujbal, & Sandhya, 2013), LasunadiVati, Marichyadivati, and Kaphaketu rasa (Rout, Rout, & Mishra, 2007). Unani formulation: Hab-e-Azarakhi (Jain & Dashora, 2012) dosage forms.
2. **Vista Nutrition Curcumin with Piperine (pill) Explanation:** Piperine with vista nutrition's curcumin capsules has anti-inflammatory, anti-oxidant effects. It contains piperine and curcumin that

restrains the enzyme called CYP3A4 to boost the oral bioavailability of compounds.

- 3. Zenith Nutrition Curcumin with Piperine (Pills) Explanation:** Zenith Nutrition Curcumin with Piperine having piperine and curcumin. The dynamic part of turmeric is responsible for its prosperous color and possible health reimbursement. The influential antioxidant helps in controlling a well inflammatory reply, in defense of cells from free radical damage, guard of brain cells, in controlling healthy liver still beneath demanding conditions.

#### 4.10.3 FOLK USES OF *P. LONGUM*

- 1. Asthma:** Pepper-pea size tablets, prepared from *P. longum* fruit and *Calotropis gigantea* flowers in identical amount is given two times every day awaiting cure. Pippali is very useful for asthma because it has bronchodilator, decongestant, and expectorant activities. Thus, *P. longum* having Kapha balancing property.
- 2. Diarrhea:** Powder of *P. longum* helps to control diarrhea because of it have Vata balancing qualities. It also enhanced the stomach fire because of its appetizer qualities which helps to manage abnormal motion incidences.
- 3. Menstrual Disorders:** *P. longum* helps to control menstrual cycle problems for example dysmenorrhea. In Ayurvedic medicines, menstruation is managed and governs by Vata dosha. *P. longum* has Vata consideration property and provides support in dysmenorrhea.
- 4. Cough:** Mixture of long pepper and *Adhatoda vasica* leaves, which is given two teaspoons to thrice in every day until make well.
- 5. Hair Tonic:** Paste made with *P. longum* and leaves of neem mixed with gingely oil and cow's milk and are useful to the scalp everywhere there are hair loss.

#### 4.11 MARKET TRADE AND ITS APPLICATION

Current market situation and export potential cultivation of medicinal and aromatic plants is fast replacing the cultivation of conventional crops in India. The country is expected to be the main player in the global market for herbal product-based medicines. The export of herbal materials and medicines is estimated to be around 500 crores. *P. longum* is being frequently

exported in huge quantities to countries such as Austria, Australia, USA, Russia, Canada, Philippines, Hungary, Europe, South East Asian countries such as Singapore, Africa, and Japan and Pakistan, etc. The price varies in diverse countries ranging from Rs. 350 to Rs. 3,000 or more per Kg. Some of the companies that sell long piper in India and also export are – M/S World Wide Enterprise (West Bengal), Sathva bioactives Pvt Ltd (Karnataka), Mother Herbs Pvt Ltd (Delhi), ARAMACS (Delhi), Nutramine Life Sciences (Delhi), Alchemy Ghemicals (Madhya Pradesh), Suyash Herbs Export Pvt Ltd (Gujrat), Genia nature Herbs Private Ltd (Tamil Nadu), Enjay Marketing Services Pvt Ltd (Maharashtra), Mazzy Exports (Chennai), Jairmdass Khushiram (Maharashtra), BIOPREX/LABS (Maharashtra) and R P Enterprises (Andhra Pradesh), etc. These companies buy long piper from the cultivators, clean, dry in their dispensation unit and pack in 1, 5, or 25 Kg bags for export.

#### **4.11.1 SPICES INDUSTRY**

*P. longum* may be establish in the multifaceted spice combinations of Morocco and also, it is an significant component in Ethiopia cuisine, anywhere *P. longum* is generally establish in the conventional meat stews collectively among nut meg, clove, black pepper, turmeric, and bereberes, a conventional Ethiopian spice combination, which simulate to Indian masale, are use to flavor mutton dishes. Moreover, hot, and spicy taste of *P. longum*, while it gets a sweet flavor.

#### **4.11.2 BIOTECHNOLOGY ASPECTS**

*P. longum* has considered as industrially valued medicinal aromatic plant that presently gained it's require because of the occurrence of essential oils, alkaloids, fatty acid, flavonoids, and glycosides. It is mainly employed in flavoring, fragrance, and pharmaceutical based industries. Tissue culture technique might be used to generate huge number of clonal propagules. Thus, clonal propagation technique is fairly required to have homogeneous *P. longum* plants obtained from germplasm to recover the improved global demand. The information regarding plant genetics, their phytochemistry, and other applicable technologies provide more resources to produce commercial crop.



### 4.11.3 INSECT AND PESTS REPELLENT

Piperoctadecalidine and piperonaline amides were obtained from fruits of *P. longum*, however plant have been reported to containing several insecticidal effects that might be useful to manage insect and pests control in agricultural fields.

### 4.11.4 IMMUNITY BUSTER PRODUCTS

Piperine has derived from fruits of *P. longum*, which have Immunity buster activity. Hence it is a safe and good alternative Immunity buster product.

### 4.11.5 ANTI-VENOM PRODUCT

Fruits of *P. longum* have been conventionally used against snakebites in southern and north-eastern areas of India. This plant having excellent anti-snake venom properties, on the other hands piperines are one of the components which are reliable for the efficient venom neutralizing capacity of the *P. longum* plant.

## 4.12 INTERNATIONAL PATENT OF *P. LONGUM* LINN.

Few international patent of *P. longum* showing in Table 4.7.

**TABLE 4.7** Some International Patent of *P. longum*

Sl. No.	Publication Number	Publication Date	Title
1.	CN103202898B *	2014-04-16	Traditionally Chinese medicine composition and formulation method thereof.
2.	CN104232312A *	2014-12-24	Long pepper extort and formulation method thereof.
3.	CN102649784A *	2012-08-29	Extracting method of piperlonguminine from <i>Piper longum</i> thereof.
4.	CN102389388A *	2012-03-28	Toothpaste preparation by <i>Piper longum</i> and formulation.
5.	CN101791336B *	2011-09-21	<i>Piper longum</i> extract preparation, method, and applications thereof.
6.	CN1322543A *	2001-11-21	Preparation of antilipemic medicine.

#### 4.13 CONCLUSION AND FUTURE ASPECTS

*P. longum* L. possesses medicinal appositeness from ancient time, but now days requires to build up up to date drugs with efficient widespread examination for its bioactivity, method, toxicity, and also pharmacotherapeutics, as well as after suitable consistency and clinical cases. The researchers of all about the universally in the structural change and fusion of novel related to privileged molecules of major phytochemical of *P. longum*. Phytochemical are accredited to the broad array of biological performance. It possesses numerous remedies as well as industrially helpful planning have been marketed, which give rise to support amongst scientists in analyzing this medicinal significant affiliation. While, it is extremely fine proof from the literatures that major phytochemicals have got amazing probability, hence the suitable change in the molecule and combination of it's idiomatic to assuage the toxicity with improved economic asset and with high-quality beneficial uses.

#### KEYWORDS

- **ayurvedic medicine**
- **pharmacology**
- **phytochemistry**
- ***Piper longum***
- **piperaceae**
- **piperine**
- **spices industry**
- **traditional evidence**

#### REFERENCES

- Agrawal, A., Rao, C. V., Sairam, K., Joshi, V., & Goel, R., (2000). Effect of *Piper longum* Linn, *Zingiber officianalis* Linn and *Ferula* species on gastric ulceration and secretion in rats. *Indian. J. Exp. Biol.*, 38, 994–998.
- Agrawal, A., Rao, C. V., Sairam, K., Joshi, V., & Goel, R., (2000). Effect of *Piper longum* Linn, *Zingiber officianalis* Linn and *Ferula* species on gastric ulceration and secretion in rats. *Indian. J. Exp. Biol.*, 38, 994–998.
- Ali, M. A., Alam, N., Yeasmin, M., Khan, A., Sayeed, M. A., & Rao, V., (2007). Antimicrobial screening of different extracts of *Piper longum* Linn. *Res. J. Agri. Biol. Sci.*, 3(6), 852–857.

- Ali, M. A., Alam, N., Yeasmin, M., Khan, A., Sayeed, M. A., & Rao, V., (2007). Antimicrobial screening of different extracts of *Piper longum* Linn. *Res. J. Agri. Biol. Sci.*, 3(6), 852–857.
- Aneja, K. R., Joshi, R., Sharma, C., & Aneja, A., (2010). Antimicrobial efficacy of fruit extracts of two piper species against selected bacterial and oral fungal pathogens. *Braz. J. Oral Sci.*, 9(4), 421–426.
- Aneja, K. R., Joshi, R., Sharma, C., & Aneja, A., (2010). Antimicrobial efficacy of fruit extracts of two *Piper* species against selected bacterial and oral fungal pathogens. *Braz. J. Oral Sci.*, 9(4), 421–426.
- Anonymous, (1999). WHO monographs on selected medicinal plants (Vol. 1, pp. 1, 2). World Health Organization, Geneva.
- Arambewela, L. P., & Wijesundera, R. L. C., (1999). The volatile constituents and microbiological studies on *Kaempheria galanga*, *Hibiscus abelmoschus* and *Piper longum*. *Acta Hort.*, 501, 297–300.
- Ayurveda Health and Lifestyle Portal*. Available at: <http://www.ayurveda.com/herbs/piper-longum.htm> (accessed on 02 September 2023).
- Bao, L., Bai, S., & Borijihan, G., (2012). Hypolipidemic effects of a new piperine derivative GB-N from *Piper longum* in high-fat diet-fed rats. *Pharm. Biol.* 50(8), 962–967.
- Barua, C., Singh, A., Sen, S., Barua, A., & Barua, I., (2014). *In vitro* antioxidant and antimycobacterial activity of seeds of *Piper longum* Linn: A comparative study. *SAJ. Pharm. Pharmacol.*, 1(101), 2262–2371.
- Bezerra, D. P., Castro, F. O., Alves, A. P., Pessoa, C., Moraes, M. O., Silveira, E. R., Lima, M. A., et al., (2006). *In vivo* growth-inhibition of sarcoma 180 by piperine and piperone, two alkaloid amides from Piper. *Braz. J. Med. Biol. Res.*, 39(6), 801–807.
- Bi, Y., Qu, P. C., Wang, Q. S., Zheng, L., Liu, H. L., Luo, R., Chen, X. Q., et al., (2015). Neuroprotective effects of alkaloids from *Piper longum* in a MPTP-induced mouse model of Parkinson's disease. *Pharm. Biol.*, 53(10), 1516–1524.
- Chaithong, U., Choochote, W., Kamsuk, K., Jitpakdi, A., Tippawangkosol, P., Chaiyasit, D., et al., (2006). Larvicidal effect of pepper plants on *Aedes aegypti* (L.) (Diptera: Culicidae). *J. Vector Eco.*, 31, 138–144.
- Chatterjee, A., & Dutta, C. P., (1967). Alkaloids of *Piper longum* Linn—I: Structure and synthesis of piperlongumine and piperlonguminine. *Tetrahedron*, 23(4), 1769–1781.
- Chaudhary, S. K., Mukherjee, P. K., Maiti, N., De, A. K., Bhadra, S., & Saha, B. P., (2013). Evaluation of angiotensin converting enzyme inhibition and anti-oxidant activity of *Piper longum* L. *Indian J. Tradit. Knowl.*, 12, 478–482.
- Chaveerach, A., Mookamul, P., Sudmoon, R., & Tanee, T., (2006). Ethnobotany of the genus *Piper* (Piperaceae) in Thailand. *Ethnobot. Res. Appl.*, 4, 223–231.
- Choochote, W., Chaithong, U., Kamsuk, K., Rattanachanpicchai, E., Jitpakdi, A., Tippawangkosol, P., et al., (2006). Adulticidal activity against *Stegomyia aegypti* (Diptera: Culicidae) of three *Piper* spp. *Rev Inst Med Trop Sao Paulo*, 48, 33–37.
- Choudhary, G. P., (2006). Mast cell stabilizing activity of *Piper longum* Linn. *Indian J. Allergy Asthma Immunol.*, 20, 112–116.
- Choudhary, G., (2006). Mast cell stabilizing activity of *Piper longum* Linn. *Indian. J. Allergy. Asthma. Immunol.*, 20(2), 112–116.
- Christina, A. J., Saraswathy, G. R., Robert, S. J., Kothai, R., Chidambaranathan, N., Nalini, G., et al., (2006). Inhibition of CCl<sub>4</sub> induced liver fibrosis by *Piper longum* Linn. *Phytomedicine*, 13, 196–18.

- Christina, A., Saraswathy, G., Robert, S. H., Kothai, R., Chidambaranathan, N., Nalini, G., & Therasal, R., (2006). Inhibition of CCl<sub>4</sub>-induced liver fibrosis by *Piper longum* Linn.? *Phytomed.*, 13(3), 196–198.
- Clark, C. E., Arnold, E., Lasserson, T. J., & Wu, T., (2010). Herbal interventions for chronic asthma in adults and children: A systematic review and meta-analysis. *Primary Care Respiratory Journal*, 19, 307–314. <https://doi.org/10.4104/pcrj.2010.00041> PMID: 20640388.
- Das, J., Jha, D. K., Policegoudra, R. S., et al., (2012). Isolation and characterization of antidermatophytic bioactive molecules from *Piper longum* L. leaves. *Indian Journal of Microbiology*, 52(4), 624–629.
- Desai, S. J., Prabhu, B. R., & Mulchandani, N. B., (1988). Aristolactams and 4, 5-dioxoaporphines from *Piper longum*. *Phytochemistry*, 27(5), 1511–1515.
- Dutta, C. P., Banerjee, N., & Roy, D. N., (1975). Lignans in the seeds of *Piper longum*. *Phytochemistry*, 14(9), 2090–2091.
- Evans, W. C., (2009). *Trease and Evans' Pharmacognosy*. Elsevier Health Sciences.
- Ghoshal, S., & Lakshmi, V., (2002). Potential antiamebic property of the roots of *Piper longum* Linn. *Phytother. Res.*, 16, 689–691.
- Ghoshal, S., & Lakshmi, V., (2002). Potential antiamebic property of the roots of *Piper longum* Linn. *Phytother. Res.*, 16(7), 689–691.
- Ghoshal, S., Prasad, B. K., & Lakshmi, V., (1996). Antiamebic activity of *Piper longum* fruits against *Entamoeba histolytica* *in vitro* and *in vivo*. *J. Ethnopharmacol.*, 50(3), 167–170.
- Gupta, U. P., Nath, A., Gupta, S. C., & Shrivastava, T. N., (1980). Preparation of semisynthetic analogues of piper amides and their anti-tubercular activity. *Bull. Med. Ethenobot. Res.*, 1(1), 99–101.
- Gupta, V., & Jain, U. K., (2011). Estimation of piperine by UV-spectrophotometric method in herbal formulation, pippli churna. *Int. J. Res. Pharmaceutica Biomed Sci.*, 2(2), 550–553.
- Gupta, V., & Jain, U. K., (2011). Quantitative analysis of piperine in ayurvedic formulation by UV spectrophotometry. *Int. J. Pharma. Sci. Res.*, 2(2), 58–61.
- Gupta, V., & Jain, U. K., (2011). Status of piperine content in Ayurvedic formulation: Method standardization by HPTLC. *Res. J. Pharma. Biol. Chem Sci.*, 2(2), 524–532.
- Harwansh, R. K., Mukherjee, K., Bhadra, S., Kar, A., Bahadur, S., Mitra, A., & Mukherjee, P. K., (2014). Cytochrome P450 inhibitory potential and RP-HPLC standardization of trikatu—A Rasayana from Indian Ayurveda. *J. Ethnopharmacol.*, 153(3), 674–681.
- He, H., Guo, W. W., Xu, R. R., Chen, X. Q., Zhang, N., Wu, X., & Wang, X. M., (2016). Alkaloids from *Piper longum* protect dopaminergic neurons against inflammation-mediated damage induced by intranigral injection of lipopolysaccharide. *BMC. Complement. Altern. Med.*, 16(1), 412.
- <http://www.genome.jp/db/pcidb> (accessed on 02 September 2023).
- <http://www.plantsoftheworldonline.org/taxon/urn:lsid:ipni.org:names:682031-1> (accessed on 02 September 2023).
- <https://pubchem.ncbi.nlm.nih.gov/> (accessed on 02 September 2023).
- Huang, H., Morgan, C. M., Asolkar, R. N., Koivunen, M. E., & Marrone, P. G., (2010). Phytotoxicity of sarmentine isolated from long pepper (*Piper longum*) fruit. *J. Agric. Food Chem.*, 58(18), 9994–10000.
- Iwashita, M., Saito, M., Yamaguchi, Y., Takagaki, R., & Nakahata, N., (2007). Inhibitory effect of ethanol extract of *Piper longum* L. on rabbit platelet aggregation through antagonizing thromboxane A2 receptor. *Phytomedicine*, 14, 853–855.

- Iwashita, M., Saito, M., Yamaguchi, Y., Takagaki, R., & Nakahata, N., (2007). Inhibitory effect of ethanol extract of *Piper longum* L. on rabbit platelet aggregation through antagonizing thromboxane A2 receptor. *Biol. Pharm. Bull.*, 30(7), 1221–1225.
- Jagdale, S., Kuchekar, B., Chabukswar, A., Lokhande, P., & Raut, C., (2009). Anti-oxidant activity of *Piper longum* Linn. *Int. J. Biol. Chem.*, 3(3), 119–125.
- Jagdale, S., Kuchekar, B., Chabukswar, A., Lokhande, P., & Raut, C., (2009). Anti-oxidant activity of *Piper longum* Linn. *Int. J. Biol. Chem.*, 3(3), 119–125.
- Jain, T., & Dashora, K., (2012). Spectrophotometric fingerprinting method for Unani formulation Hab-e-Azarakhi. *Asian J. Pharm. Tech.*, 2(1), 1–3.
- Jalalpure, S. S., Patil, M. B., Prakash, N. S., Hemalata, K., & Manvi, F. V., (2003). Hepatoprotective activity of the fruits of *Piper longum* Linn. *Indian Journal of Pharmaceutical Sciences*, 65, 363.
- Jiang, Z. Y., Liu, W. F., Huang, C. G., et al., (2013b). New amide alkaloids from *Piper longum*. *Fitoterapia*, 84, 222–226.
- Jiang, Z. Y., Liu, W. F., Zhang, X. M., et al., (2013a). Anti-HBV active constituents from *Piper longum*. *Bioorganic & Medicinal Chemistry Letters*, 23(7), 2123–2127.
- Jin, Z., Borjihan, G., Zhao, R. G., Sun, Z., Hammond, G. B., & Uryu, T., (2009). Antihyperlipidemic compounds from the fruit of *Piper longum* L. *Phytother. Res.*, 23(8), 1194–1196.
- Johri, R., & Zutshi, U., (1992). An Ayurvedic formulation ‘Trikatu’ and its constituents. *J. Ethnopharmacol.*, 37(2), 85–91.
- Juvekar, M., Kulkarni, M., & Juvekar, A., (2008). Anti-stress, nootropic, and anticonvulsant potential of fruit extracts of *Piper longum* L. *Planta Medica*, 74(09), PA244.
- Kanaki, N., Dave, M., Padh, H., & Rajani, M., (2008). A rapid method for isolation of piperine from the fruits of *Piper nigrum* Linn. *J. Nat. Med.*, 62, 281–283.
- Kapoor, L., (2000). *Handbook of Ayurvedic Medicinal Plants* (pp. 264, 265). CRC Press.
- Khan, M., & Siddiqui, M., (2007). Antimicrobial activity of piper fruits. *IJNPR*, 6(2), 111–113.
- Khan, M., & Siddiqui, M., (2007). Antimicrobial activity of piper fruits. *IJNPR*, 6(2), 111–113.
- Khare, C. P., (2008). *Piper longum*. *Indian Medicinal Plants: An Illustrated Dictionary* (p. 491). Springer Science & Business Media.
- Khushbu, C., Roshni, S., Anar, P., Carol, M., & Mayuree, P., (2011). Phytochemical and therapeutic potential of *Piper longum* Linn a review. *International Journal of Research in Ayurveda and Pharmacy*, 2, 157–161.
- Kilari, E. K., Rao, L. S. N., Sreemanthula, S., & Kola, P. K., (2015). Anti-stress and nootropic activity of aqueous extract of *Piper longum* fruit, estimated by noninvasive biomarkers and Y-maze test in rodents. *Environ. Exp. Biol.*, 13, 25–31.
- Kim, K. S., Kim, J. A., Eom, S. Y., Lee, S. H., Min, K. R., & Kim, Y., (2006). Inhibitory effect of piperlonguminine on melanin production in melanoma B16 cell line by downregulation of tyrosinase expression. *Pigment Cell Res.*, 19, 90–98.
- Kirtikar, K. R., & Basu, B. D., (1980). *Indian Medicinal Plants* (pp. 21–28). Mumbai, India: Orients Longman.
- Kokate, C. K., D’cruz, J. L., & Nimbker, A. Y., (1980). Evaluation of fruits of *Piper longum* and leaves of *Adhetoda vasica* for anthelmintic activity. *Indian Drugs*, 17, 99–101.
- Kokate, C., Chaudhari, G., & Nimbkar, A., (1980). *Search for Anthelmintics of Plant Origin: Activities of Volatile Principles of Acorus Calamus and Piper Longum Against Ascaris Lumbricoides* (p. 4). Asian Symposium on Medicinal Plants and Spices, Bangkok (Thailand).

- Koorse, K. G., Samraj, S., John, P., Narayanan, P. M., Devi, S., Usha, P., Sunilkumar, S., & Gleeja, V., (2018). Anthelmintic activity of fruit extract and fractions of *Piper longum* L. *in vitro*. *Pharmacog. J.*, 10(2), 333–340.
- Krishna, M. S., Joy, B., & Sundaresan, A., (2015). Effect on oxidative stress, glucose uptake level and lipid droplet content by Apigenin 7,4'-dimethyl ether isolated from *Piper longum* L. *J. Food Sci. Technol.*, 52(6), 3561–3570.
- Kumar, A., Panghal, S., Mallapur, S., Kumar, M., Ram, V., & Singh, B., (2009). Antiinflammatory activity of *Piper longum* fruit oil. *Indian J. Pharm. Sci.*, 71(4), 454.
- Kumar, G. P., Anilakumar, K., & Naveen, S., (2015). Phytochemicals having neuroprotective properties from dietary sources and medicinal herbs. *Pharmacog. J.*, 7(1), 1–17.
- Kumar, S., Arya, P., Mukherjee, C., Singh, B. K., Singh, N., Parmar, V. S., Prasad, A. K., & Ghosh, B., (2005). Novel aromatic ester from *Piper longum* and its analogues inhibit expression of cell adhesion molecules on endothelial cells. *J. Biochem.*, 44(48), 15944–15952.
- Kumar, S., Kamboj, J., & Sharma, S., (2011). Overview for various aspects of the health benefits of *Piper longum* Linn. fruit. *Journal of Acupuncture and Meridian Studies*, 4, 134–140. [https://doi.org/10.1016/S2005-2901\(11\)60020-4](https://doi.org/10.1016/S2005-2901(11)60020-4) PMID: 21704957.
- Kumar, S., Sharma, S., & Vasudeva, N., (2013). Screening of antidiabetic and antihyperlipidemic potential of oil from *Piper longum* and piperine with their possible mechanism. *Expert. Opin. Pharmacol.*, 14(13), 1723–1736.
- Kumar, S., Sharma, S., & Vasudeva, N., (2013). Screening of antidiabetic and antihyperlipidemic potential of oil from *Piper longum* and piperine with their possible mechanism. *Expert. Opin. Pharmacol.*, 14(13), 1723–1736.
- Kumari, M., Ashok, B., Ravishankar, B., Pandya, T. N., & Acharya, R., (2012). Anti-inflammatory activity of two varieties of Pippali (*Piper longum* Linn.). *Ayu*, 33(2), 307.
- Lakshmi, V., Kumar, R., Agarwal, S. K., & Dhar, J. D., (2006). Antifertility activity of *Piper longum* Linn. in female rats. *Nat. Prod. Res.*, 20, 235–239.
- Lakshmi, V., Kumar, R., Agarwal, S., & Dhar, J., (2006). Antifertility activity of *Piper longum* Linn. in female rats. *Nat. Prod. Res.*, 20(3), 235–239.
- Lee, S. A., Hong, S. S., Han, X. H., Hwang, J. S., Oh, G. J., Lee, K. S., et al., (2005). Piperine from the fruits of *Piper longum* with inhibitory effect on monoamine oxidase and antidepressant/like activity. *Chem. Pharm. Bull.*, 53, 832–835.
- Lee, S. A., Hwang, J. S., Han, X. H., Lee, C., Lee, M., Choe, S. G., et al., (2008). Methylpiperate derivatives from *Piper longum* and their inhibition of monoamine oxidase. *Arch. Pharm. Res.*, 31, 679–683.
- Lee, S. W., Kim, M. S., Park, M. H., Park, S. J., Lee, W. S., Chang, J. S., & Rho, M. C., (2010). Alkamides from *Piper longum* and *Piper nigrum* as inhibitors of IL-6 action. *Bull. Korean Chem. Soc.*, 31(4), 921–924.
- Lee, S., Park, B., Kim, M., Choi, W., Kim, H., Cho, K., Lee, S., & Hoi-Seon, L., (2001). Fungicidal activity of piperonaline, a piperidine alkaloid derived from fruits of long pepper, *Piper longum*, against *Phytopathogenic fungi*. *Crop Prot.*, 20(6), 523–528.
- Li, K., Zhu, W., Fu, Q., et al., (2013). Purification of amide alkaloids from *Piper longum* L. using preparative two-dimensional normal-phase liquid chromatography× reversed-phase liquid chromatography. *Analyst*, 138(11), 3313–3320.
- Liu, W., Jiang, Z., Chen, J., et al., (2009). Chemical constituents from *Piper longum*. *China Journal of Chinese Materia Medica*, 34(22), 2891–2894.

- Madhu, S., Vijayan, V., & Shaikath, A., (2011). Bioactivity guided isolation of mosquito larvicide from *Piper longum*. *Asian Pac. J. Trop. Med.*, 4(2), 112–116.
- Madhusudhan, P., & Vandana, K., (2001). Tetrahydropiperine, the first natural aryl pentanamide from *Piper longum*. *Biochem. Syst. Ecol.* 29(5), 537–538.
- Maheshari, M. L., Vasantha, K. T., Sharma, N., Chandel, K. P., & Patchouli, S., (1993). An Indian perspective. *Indian Perfumer*, 37, 9–11.
- Min, K. R., Kim, K., Ro, J. S., Lee, S. H., Kim, J. A., Son, J. K., & Kim, Y., (2004). Piperlonguminine from *Piper longum* with inhibitory effects on alpha-melanocyte-stimulating hormone-I induced melanogenesis in melanoma B16 cells. *Thieme-connect, Planta Med.*, 70(12), 1115–1118.
- Multilingual Multiscript Plant Name Database*. Available at: <http://www.plantnames.unimelb.edu.au/Sorting/Piper.html> (accessed on 02 September 2023).
- Mustafa, R., Hamid, A. A., Mohamed, S., & Bakar, F. A., (2010). Total phenolic compounds, flavonoids, and radical scavenging activity of 21 selected tropical plants. *J. Food Sci.*, 75(1), C28–C35.
- Nabi, S. A., Kasetti, R. B., Sirasanagandla, S., Tilak, T. K., Kumar, M. V. J., & Rao, C. A., (2013). Antidiabetic and antihyperlipidemic activity of *Piper longum* root aqueous extract in STZ induced diabetic rats. *BMC Complementary and Alternative Medicine*, 13, 37. <https://doi.org/10.1186/1472-6882-13-37> PMID: 23414307.
- Nabi, S. A., Kasetti, R. B., Sirasanagandla, S., Tilak, T. K., Kumar, M. V. J., & Rao, C. A., (2013). Antidiabetic and antihyperlipidemic activity of *Piper longum* root aqueous extract in STZ induced diabetic rats. *BMC Complement. Altern. Med.*, 13(1), 37.
- Nair, K. K. N., (2000). *Manual of Non-wood Forest Produce Plants of Kerala* (pp. 268–270). Kerala Forest Research Institute, Kerala.
- Natarajan, K. S., Narasimhan, M., Shanmugasundaram, K. R., & Shanmugasundaram, E. R., (2006). Antioxidant activity of a salt/spice/herbal mixture against free radical induction. *J. Ethnopharmacol.*, 105, 76–83.
- Nile, S. H., Keum, Y. S., Nile, A. S., Jalde, S. S., & Patel, R. V., (2018). Antioxidant, anti-inflammatory, and enzyme inhibitory activity of natural plant flavonoids and their synthesized derivatives. *J. Biochem. Mol. Toxicol.*, 32(1), e22002.
- Pandey, J. K., & Singh, D. K., (2009). Molluscicidal activity of *Piper cubeba* Linn., *Piper longum* Linn. and *Tribulus terrestris* Linn. and their combinations against snail *Indoplanorbis exustus* Desh. *Indian J. Exp. Biol.*, 47, 643–648.
- Patel, S. G., Patel, J. K., & Patel, K., (2012). Comparison and quantification of marker compound of triphala guggulu by using HPTLC method. *Am J. Pharm. Tech Res.*, 2(4), 999–1013.
- Pathak, N., & Khandelwal, S., (2006). Modulation of cadmium induced alterations in murine thymocytes by piperine: Oxidative stress, apoptosis, phenotyping, and blastogenesis. *Biochem Pharmacol.*, 72(4), 486–497.
- Pattanaik, S., Hota, D., Prabhakar, S., Kharbanda, P., & Pandhi, P., (2006). Effect of piperine on the steady state pharmacokinetics of phenytoin in patients with epilepsy. *Phytother Res.*, 20, 683–686.
- Pradee, C. R., & Kuttan, G., (2002). Effect of piperine on the inhibition of lung metastasis induced B16F-10 melanoma cells in mice. *J. Clin. Exp. Meta.*, 19(8), 703–708.
- Rahman, T., & Rahmatullah, M., (2010). Proposed structural basis of interaction of piperine and related compounds with monoamine oxidases. *Bioorg. Med. Chem. Lett.*, 20, 537–540.

- Rode, S., Bhujbal, P., & Sandhya, P., (2013). Quantification of piperine and 18- $\beta$  glycyrrhetic acid in herbal formulation “eladi gutika.” *Acta Chromatogr.*, 25(1), 135–146.
- Rout, K. K., Rout, O. P., & Mishra, S. K., (2007). Estimation of piperine in commercial Ayurvedic formulations. *J. Planar. Chromat.*, 20, 447–450.
- Ru, J., Li, P., Wang, J., et al., (2014). TCMSP: A database of systems pharmacology for drug discovery from herbal medicines. *Journal of Cheminformatics*, 6(1), 13.
- Sahi, S., Tewatia, P., & Ghosal, S., (2012). *Leishmania donovani* pteridine reductase 1: Comparative protein modeling and protein–ligand interaction studies of the leishmanicidal constituents isolated from the fruits of *Piper longum*. *Journal of Molecular Modeling*, 1–9.
- Samudram, P., Vasuki, R., Rajeshwari, H., Geetha, A., & Moorthi, P. S., (2009). Antioxidant and antihepatotoxic activities of ethanolic crude extract of *Melia azedarach* and *Piper longum*. *J.M.P.R.*, 3(12), 1078–1083.
- Saraf, A., & Saraf, A., (2014). Phytochemical and antimicrobial studies of medicinal plant *Piper longum* Linn. *I.J.P.P.R.*, 6(2), 213–222.
- Sarkar, B., Tiwari, S., Patel, R., & Dubey, G., (2011). High performance thin layer chromatographic method for quantification of piperine in an ayurvedic formulation. *Asian J. Pharmacy Life Sci.*, 1(2), 128–432.
- Sarwar, A. H. M. G., Nirala, R. K., Arif, M., Khillare, B., & Thakur, S. C., (2015). Spermicidal activity of the hexane extract of *Piper longum*: An *in vitro* study. *Nat. Prod. Rep.*, 29(12), 1166–1169.
- Sarwar, A., Sharma, S., Arif, M., Thakur, S. S., Athar, F., Khillare, B., & Thakur, S. C., (2014). *Piper longum* hexane fraction induces infertility by modulation of inflammatory mediators and gonadotripin insufficiency in female rats. *Int. J. Pharm. Pharm. Sci.*, 2, 416–420.
- Sarwar, A., Sharma, S., Arif, M., Thakur, S. S., Athar, F., Khillare, B., & Thakur, S. C., (2014). *Piper longum* hexane fraction induces infertility by modulation of inflammatory mediators and gonadotripin insufficiency in female rats. *Int. J. Pharm. Pharm. Sci.*, 2, 416–420.
- Satyavati, G., Gupta, K., Ashok, & Tandon, N., (1987). *Medicinal Plants of India* (Vol. 2). Indian Council of Medical Research, New Delhi.
- Sawangjaroen, N., Sawangjaroen, K., & Poonpanang, P., (2004). Antiamoebic effects of *Piper longum* fruit, *Piper sarmentosum* root and *Quercus infectoria* nut gall on caecal amoebiasis in mice. *J. Ethnopharmacol.*, 91(2, 3), 357–360.
- Sawangjaroen, N., Sawangjaroen, K., & Poonpanang, P., (2004). Effects of *Piper longum* fruit, *Piper sarmentosum* root and *Quercus infectoria* nut gall on caecal amoebiasis in mice. *J. Ethnopharmacol.*, 91(2, 3), 357–360.
- Selvendiran, K., & Sakthisekaran, D., (2004). Chemopreventive effect of piperine on modulating lipid peroxidation and membrane bound enzymes in benzo (a) pyrene induced lung carcinogenesis. *Biomed Pharmacother.*, 58(4), 264–267.
- Shailajan, S., Sayed, N., Joshi, H., & Tiwary, B., (2011). Standardization of an Ayurvedic formulation: Trikatu churna using bioanalytical tools. *Int. J. Res. Ayur Pharma*, 2(6), 1676–1678.
- Sharma, A. K., Kumar, S., Chashoo, G., Saxena, A. K., & Pandey, A. K., (2014). Cell cycle inhibitory activity of *Piper longum* against A549 cell line and its protective effect against metal-induced toxicity in rats. *Indian J. Biochem. Biophys.*, 51(5), 358–364.
- Sharma, A. K., Kumar, S., Chashoo, G., Saxena, A. K., & Pandey, A. K., (2014). Cell cycle inhibitory activity of *Piper longum* against A549 cell line and its protective effect against metal-induced toxicity in rats. *Indian J. Biochem. Biophys.*, 51, 358–364.



- Shenoy, P., Nipate, S., Sonpetkar, J., Salvi, N., Waghmare, A., & Chaudhari, P., (2013). Anti-snake venom activities of ethanolic extract of fruits of *Piper longum* L. (*Piperaceae*) against Russell's viper venom: Characterization of piperine as active principle. *J. Ethnopharmacol.* 147(2), 373–382.
- Shoji, N., Umeyama, A., Saito, N., Takemoto, T., & Kajiwara, A., (1986). Ohizumi dehydropiperonaline, an amide possessing coronary vasodilating activity, isolated from *Piper longum* L. *J. Pharm. Sci.*, 75, 1188, 1189.
- Singh, M., Varshneya, C., Telang, R. S., & Srivastava, A. K., (2005). Alteration of pharmacokinetics of oxytetracycline following oral administration of *Piper longum* in hens. *J. Vet. Sci.*, 6, 197–200.
- Singh, N., Kumar, S., Singh, P., Raj, H. G., Prasad, A. K., Parmar, V. S., & Ghosh, B., (2008). *Piper longum* Linn. Extract inhibits TNF- $\alpha$ -induced expression of cell adhesion molecules by inhibiting NF- $\kappa$ B activation and microsomal lipid peroxidation. *Phytomedicine*, 15(4), 284–291.
- Singh, T. U., Kumar, D., Tandan, S. K., & Mishra, S. K., (2009). Inhibitory effect of essential oils of *Allium sativum* and *Piper longum* on spontaneous muscular activity of liver fluke, *Fasciola gigantica*. *Exp. Parasitol.*, 123(4), 302–308.
- Singh, T., Kumar, D., & Tandan, S., (2008). Paralytic effect of alcoholic extract of *Allium sativum* and *Piper longum* on liver amphistome, *Gigantocotyle explanatum*. *Indian J. Pharmacol.*, 40(2), 64.
- Singh, T., Kumar, D., Gupta, P., & Tandan, S., (2007). Inhibitory effects of alcoholic extracts of *Allium sativum* and *Piper longum* on gross visual motility and glucose uptake of *Fasciola gigantica* and *Gigantocotyle explanatum*. *J. Vet. Parasitol.*, 21(2), 121–124.
- Srinivasan, R. P., Jamil, K., Madhusudhan, P., Anjani, G., & Das, B., (2001). Antibacterial activity of isolates from *Piper longum* and *Taxus baccata*. *Pharmaceutical Biology*, 39, 236–238.
- Sumy, O., Ved, D. K., & Krishnan, R., (2000). *Tropical Indian Medicinal Plants, Propagation Methods*, 268–269.
- Sunila, E. S., & Kuttan, G., (2004). Immunomodulatory and antitumor activity of *Piper longum* Linn. and piperine. *Journal of Ethnopharmacology*, 90, 339–346. <https://doi.org/10.1016/j.jep.2003.10.016> PMID: 15013199.
- Sunila, E. S., & Kuttan, G., (2005). Protective effect of *Piper longum* fruit ethanolic extract on radiation induced damages in mice: A preliminary study. *Fitoterapia*, 76, 649–655.
- Sunila, E., & Kuttan, G., (2006). *Piper longum* inhibits VEGF and proinflammatory cytokines and tumor-induced angiogenesis in C57BL/6 mice. *Int. Immunopharmacol.*, 6(5), 733–741.
- Tewtrakul, S., Hase, K., Kadota, S., Namba, T., Komatsu, K., & Tanaka, K., (2000). Fruit oil composition of *Piper chaba* Hunt., *P. longum* L. and *P. nigrum* L. *JEOR*, 12(5), 603–608.
- The Wealth of India: A Dictionary of Indian Raw Materials and Industrial Products Raw Materials Series*, (1969). (Vol. VIII, pp. 96–99). Publications and Information Directorate, Council of Scientific & Industrial Research, New Delhi.
- Thomas, M., Sujatha, K., & George, S., (2009). Protective effect of *Piper longum* Linn. on monosodium glutamate induced oxidative stress in rats. *J. Exp. Biol.*, 47, 186–192.
- Thomas, M., Sujatha, K., & George, S., (2009). Protective effect of *Piper longum* Linn. on monosodium glutamate induced oxidative stress in rats. *J. Exp. Biol.*, 47, 186–192.
- Tripathi, D. M., Gupta, N., Lakshmi, V., Saxena, K. C., & Agrawal, A. K., (1999). Anti-giardial and immunostimulatory effect of *Piper longum* on giardiasis due to *Giardia lamblia*. *Phytother Res.*, 13, 561–565.

- Vaghasiya, Y., Nair, R., & Chanda, S., (2007). Investigation of some piper species for anti—Bacterial and anti—Inflammatory property. *Int. J. Pharmacol.*, 3(5), 400–405.
- Varughese, T., Unnikrishnan, P. K., Deepak, M., Balachandran, I., & Rema, S. A., (2016). Chemical composition of the essential oils from stem, root, fruit, and leaf of *Piper longum* Linn. *J. Essent Oil. Bear. Pl.*, 19(1), 52–58.
- Vedhanayaki, G., Shastri, G. V., & Kuruvilla, A., (2003). Analgesic activity of *Piper longum* Linn. root. *Indian J. Exp. Biol.*, 41(6), 649–651.
- Vedhanayaki, G., Shastri, G. V., & Kuruvilla, A., (2003). Analgesic activity of *Piper longum* Linn. root. *J. Exp. Biol.*, 41(6), 649–651.
- Vyas, A., Jain, V., Singh, D., et al., (2011). TLC densitometric method for the estimation of piperine in ayurvedic formulation Trikatu Churna. *Orient J. Chem.*, 27(1), 301–304.
- Wakade, A. S., Shah, A. S., Kulkarni, M. P., & Juvekar, A. R., (2008). Protective effect of *Piper longum* L. on oxidative stress induced injury and cellular abnormality in adriamycin induced cardiotoxicity in rats. *Indian J. Exp. Biol.*, 46, 528–533.
- Wakade, A. S., Shah, A. S., Kulkarni, M. P., & Juvekar, A. R., (2008). Protective effect of *Piper longum* L. on oxidative stress induced injury and cellular abnormality in adriamycin induced cardiotoxicity in rats. *Indian J. Exp. Biol.*, 46, 528–533.
- Wiert, C., (2013). *Lead Compounds from Medicinal Plants for the Treatment of Cancer* (p. 35). Academic Press Waltham.
- Yadav, V., Chatterjee, S. S., Majeed, M., & Kumar, V., (2015). Long lasting preventive effects of piperlongumine and a *Piper longum* extract against stress triggered pathologies in mice. *J. Intercultural Ethnopharmacol.*, 4(4), 277.
- Yang, J., Su, Y., Luo, J. F., Gu, W., Niu, H. M., Li, Y., Wang, Y. H., & Long, C. L., (2013). New amide alkaloids from *Piper longum* fruits. *Nat. Prod. Bioprospect.*, 3(6), 277–281.
- Yang, Y. C., Lee, S. G., Lee, H. K., Kim, M. K., Lee, S. H., & Lee, H. S., (2002). A piperidine amide extracted from *Piper longum* L. fruit shows activity against *Aedes aegypti* mosquito larvae. *J. Agric. Food Chem.*, 50(13), 3765–3767.
- Yang, Y. C., Lee, S. G., Lee, H. K., Kim, M. K., Lee, S. H., & Lee, H. S., (2002). A piperidine amide extracted from *Piper longum* L. fruit shows activity against *Aedes aegypti* mosquito larvae. *J. Agric. Food Chem.*, 50(13), 3765–3767.
- Yende, S. R., Sannapuri, V. D., Vyawahare, N. S., & Harle, U. N., (2010). Antirheumatoid activity of aqueous extract of *Piper longum* on Freund's adjuvant-induced arthritis in rats. *Int. J. Pharm. Sci. Res.*, 1(9), 129–133.
- Zhang, K., Chen, C., Wang, D., & Wu, Y., (1996). A new dimer of amide from *Piper longum*. *Acta Bot. Yunnanica*. 18(3), 353–355.
- Zheng, L., Wang, H., Ba, Y., Liu, H., Wang, M., Guo, W., Wu, X., & Yang, H., (2014). Protective effect of alkaloids from *Piper longum* in rat dopaminergic neuron injury of 6-OHDA-induced Parkinson's disease. *Zhongguo. Zhong. Yao. Za. Zhi*, 39(9), 1660–1665.

## CHAPTER 5

---

# Pomegranate (*Punica granatum*): A Medicinal and Commercial Perspective

SHILPA VAKSHASYA<sup>1</sup> and GOPAL DIXIT<sup>2</sup>

<sup>1</sup>*St. Alloysius College, Pilibhit, Uttar Pradesh, India*

<sup>2</sup>*Upadhi PG College, (MJP Rohilkhand University), Pilibhit, Uttar Pradesh, India*

---

### ABSTRACT

Pomegranate is considered as one of the primitive and most important nutritive plant cited in Ayurveda, Unani, and other traditional systems of medical practice. Pomegranate fruit is considered a good astringent, exhilarant, anti-fatigue, and appetizer. In this chapter, we compile the medicinal perspectives of pomegranate, cited in the different systems of medicine. This also includes edible and other medicinal properties, cultivation, propagation, harvesting, processing, grading, storage, value addition, marketing, and trade along with recommendations and future vision for research and development.

### 5.1 INCEPTION

It is most extensively used, nutritive and ancient edible juicy plant of human civilization which has been used as medicine by humans. Due to its usefulness, pomegranate is considered a unique and most fascinating fruit plant which occupies a top position amongst the angiosperms in the plant kingdom, primarily due to its characteristic features and medicinal properties. Economically, the pomegranate plant is important as far as the needs of human beings are concerned as it provides juice, oil, tan, dye, and medicine

(Kumari et al., 2012). It is a popular fruit and is estimated 20% part of total fresh fruits. Several types of pomegranates are found in the world which is distinguished by the shape, color with variation in size and thickness of the rind in cultivated and wild species. Similarly color variation is found in different cultivars. Seeds size and juice content also varies among different varieties. Pulp color ranges from white to transparent in few varieties and pink and blood red is found in other better quality fruits. Taste of pulp is also showing significant variation from sweet and aromatic to sour and insipid. Seed coat shows variation in hardness, some are soft seeded to seedless. This absence of seeds is due to the lignifications of testa. Different varieties of pomegranate are growing with different varietal names (Table 5.1).

Pomegranate is considered as natural source of both ascorbic and folic acid. Its cultivation also contributes to the economic uplifting of rural and ethnic people living in the vicinity of forests. Bearing in mind the economical potential benefits, the Centre of Research in Ethnomedicobotany in Pilibhit has selected this popular fruit plant among the tribal and rural people for their socio-economic uplifting through large scale pomegranate cultivation. People were given in house and field training from cultivation to harvesting, which is necessary for the varietal selection of the Genus.

## 5.2 ORIGIN AND DISTRIBUTION

As far as the origin of pomegranate is concerned, it is considered as Iranian fruit where it is naturally growing in the wild state. As a highly valuable fruit it has been cultivated in the Mediterranean region and Southern Asia for more than 5,000 years ago. It was also reported from the Hanging Gardens of Babylon. Wild species still exist in certain places of Syria, in Gilead and Mount Carmel. As far as the origin of this fruit is concerned there was some confusion as De Candolle Vavilov believed that it originated in Iran and South West Asia. According to some religious beliefs, during the time of the Prophet Moses, high quality pomegranate was cultivated throughout Palestine, Lebanon, Turkey, and Syria. A good quality pomegranate was also cultivated in the city of Rimmon hence known as Rummon. In India and other Mediterranean and eastern countries, it was introduced after the invasion of Mughals. From here visitors, religious leaders, emperors spread its cultivation to neighboring countries. In Britain and other European countries, it was found after the influence of Islam around the 13<sup>th</sup> century. Traders from European countries and Spain took the fruit plant to countries

like Mexico and onwards to the USA for cultivation. Therefore, its widespread cultivation gradually reaches other countries and now widely spread to different climatic zones and available globally. However, the best quality of pomegranate comes from Turkey, Iran, Morocco, Afghanistan, and Spain. India also produces the Khandari and Sholapur pomegranate varieties which are considered a high quality fruit. Pomegranate cultivation provides an economic base to ethnic, rural, and tribal people.

### 5.3 TAXONOMY

Botanical characteristics are presented as follows:

- Botanical Name: *Punica granatum* L.
- Family: Punicaceae (Lytheraceae).
- Vernacular Name: Anaar.
- Trade Name: Pomegranate.

Pomegranate is a perennial, deciduous small tree or shrub of about 5–10 meters height with profuse branching with minute spines erected on the stem.

### 5.4 MORPHOLOGY

The plant is branched with spiny covering on it. The stem bark is smooth and dark gray and leaves are oblong or ob-ovate with shining surfaces and opposite or whorled. The scarlet red flowers are borne solitary or in groups of 2–4. Sepals are thick and fleshy and 5–8 in number. The fruit is balausta (a multilocular, multiseed fruit) and crowned with persistent calyx where pericarp is leathery and tough with two whorls of carpel one above the other, bearing seeds irregularly. A radial elongation of the outer integument of the seeds constitutes the juicy edible part of the fruits. The interior part of the fruits is separated into compartments by white membranous walls filled with angular seeds. The seeds weight represents more than 50% in most fruits.

### 5.5 PHENOLOGY

The phenology of pomegranate:

- i. **Leaf Fall:** December to February.
- ii. **Leafing:** January to February.

**iii. Flowering:** February to March; June to July and September.

**iv. Fruiting:** March to April; August to November.

The phenological occurrence of the fruit plant depends mainly on the climatic conditions of the different regions where pomegranates are grown. In southern and central parts of India, it flowers throughout the year; however the rainy season is most suitable for flowering in most of *Punica* cultivars. Artificial induction of flowering has been done for early flowers in the monsoon season. Spring flowering gives lower quality fruits in summer. Hence artificial flowering induction is a must like that of Citrus. For this particular purpose, manuring, and irrigation are completed in May before the ripening of the fruits in November and December.

## 5.6 CHARACTERISTIC FEATURES OF THE FRUIT

Fruits are borne terminally on short spurs arising from old shoots. Fruit shapes are globose, ob-ovate, crowned by persistent calyx with a tough woody rind. The number and position of the fruits varies from species to species. Similarly, the color of fruits also differs with the stage of development and display green color while young and pink to red at maturity.

## 5.7 AREAS AND PRODUCTION

Geographically, pomegranate limits its natural distribution between 40° N and 26° N latitude from North to South. Pomegranate is considered as one of the native plant of Iran to north India. It is widely cultivated in the Asia; Middle East, USA to Arizona. Pomegranate is extensively grown in all parts of India, Malaya, and Africa. In India, total pomegranate cultivation area is 107,000 hectare and production is approximately 743,000 tons. Maharashtra state of India is the leading pomegranate producer with 78% of total land area and approx 84% of the total production in India; this is followed by Karnataka, Andhra Pradesh, Gujarat, and Tamil Nadu states.

## 5.8 UNIVERSAL DISTRIBUTION

Natural populations of pomegranate have been found in Asian countries like Iran, Israel, Japan, and Jordan. The countries where the plant has been

naturalized and is now cultivated are Afghanistan, Armenia, Azerbaijan, Bangladesh, China, Cyprus, Georgia, India, Myanmar, Pakistan, Syria, Turkey, and Turkmenistan in Asia; in Africa, Cape Verde, Egypt, Kenya, Morocco, and Tunisia; Mexico and the USA in North America; Argentina, Brazil; and Chile in South America.

## **5.9 AGRO-ECOLOGICAL REGIONS**

Pomegranate is found cultivated in most agro-ecological regions. The most important regions are:

- i. Semi-arid eco-region with alluvium derived soil.
- ii. Semi-arid eco-region with medium deep soil.
- iii. Semi-arid eco-region with shallow medium soil.
- iv. Semi-arid eco-region with red soil.
- v. Semi-arid eco-region with alluvial soil.
- vi. Semi-arid eco-region with black soil.
- vii. Semi-arid eco-region with lateritic soil.
- viii. Semi-arid eco-region with red lateritic and alluvium derived soil.

### **5.9.1 ECO-FLORISTIC REGIONS**

- i. North-west Himalayas with a similar climate to the Mediterranean region.
- ii. Western Himalayas including parts of Jammu, Himachal Pradesh and Uttarakhand under tropical rainy seasons.
- iii. Wet evergreen forests of West Bengal including Western Ghats.
- iv. Deccan desert from Bijapur to Malegaon, North Gujarat plains and the piedmonts of Aravalli hill ranges.

### **5.9.2 TYPES OF FOREST**

- i. Moist deciduous forests.
- ii. Dry deciduous forests.
- iii. Semi evergreen forests.
- iv. Pine forests.
- v. Broad leaved hill forests.

### **5.9.3 HABITAT AND VULNERABILITY**

Naturally pomegranate grows extensively both in cultivated and in the wild. Hence, the plant is not included in the list of vulnerable plants and is widely available in cultivated areas.

## **5.10 COMPOSITION AND USES**

The plant and plant parts display important therapeutic properties which are used for various human conditions and activities.

### **5.10.1 PLANT PARTS USED**

- 1. Bark:** The dried barks have been used for the expulsion of tape worms in human beings. It is used in the form of decoction. Antibiotic properties are found in the extracts of different parts of plant and used widely in ethno-medicine.
- 2. Flower:** Fresh flowers yield a red dye which is often used to dye clothes.
- 3. Fruit:** Ripen fruits are peeled off using a knife and clusters of fruits are ready to consume or to make juice.
- 4. Rind:** It is considered as a good source of yellow dye for the textile industries. Due to the presence of some alkaloids, it is often used as an astringent.
- 5. Seed:** The seeds oil contains punicic acid. Chemically, it possesses antibacterial properties and is used as a stomachic and condiment.

### **5.10.2 JUICE**

The plants are extensively cultivated for the juice and for various purposes. The fresh juice is often used as cooling and refrigerant mixture in medicine to treat dyspepsia and directly consumed as hemoglobin enhancer in anemic patients. Due to the acidic nature found in the juice, it blends easily with other juices. Pomegranate juice may be converted as high quality syrup for future use. It is also used in the preparation of grenadine, commonly used



non-alcoholic syrup which is characterized by tart and sweet flavor and a deep red color. It is also used as a topping on ice creams. In places like in Eastern Europe, Middle East, and Asia, the juice has been used to prepare of wine after the process of fermentation which contains high amounts of antioxidants used for many health benefits; anti aging, artery problems and lowering cholesterol level.

### **5.10.3 POMEGRANATE SAUCE**

In some rural parts of India, people prepare a sauce or ketchup made with pomegranate juice by adding equal amount of sugar and heated to make it thick and viscous.

### **5.10.4 MEDICINAL USES**

Medicinally, pomegranate is extensively used in the treatment of various human and veterinary ailments around the world. The juice of wild pomegranate is often used to produce citric acid and sodium citrate for different pharmacological uses. It is considered a useful in the treatment of dyspepsia and leprosy. The juice from the young fruits and leaves is mildly laxative and very useful as a cooling agent for stomach complaints and in cardiac pain. In some parts of the world, flower buds are used in bronchitis and whooping cough. The extracts of the bark, leaves, unripe fruits, fruit rind contain high amount of tannin and it is recommended as an astringent to stop diarrhea, dysentery, and hemorrhages. The leaves, roots, bark, and seeds have anti-inflammatory, antispasmodic, and anthelmintic properties (Aziz et al., 2018).

### **5.10.5 TANNING**

Most parts of the plants have tanning properties but the fruits rind, stem bark, root bark, and leaves possess large amount of tanning alkaloids (Zhang et al., 2010). From ancient times in Mediterranean and east countries, roots, and stem bark are extensively used in the production of tanning materials (Dwivedi, 1993). The bark of tree has been used in the production of Moroccan leather.

**TABLE 5.1** Plant Parts with Tannin Contents

<b>Plant Parts</b>	<b>Tannin Content (%)</b>
Bark of stem	23
Bark of roots	28
Green leaves	10
Fruit rind	26

### **5.10.6 COMMERCIAL DYE**

The rind from the ripen fruits and stem bark are commonly used for the production of dyeing materials for different industries. From the age of early human civilization as evidenced from Mesopotamia (2000 BC) and from Egypt (1500 BC), a yellow dye has been extracted from the fruit rind and the stems of barks and used to dye different textile products (Rajappa et al., 1995). Similarly, a red dye has been obtained from the red flowers and the rind from unripe fruits. A red or black dye can be used as an ink for various purposes. It is coppery brown in color and does not require any mordant (a dye fixative substance used to set dyes on fabrics that forms a coordination complex with the dye) because it contains natural mordant like tannic acid. In parts of India, a yellow dye is obtained from the rind of dried fruits and often used for hair coloring and for dyeing clothes. To produce an olive, pond green to yellow ochre color, the rind extracts of pomegranate is mixed with turmeric, indigo, or iron sulfate and alum; while straw color is obtained by mixing the extract of the outer pod of the fruit with alum and caustic soda (Rajappa et al., 1995). The dyeing process runs as follows: pomegranate pods are grounded to powder; the powder is mixed with a gallon of water and the mixture allowed boiling. After boiling the container is removed from the heat; the cloth material is kept in the water for approx 20 minutes and then washed to reveal the yellow color in the textile fibers. Dwivedi (1993) prepared a color chart obtainable from different parts of pomegranate (Table 5.2).

**TABLE 5.2** Color Dye Yielded by Different Parts of the Plant

<b>Plant Parts</b>	<b>Color/Dye</b>
Rind of fruits	Yellow and black
Stem bark	Yellow
Roots	Yellow/red
Flowers	Red

Similarly, crimson red dye is obtained from the pomegranate flowers and used extensively for dyeing Kashmiri shawls and traditional carpets.

### 5.10.7 CHEMICAL COMPOSITION AND FOOD VALUE

Pomegranate fruits contain sugar, vitamin C, high amount of Fe and Ca in lesser quantity along with other valuable compounds (*see* Table 5.3). They contain pectin as calcium pectate. The seeds without juicy coat contain moisture, fatty, and nitrogenous substances, starch, fibers, and ash. The seeds are a good source for drying oil (oil that hardens on exposure to air). The fresh rind of the fruits contain 0.8% wax, 4.5% resin, 1.8% mannitol along with sugars, gums, insulin, mucilage, tannin, gallic acid, and calcium oxalate. Tannin is found in almost every part of the tree, like the dried rind, stem bark, root bark and leaves. Different alkaloids are found in roots and bark which varies from 0.3 to 0.6%. Major alkaloids are pelletierine (C<sub>8</sub>H<sub>15</sub>ON), isopelletierine { $\alpha$ -(2-piperidyl)-propane- $\beta$ -one} (C<sub>8</sub>H<sub>15</sub>ON), pseudo-pelletierine (C<sub>9</sub>H<sub>15</sub>ON) and methyl pelletierine (C<sub>8</sub>H<sub>17</sub>ON).

**TABLE 5.3** Food Value of 100 Gram of Edible Part of Pomegranate

Calorific value	65–75 kcal
Moisture content	72.6–86.4
Protein	0.05–1.6 gm
Fat	Trace to 0.5 gm
Carbohydrates	15.4–20.0 gm
Fiber content	3.5 to 4.5 gm
Ash	0.35–0.70 gm
Calcium	3–12 mg
Phosphorus	8–37 mg
Iron	0.3–1.2 mg
Sodium	3 mg
Potassium	259 mg
Carotene	NT
Thiamine	0.003 mg
Riboflavin	0.012–0.03 mg
Niacin	0.180–0.03 mg
Ascorbic acid	4–4.2 mg
Citric acid	0.50–3.5 mg
Boric acid	0.005 mg

### 5.10.8 TOXICITY

Although the presence of tannin in the edible part in less than 0.25%, it is nonetheless considerable. Bassiri-Jahromi et al. (2015) have shown that the presence of tannin is carcinogenic to humans and prolonged consumption may leads to health problems. Although the bark of the roots and the stem contain the alkaloid isopelletierine, an effective anthelmintic for tapeworms, an overdose produces emetic, purgative symptoms and causes pupils' dilation, sight dimness, muscular weakness and paralysis (Patel et al., 2008).

### 5.10.9 ADULTERATION

Substitute adulterants have not been identified so far.

## 5.11 SOIL AND CLIMATE

Climatic conditions are equally important factor in successful cultivation of pomegranate. Main climatic conditions required are as in subsections (Table 5.4).

**TABLE 5.4** Climatic Conditions for Pomegranate Cultivation

Altitude range	500–2,000 meter
Annual rain	700–2,500 mm
Climate season	Winter, bimodal
Duration of summers	3 month
Average annual temperature	24–40°C
Mean maximum temperature	36–45°C
Mean minimum temperature	3–12°C
Absolute minimum temperature	> –10°C

### 5.11.1 SOIL FACTORS

The soil's conditions are the basic requirement for the optimum growth and development of pomegranate plants; calcareous, alkaline soils, deep acidic, loamy, and broad range of soils are the most suitable types of soils. It is commonly believed that pomegranate thrives well on poor soils, too, where other fruit plants are unable to flourish. In some places in India, it grows fairly well on rock-strew gravel type of soil. However, the most suitable types of soil factors are:

- Texture: Fine
- Drainage: Proper
- Nature: Basic
- Tolerance: Infertile

## 5.12 VARIETIES AND CULTIVARS

Pomegranate prefers to grow in cool as well as summer climatic conditions. However, while the plant tolerates well frosty climate and desert conditions, it prefers well irrigated soil that also resists drought conditions. Pomegranate plants are permitted to grow straight by main trunk while regular cutting of small branches, limiting the pruning requirements. The growth of new shoots is encouraged while shoot sapping should be removed regularly to allow a better growth.

### 5.12.1 CULTIVARS AND SUB-SPECIES

Taxonomically, *Punica granatum* has two sub species which are based on contained pigments. Both these pomegranate species are found distributed in separate localities as *chlorocarpa* and mainly reported in plants growing in the trans Caucasus region while *porphyrocarpa* is found in plants growing in central Asian countries.

In the Asian subcontinent regions like those of India, several cultivars of pomegranate are common, i.e., with white flowers, ornamental, and with double flowers. The white flower variety has a poor quality of fruits. Cultivated species contains 12–16% of sugar with an acidity varying from 1.5 to 2.5%. Farmers prefer to grow fleshy, juicy pulped seeded varieties. Soft seeded varieties are considered as seedless varieties (Table 5.5).

**TABLE 5.5** Common Types of Pomegranate Varieties

<b>Musket Red</b>	Fruit small to medium in size, rind is thick, Testa fleshy with sweet juice, seeds are soft.
<b>Paper Shell</b>	Fruit round, fruit size medium to large, rind comparatively thin, fleshy Testa red to pink in color with sweet juice, seeds are soft.
<b>Spanish Rubi</b>	Fruit round, red colored with thin covering, Testa is rose colored, pulp is aromatic and sweet.
<b>Musket White</b>	Fruit is large, creamy white, rind is thin, pulp fleshy cream colored, pulp is sweet, and seeds are hard.
<b>Wonderful</b>	Fruit is ovate, big size, red colored, rind thick, medium hard seeded.

### 5.13 GENETICS

Pomegranate (*Punica granatum* L.) is a common angiosperm fruit plant, genetically diploid ( $2n = 16$ ) with little variation from wild species of western Himalayas. Meiotic studies of hilly cultivars show the presence of 'B' chromosomes instead of 8 bivalents at diakinesis and metaphase I. Sheidai et al. (2012) studied a few pollen mother cells and confirmed the presence of 8 bivalents Number of 'B' chromosomes ranging from 0 to 4 which showed 100% pollen fertility. Diploid varieties from Mussoorie hills with  $2n = 14$ , 16, or 18 have also been reported (Gill et al., 1984).

### 5.14 PROPAGATION AND ROOTSTOCK

In most cases, seeds naturally propagate pomegranate. In some places of Maharashtra state, it is also vegetative propagated by stem cuttings. Natural dispersal of seeds is done by particular fruit eating bats or other wild animals that eat ripe fruits. Seeds on the soil germinate just after the onset of the monsoon, and some seeds become dormant due to the presence of inhibitory compounds and unsuitable ecological condition, while these beneath the soil germinate better and faster. Seedlings exhibit good competitive ability with surrounding weeds and grasses.

#### 5.14.1 VEGETATIVE PROPAGATIONS

Vegetative propagation is one of the most important methods for reproducing pomegranate plants worldwide. This method tends to be more reliable for preserving and multiplying selected varieties. Vegetative propagation of selected cultivars has been facilitated with 25–50 cm long stem cuttings. Application of growth promoting hormone IBA is quite suitable for the proper development of roots and for better survival rate. These cuttings are planted in nurseries for growth and development under controlled conditions. The following year, the rooted cuttings with suitable growth are transplanted to the orchard.

For the cultivation of good quality pomegranate plants, fruit growers and farmers frequently used budding and grafting practices to develop the best cultivars.

### 5.14.2 MICROPROPAGATION

To maintain genetic fidelity of pomegranate, clonal propagation is the only option for biotechnologists. Similarly, *in vitro* propagation technique is found highly effective for the production of quality seedlings. Gorad et al. (2018) suggested *in vitro* propagation of young leaves and petals selected from explants and placed in the MS medium (Murashige & Skoog, 1971). White pH (WPH medium) is often used for callus induction with different levels of hormones like 2, 4-D, and NAA. Sub-culture of callus is prepared for shoot initiation and NAA useful for root induction process in pomegranate.

### 5.14.3 SEEDS SOWING

Direct sowing of mature seeds is completed during the months of July to September depending on the climatic and soil conditions of the locality.

## 5.15 PLANTING, IRRIGATION, AND NUTRIENT MANAGEMENT

Development of a good nursery involves several steps:

1. **Sowing:** With this popular method, mature fruits are selected and their pulp is completely removed from seeds. Sun dried seeds are sown in the soil filled with poly bags and allowed to germinate. The germination occurs after 20–22 days of sowing. Proper watering and care is required for proper growth and the development during transplantation. The well developed two months old seedlings are transplanted in a suitable soil. Seedlings are planted in the prepared pits of 60×60×60 cm which are filled with a mixture of farmyard manure and soil. The transplantation nursery phase is over in 3 to 4 months. The sowing of seeds to the planting of seedlings process should be completed between August to December.
2. **Culture:** Well rooted seedlings are transplanted in pre-fertilized pits and separated 4 to 5 m apart depending the nature and fertility of the soil in the field. Young plants are cut back to 65–75 cm following the transplantation and followed by the branching, pruning of lower branches to clear the main stem. The plant produces fruits only at the tips of new branches. It is therefore recommended that branches be pruned regularly in the first three years to maximize the number

of new shoots in all directions. This process allows a strong, well framed plant that can yield better fruiting. After three years of plant pruning and shaping, only the dead branches and shoot should be removed as needed.

3. **Manuring:** The process of manuring usually starts before the transplantation at the rate of 20 kg per seedling. Calculated amount of cattle manure is applied yearly as monsoon breaks. It is advised to apply 2 kg of groundnut cake to further enhance the fruit development. In addition, ammonium sulfate  $(\text{NH}_4)_2 \text{SO}_4$ , wood ash, lime, and farmyard manure is added as it effectively improve the quality of the fruit.
4. **Watering:** Irrigating at regular intervals is required for maximizing the plant growth, the flowering and the fruiting of pomegranate. During and following the flowering and the fruiting season, regular, and abundant watering is necessary so that the fruits can reach a descent shape and size which prevent them from cracking due to moisture conditions.

## 5.16 TRAINING AND PRUNING

Training and pruning is one of the most important steps for the overall development of plants to get the desired yield. In this process, the side branches are removed regularly with a sharp tool. Fruits are produced terminally on the branches arising from the main stem. Pruning is performed yearly to allow the emergence of new shoots from all sides of the tree. This process allows for a successful flowering and fruiting.

## 5.17 PEST AND DISEASE MANAGEMENT

### 5.17.1 MAJOR DISEASES

Like other fruit plants, pomegranate also faces a serious problem from different pests and diseases. However, the major problem is fruit splitting and cracking. This may occur due to the hardening of the fruit skin because of a shortage of moisture content and the sudden expansion of the inner part of the fruit after rain or watering of the field. Sometimes, more than 50% of the fruits become affected and finally crack. To avoid this cracking



condition, premature harvesting is recommended; however, the quality of fruits is below standard. To overcome the cracking problem of the fruits, regular manuring followed by watering is necessary to maintain moisture in the fruits. In Uttar Pradesh for instance where pomegranate is cultivated, growers spread brick powder around the soil of the tree based on the belief that the fruit color and taste will be improved; however, this practice is not scientifically proven. Nonetheless, it probably induces the moisture retention capacity of the soil which in turn reduces the cracking of fruits.

The pomegranate butterfly (*Virochola isocrates*) also damages pomegranate plants by laying eggs on the floral buds and on the calyx of developing fruits. Caterpillars emerge from the eggs and enter the fruits through the calyx and imposes heavy loss due to rotting inside the fruits. To protect the fruits from this infestation, a spray of calcium arsenate is applied after the fruit set. Similarly, dusting of a mixture of Paris green (9lb), lime (5lb), talc (15lb) and flour (4oz) is also effective to control the fruit borers. However, the dusting of DDT (Di Chloro Di Ethyl Tri Chloro Ethane) and BHC (Benzene Hexa Chloride) is not effective.

Another serious issue for the pomegranate is twig dieback caused by *Pleuro placonema* or *Ceuthospora phyllosticta*. The fungus *Aspergillus castaneusis* is responsible for the discoloration of the fruits and seeds to a great extent. *Sphaceloma punicae* causes the disfiguring of fruits during the development process. *Phomopsis* *sps.* or *Zythia versoniana* is mainly responsible for the dry rot on pomegranate crop and causes up to 80% of pomegranate loss in the field. Another fungus *Alternaria solani* causes post harvest rot and cracking of the fruits. A bark eating caterpillar, *Aleurodes* *sps.* has also been reported during crop infestation.

### 5.17.2 MINOR DISEASES

Pomegranate plants are also affected to an extent by fungal leaf and fruit spot diseases. Other damages are caused due to white flies, thrips, mealy bugs, and scale insects. Similarly, *Euproctis* *sps.* and *Archyophora dentula* are responsible for defoliation. In North India, termites may also infest tree trunks.

Farmers often apply conventional and innovative practices like enveloping ripen fruits with old newspapers for the sustainable management of various insects and pests, learnt from experience transmitted through generations. Heavy rain at the time of ripening of the fruit may cause soft rot in the fruits.

## **5.18 HARVESTING AND YIELD**

### **5.18.1 HARVESTING TIME**

According to seasonal changes, harvesting time has been divided into three flowering seasons viz. winter, summers, and autumn. In most parts of India, harvesting time is between November and December.

### **5.18.2 MATURITY INDICES AND HARVESTING METHODS**

Mature and slightly dark colored fruits are plucked from the plants once they are hard and are properly shaped and a good size. Good varieties of pomegranate start fruiting in approx four years after their transplantation. Average ripening time of fruit varies from cultivar to cultivar, however in most cases the fruits are ready between 6 and 7 months after flowering. Treatment of ethylene is not effective in the ripening of the fruit. Fruits are ready to harvest when the skin of the fruit becomes slightly yellow. In ideal conditions, fruits are picked before over maturity to avoid the cracking of the rind. Sometimes however, adverse atmosphere may leads to the cracking of the fruit. In natural conditions of seed dispersal, ultimate splitting of ripen fruit occurs frequently.

### **5.18.3 MECHANIZATION AND YIELD**

Hand picking or other mechanical methods have been frequently applied to pull off the ripe fruit for further processing. Selected fruits are picked in such a way that shoots are not left, to avoid any possible further damage during packing and handling processes. It is essential that the collected fruits are not exposed under the sun light as it may produce wrinkles and dull coloration of rind. Yield of pomegranate varies from cultivar to cultivar and ranges from 70 to 180 fruit per tree.

## **5.19 POST-HARVEST HANDLING AND STORAGE**

### **5.19.1 SORTING, GRADES, AND GRADING**

Grading and sorting of ripen fruits is done according to the fruits' size, appearance, color, as fruit may be red, pink, white, and black. Red colored fruits are of a superior quality. Similarly, the size of fruit also plays an important role in sorting and grading of the fruits. Variety of pomegranate is a key factor in

post harvest handling. Though there are no definite criteria or prescribed and recorded standards of grading and sorting of the ripe fruit, these practices are mainly based on the experience of generations of growers. Based on these practices, at least three grades of fruits have been maintained as local, fine, and of export quality.

### **5.19.2 STORAGE: DURATION AND BIOCHEMICAL CHANGE**

The harvested fruits can be stored for a long period of time to increase the flavor, juice, and quality. Because of the hard and tough rind, they can be stored for a long time. In cold storage conditions, the fruit stays fresh for a long time at a temperature of 10°C; however, it starts shrinking and deteriorating after a few hours of being removed from cold storage. For long storage duration, 0–4°C temperatures, 80% relative humidity is required to keep the fruit intact and unspoiled for 7 to 8 months. As and when needed, the fruits are stored in well aerated places with controlled temperature facilities. The prolonged keeping of fruit leads to internal breakdown, fading, streaky pulp and low flavor.

### **5.19.3 PACKING**

After harvesting, the ripe fruits are graded for different sizes and grades. They are packed separately accordingly. Usually, the fruits are packed in Corrugated Fiber Board (CFB) carton to carry 5 kg. Fruits are arranged in circular rows and separated from each other with separators. The fruits are wrapped in dry papers and stored inside the carton with 40–50 fruits. Fruits are kept in layers in cardboard boxes each containing approx 20 kilograms and stored at 0°C and 80% humidity for bulk storage. Thin cardboard sheets are used as separator. The packing of the fruits is an important step for marketing. Producers bring ripen fruits in bags to the buyers and wholesalers repack them in specific fruit cartons.

### **5.19.4 COLLECTION AND PROCESSING OF POMEGRANATE**

The delivery of high quality fruits from growers is a main motivation for buyers. In the state of Mharastra, the horticulture and agriculture department provided a local unit for pomegranate growers. They are promoted to cultivate

improved varieties and receive guidance from scientists for cultivation to harvesting. Once the fruit growers receive a good income from buyers, they train other villagers to follow the initiative. The Government of India has encouraged the development of cold storage spaces for safe and long duration storage of ripen fruits in and around the pomegranate producing areas. This may be governed by co-operative societies or through public private partnership (PPP). Furthermore, the grading of fruit should be based on quality control that is scientifically proven. Similarly, the grinding process and transportation systems are under mechanical operation for quick and time bound extraction. The horticulture departments of different states of India are advised to conduct disease and pest control practices under pathological observations. In addition, efforts have been made to cultivate the latest varieties, using non-chemical practices for sustainable, environment friendly and cost effective production of pomegranate. Bearing in mind that the packaged fruits are transported rapidly from one location to another, it is recommended that machine operated systems should be used as much as possible to fasten the processing of fruit and also to avoid unnecessary touching.

#### **5.19.5 ADDED VALUE**

Pomegranate fruits are mainly consumed as value added fruit juice and dehydrated high quality products for their sensory and nutritional aspects. Arils are highly perishable with shelf life of less than 20 hours. Hence, the use of low temperature storage under radiation processing to increase the shelf life of fresh juice is vital. Fresh juice extracted from mature fruit is sweet in taste with a rich flavor. The extracted juice from the whole fresh fruit contains high amount of tannin from the rind which can be separated out by gelatin processes. Filtration of fresh juice is performed and preserved either through pasteurization or by adding some preservatives such as sodium benzoate before bottling. Fruit juices proved as very good anti oxidant lowers high blood pressure and rejuvenate damaged liver. To minimize the adverse effects of chemical preservatives, minimum processed products from pomegranate are produced commercially.

#### **5.20 CHARACTERIZATION OF PHYTOCONSTITUENTS**

Regarding the physico-chemical characterization of pomegranate, the fruit contains some steroid hormones which have antioxidant properties. The chemical composition of the fruit varies according to the cultivar, growing

area and growing season, cultivation practices, harvesting, climatic conditions and storage. The rind which represents half of the total weight of the fruit has many important bioactive compounds; polysaccharides, minerals like calcium, potassium, nitrogen, phosphorus, sodium, and magnesium. Edible part of the fruit consists of juicy aril (a specialized outgrowth from a seed that completely covers the seed) and seeds in 40% and 10% respectively. The aril usually contains 85% water, 10% sugars (glucose and fructose), pectic substances, acidic contents as ascorbic acid, citric acid, and malic acid, along with phenolics and flavonoids. The seeds contain oil mainly composed of triacylglycerols. Pomegranate contains a diverse range of chemical substances which include phenols, sugars, fats, flavoring compounds, different amino acids, terpenes, and alkaloids. These bioactive components have anticancer and strong antioxidant activity as they contain ellagitannins, anthocyanins, and hydrolysable tannins.

### 5.21 BIOPROSPECTS

The bioprospects of pomegranate are broad and used in Traditional, Chinese, *Ayurvedic*, *Unani* systems of medicine; for instance in herbal medicines as appetizer, hematanic syrup, and antioxidant agent. Regarding the bioprospects of pomegranate, the juice from extracted from the arils stands as one of the important methods. Fresh juice is frequently used domestically in the preparation of squash, syrup, nectar, jelly, concentrate, jams, and sauces. They are known for their potential health benefits due to the high anti-oxidants, mutagenic, hypertension, and liver disorder corrections. Besides, the juice has powerful control over inflammation and osteoarthritis, cancerous tumors, HIV-I, and heart disease. Pomegranate is currently considered as one of the most nutritive and productive fruit as it reduces hypertension, mutagenicity, and toxicants from the human body due to the presence of anthocyanins. Several value added products of pomegranate have been made which includes syrup, candied arils, arils in brandy, vinegar, and pomegranate wine (Hill, 1990). Further processed products like anardana juice, concentrate, syrup, and jelly were also prepared from fresh juice. Consumers tend to prefer these products over the whole fruits for the bio properties of the fruit. Its juice can be further utilized as flavoring and coloring agents and for dietetic and prophylactic treatments. Albrecht et al. (2004); and Zarfeshany et al. (2014) have reported the negative correlation of pomegranate juice with proliferation and angiogenicity. Tannins of the fruit have high anti-oxidant value and fruit exceeds the *in-vitro* anti-oxidant potential (Seeram et al., 2008).

## 5.22 AVAILABLE COMMERCIAL PRODUCTS

Due to the rich source of minerals, vitamins, and nutrients, pomegranate is used widely in traditional *Ayurveda* and *Unani* systems of medicine. Many herbal drugs have been prepared from the plant to cure dysentery, diarrhea, stomachache, inflammations, dyspepsia, bronchitis, and intestinal worms. Fresh juice is recommended to patients with gastric problems. Beverages made from pomegranate are highly nutritive and refreshing. It is regarded as a “super food” due to its protective action against several diseases. In laboratory tests, it displays antiviral, antibacterial, and antioxidant properties. In folk and traditional remedies, the fruit and the seeds are commonly used as an alternative to synthetic drugs as they contain 124 different phytochemicals; some of them being effective in human diseases in clinical trials. Commercial products have been made from whole pomegranate fruit juice and used for decades in our age old cultures for health benefits. These trade products as herbal drugs have become popular in western countries as an alternative to synthetic and allopathic medicines.

## 5.23 TECHNOLOGY TRANSFER/PATENTS OF POMEGRANATE

Germplasm collection and the establishment of a field gene bank of pomegranate was the main motivation of the National Research Center on Pomegranate. Different methods and selection have been identified for the bacterial blight disease tolerant genotypes. For the purpose of crop production, wedge grafting techniques are useful for the multiplication of grafted plants. Sustainable crop production has been possible under the Integrated Plant Nutrient Management (IPNM) system. Tissue culture and stool layering techniques are effective for fast multiplication of planting material. Orchard Health Management (OHM) schedules have been developed for the effective management of bacterial blight and other diseases and insect-pests associated with pomegranate. New chemical molecules, bio-agents, and botanicals have been evaluated for the effective management of bacterial blight and other common diseases and insect-pests.

Regarding technology transfer, most patents for machinery or technology transfer are based on the medicinal and pharmaceutical values of pomegranate. However, there is a growing concern for the patenting and the machinery related to pomegranate processing as several discoveries have been made worldwide, most patents issued from the United States. Important titles of invention that relates to methods for the treatment of hypertension, complications of atherosclerotic in diabetes, regression in

lesions, dermatological disorders, hair health, antiviral or antifungal compositions, breast enlargement system, dietary supplements, neurodegenerative disorders, skin lightening effect, bone health, skin sores and lesions treatment, antioxidants extraction, anticoagulant and anti-platelet aggregation, anti-angiogenic extracts, influenza treatment, erectile dysfunction treatment have been granted. Patent of machinery tools include apparatus for separating pomegranate seeds, scanning apparatus, hand tool for easy separation of arils, juice extractor, apparatus for extracting pomegranate seeds, pomegranate processing machine, harvesting machine. Patents are also granted for post harvesting technology which includes method for producing fruit juice, application of breathable surface coating on fruits for extended life, making digestive products, method for producing deodorized pomegranate seed oil and process of alcohol production.

## KEYWORDS

- **Asia**
- **biochemical change**
- **commercial**
- **flavonoids**
- **fruit**
- **maturity indices**
- **medicinal uses**
- **phytoconstituents**

## REFERENCES

- Albrecht, M., Jiang, W., & Kumi-Daka, J., (2004). Pomegranate extracts potently suppress proliferation, xenograft growth and invasion of human prostate cancer cells. *J. Med. Food*, 7, 274–283.
- Aziz, A. A. R., AbouLaila, M. R., Aziz, M., Omar, M. A., & Sultan, K., (2018). *In vitro* and *in vivo* anthelmintic activity of pumpkin seeds and pomegranate peels extracts against *Ascaridia galli*. *Beni-Suef Uni. J. of Basic and Applied Sciences*, 7(2), 231–234.
- Bassiri-Jahromi, S., Pourshafie, M. R., Mirabzadeh, E., Tavasoly, A., & Katiraei, F., (2015). Evaluation of pomegranate (*Punica granatum*) peel extracts toxicity in BALB/c mice. *Nat Prod. Chem. Res.* (Abstract). In: 3<sup>rd</sup> Intl. Conf. and exhibition on Pharmacology, Phytochemistry, and Natural Products.

- Dwivedi, A. P., (1993). *Tans and Dyes from Forest*. International Book Distributors, Dehradun. India.
- Gill, B. S., Bir, S. S., & Singhal, V. K., (1984). Cytological studies in some western Himalayan Woody species II polypetalae. In: Paliwal, G. S., (ed.), *The Vegetational Wealth of the Himalayas* (pp. 497–515).
- Gorad, D. S., Kallalbandi, B. M., Sgaikh, S. A., & Mal, A. S., (2018). *In vitro* propagation of pomegranate. *Intl. J. Ad. Res. Ideas and Innov. in Tech.*, 4(4), 159–165.
- Hill, A. F., (1990). *Economic Botany*. Tata Mc Graw Hill Publishing Co. Ltd., New Delhi.
- Kumari, A., Dora, J., Kumar, A., & Kumar, A., (2012). Pomegranate (*Punica granatum*): Overview. *Int. J. Pharma and Chem. Sci.*, 1(4), 1218–1222.
- Patel, C., Dadhaniya, P., Hingorani, L., & Soni, M. G., (2008). Safety assessment of pomegranate fruit extract: Acute and sub chronic toxicity studies. *Food Chem Toxicol.*, 46(8), 2728–2735.
- Rajappa, J., Agarwal, A., & Shrividya, J., (1995). *Resource -file on Natural Dyes*. Workshop on Natural Dyes at Department of Textile Technologies, Anna University, Chennai.
- Seeram, N. P., Aviram, M., & Zhang, Y., (2008). Comparison of anti-oxidant potency of commonly consumed polyphenol –rich beverages in the United States. *Journal of Agriculture and Food Chemistry*, 56(4), 1415–1422.
- Sheidai, M., Kolahizadeh, S., Noormohammadi, Z., Azani, N., & Nikoo, M., (2012). Correlation between geography and cytogenetic diversity in pomegranate (*Punica granatum* L.) cultivars in Iran. *Acta Bot. Brasilica*, 26(4), 953–965.
- Zarfeshany, A., Asgary, S., & Javanmard, S. H., (2014). Potent health effects of pomegranate. *Adv. Biomed. Res.*, 3, 100.
- Zhang, L., Gao, Y., Zhang, Y., Liu, J., & Yu, J., (2010). Changes in bioactive compounds and antioxidant activities in pomegranate leaves. *Scientia Horticulturae*, 123(4), 543–546.



## CHAPTER 6

---

# Rhubarb (*Rheum* sp.): A Rare and Endangered Medicinal Plant of the Himalayas

MEENAKSHI THAKUR

*College of Horticulture and Forestry (Dr. Y.S. Parmar University of Horticulture and Forestry), Neri, Hamirpur, Himachal Pradesh, India*

---

### ABSTRACT

*Rheum* species belong to the Polygonaceae family and are found in the temperate and subtropical regions of Asia continent. The species belonging to the genus *Rheum* are known as Rhubarb. Indian or Himalayan Rhubarb includes *Rheum australe*, *R. webbianum*, *R. moorcroftianum*, and *R. spiciforme*. These species are found at altitudes that range from 3,000 to 5,200 m above sea level (asl). *Rheum* species are increasingly threatened and different agencies such as IUCN, WWF, and UNEP have included them into endangered plants lists. *Rheum* species have been used in traditional medicine due to their various properties such as astringent, antiseptic, antidiabetic, antiviral, antimicrobial, antitumor, anti-inflammatory, cytotoxic, diuretic, liver stimulant, nephroprotective, purgative, stomachic, anti-cancerous, and tonic. These species are also used for the treatment of boils, wounds, bone fractures, backache, joint, and rheumatic pains. They are also used in cosmetics, textile, and food industry as colorant. Leaves of *Rheum* species are cooked and eaten as vegetable. In India, annual trade of *R. australe* rhizomes is estimated to about 100–200 MT. The therapeutic properties of *Rheum* species are mainly attributed to the presence various derivatives of anthraquinones (emodin, emodin glycoside, aloe-emodin, chrysophanol, chrysophanol glycoside, rhein, and physcion); stilbenoids

(resveratrol, piceatannol, and their glycosides); anthocyanins; flavonoids; anthraglycosides and polyphenols. This chapter covers the various aspects of high value medicinal plant – Himalayan Rhubarb that are important for their conservation.

## 6.1 GENERAL INTRODUCTION

*Rheum* (family Polygonaceae) commonly called Rhubarb, includes approximately 60 species which are mainly distributed in the temperate and subtropical parts of Asia (Li, 1998; Anjen et al., 2003; Cao et al., 2017). In the Indian subcontinent 10 species of *Rheum* have been recorded (Ganie, 2014). The name Rhubarb is originated from the Latin word *rha* which means “river” and *barb* which means “barbarian land.” In ancient times, the Romans imported the roots of Rhubarb from barbarian lands which are situated outside the Volga or Rha river. According to Lindley’s Treasury of Botany, the word ‘Rhubarb’ is originated from the Greek word *rheo* which means “to flow.” Rhubarbs are mainly of three types – Chinese, Indian or Himalayan, and Rhapontic. The Chinese Rhubarb consists of the roots and rhizomes of *R. officinale* and *R. palmatum*. The Indian Rhubarb constitutes the rhizomes of *R. australe*, *R. webbianum*, *R. moorcroftianum* and *R. spiciforme*. *Rheum rhaponticum* is the Rhapontic Rhubarb (Khare, 2007). Table 6.1 represents the Indian *Rheum* species along with their common names, habitat, and medicinal properties.

*Rheum australe* D. Don. (*Rheum emodi* Wall. Ex. Meissn.) is commonly known as Himalayan Rhubarb or red-veined pie plant. This plant is found in the temperate and subtropical areas of the Himalaya from Kashmir to Assam, at elevations ranging from 3,300 to 5,200 m asl (Pandith et al., 2014). It is indigenous to India, Nepal, Myanmar, and Pakistan. It is widely used in traditional medical practices including Ayurveda, homeopathy, Chinese, Unani, and Tibetan systems (Bhatia et al., 2011). Additionally, it is used as a natural colorant in cosmetics, textiles, and food (Malik et al., 2009). *Rheum moorcroftianum* Royle is also found in the Himalaya at altitudes of 3,000 to 5,200 m asl, mainly in Garhwal and Kumaon. *Rheum webbianum* Royle is found in the western and central Himalaya at altitudes of 3,000 to 5,000 m asl (Khare, 2007). *Rheum spiciforme* Royle is present in Kashmir and in the drier areas of Sikkim and Kumaon at altitudes ranging from 1,700 to 5,500 m asl.

*Rheum* is a perennial herbaceous genus with valuable medicinal properties which is being used in traditional medicine since ancient times (Saggoo & Farooq, 2011). The rhizomes and roots of *Rheum* are often used as

**TABLE 6.1** *Rheum* Species Present in the Indian Subcontinent

Botanical Name	Common Name	Habitat	Properties
<i>Rheum australe</i> D. Don [ <i>Rheum emodi</i> Wall. ex Meissn.]	Indian Rhubarb, Himalayan Rhubarb	Sub-alpine Himalaya covering Kashmir to Sikkim with altitude ranging from 3,300–5,200 m asl.	Purgative, astringent, and aperient. Used for atonic dyspepsia. However, it is not advised for patients of rheumatism, gout, and epilepsy.
<i>Rheum moorcroftianum</i> Royle	Archa, Chukri, Chuchi, Lechu, Revandehini, Rhubarb, Usharerevand	Kashmir, Garhwal, and Kumaon at altitudes of 3,000–5,200 m asl.	Exhibits properties similar to those of <i>R. australe</i> .
<i>Rheum webbianum</i> Royle	Archa	Western and central Himalaya at altitudes of 3,000–5,000 m asl.	Antispasmodic, muscle relaxant and antiseptic.
<i>Rheum spiciforme</i> Royle	Spiked Rhubarb	Kashmir, Kumaon, and Sikkim at altitudes of 2,700–4,800 m asl.	Purgative.

Source: Adapted from: Khare (2007).

purgative, laxative, and tonic. The dried root powder is also used for quick healing of ulcers and wounds and for cleaning teeth (Kaul, 1997). Its small dosage is given for treating indigestion and stomach disorders (Ballah & Churasia, 2009). *Rheum* rhizomes have also been reported as a potent source of anticancer drug (Rajkumar et al., 2010). Extracts prepared from its roots, bark, and leaves have been used to treat constipation since very old times and are still used in different herbal preparations (Wang et al., 2007).

The biological activities of *Rheum* species is attributed to the presence of numerous phytoconstituents such as essential oil, anthraquinones (emodin, aloe-emodin, chrysophanol, rhein, physcion), dianthrone, stilbenes, anthocyanins, flavonoids, anthraglycosides, polyphenols, chromene, chromanone, chromone glycosides and vitamins (Agarwal et al., 2001; Singh et al., 2010). These phytochemicals of Rhubarb exhibit various bioactivities such as cytotoxic, antioxidant, antimicrobial, antifungal, antitumor, antidiabetic, anti-proliferative, and immune-stimulating properties (Matsuda et al., 2001; Babu et al., 2003; Radika et al., 2010; Zargar et al., 2011).

## 6.2 AREA AND PRODUCTION

*Rheum* species particularly from Kashmir Himalaya are threatened of extinction due to the commercial exploitation. These are incorporated in the lists of

endangered plants by various agencies like IUCN, WWF, and UNEP (Kabir et al., 2015). For trading *Rheum* internationally, either a ‘certificate of cultivation’ or a ‘legal procurement certificate’ is required from the designated authorities of the forest (Nautiyal et al., 2002). The Government of India has also setup various schemes that encourage farmers to cultivate *Rheum* species. In Indian market, the dried roots of *Rheum* species are sold at 50–55 INR per kg. Under the National Ayush Mission of National Medicinal Plant Board, 50% subsidy is allocated for the cultivation of *Rheum australe*. For the year 2016–2017, the cost of cultivation of *R. australe* was 1,18,592 INR per acre (National Medicinal Plant Board, Ministry of Ayush, GOI).

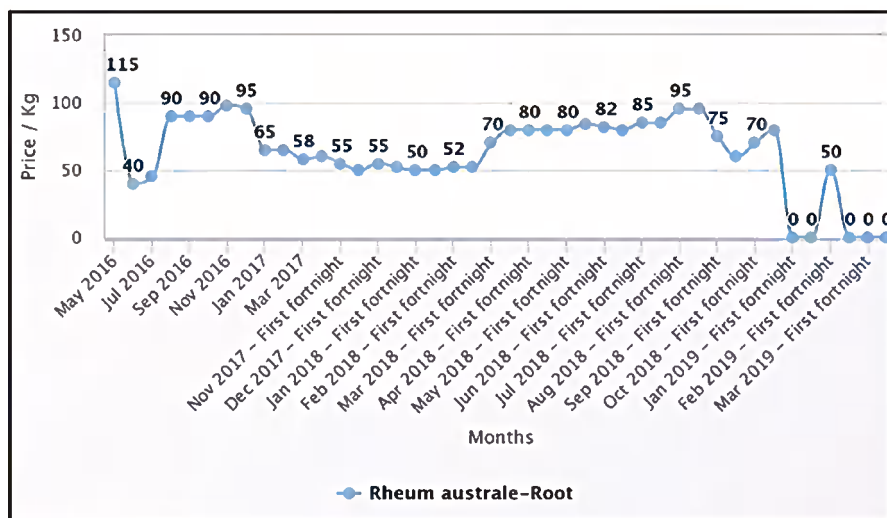
### 6.3 MARKETING AND TRADE

In modern medicine, medicinal plants are used directly or indirectly as a source of bioactive compounds for the synthesis of drugs or as markers to discover novel bioactive constituents. This involves a new approach of integrated drug discovery in which traditional knowledge synergizes with extraction of crude drug from plant sources (Katiyar et al., 2012). As per the World Health Organization estimation, the yearly demand for medicinal plant based raw material for drug preparation is approximately 14 billion USD with an annual increase 15 to 25%. India stands in second position (next to China) as largest supplier of raw material of medicinal plants. In India, the estimated trade of medicinal plants is 1 billion USD per year (Kala et al., 2006). Table 6.2 shows the estimated annual trade of *Rheum* species in India. In India, the roots of *R. australe* are mainly traded with an estimated annual trade of 100–200 MT. Figure 6.1 depicts the market price of *R. australe* roots in New Delhi, India.

**TABLE 6.2** Estimated Annual Trade of *Rheum* Species in India

Botanical Name	Trade Name	Part Used	Estimated Annual Trade (MT)	Market Rate (INR)
<i>Rheum australe</i>	Revan Chini/ Dolu/Archa	Root (rhizome)	100–200	Dried roots: 55/– per kg Extract: 750/– per kg
<i>Rheum moorcroftianum</i>	Revand-chini/ Amlaparni	Root (rhizome)	<10	Dried roots: 50–55/– per kg Extract: 750/– per kg
<i>Rheum webbianum</i>	Revand-chini	Root (rhizome)	<10	Dried roots: 50–55/– per kg Extract: 750/– per kg

Source: Anonymous (2021).



**FIGURE 6.1** Market price of *Rheum australe* roots in New Delhi, India.

Source: Anonymous (2020).

## 6.4 COMPOSITION AND USES

*Rheum australe* is used in various traditional systems of medicine to treat numerous ailments related to the circulation, digestion, endocrine, respiratory, and skeletal systems. It is also used to treat various bacterial infections (Keser et al., 2019). These medicinal properties are due to the presence of bioactive compounds such as anthraquinones (emodin, aloe-emodin, rhein, physcion, chrysophanol, and their glycosides) and stilbenoids (piceatannol, resveratrol, and their glycosides) in addition to dietary flavonoids which are recognized for their potential health uses (Rehman et al., 2014; Pandith et al., 2018). Rhizomes of *R. moorcroftianum* contain emodin, emodin-8-O- $\beta$ -D-glucosides, chrysophanol, chrysophanol-8-O- $\beta$ -D-glucosides and physcion (Rawat et al., 1989) which are responsible for various pharmacological properties like antifungal, immune-modulatory, antioxidant, nephroprotective, and hepatoprotective activities (Zargar et al., 2011).

*Rheum webbianum* also possesses various biological activities. The roots and stems of the species are rich in anthraquinones, such as emodin (1,3,8-trihydroxy-6-methyl-9,10-anthraquinone) and rhein which are responsible for cathartic and laxative effects. Due to the presence of these bioactive compounds, Rhubarb is used sporadically as a slimming agent. Various *in vitro* and *in vivo* studies have proved that the rhizomes of *R. webbianum*

contain a bioactive compound – desoxyrhapontigenin that exhibits smooth muscle relaxant activity. The paste of fresh rhizomes is applied on burns, blisters, and boils to check the formation of scars (Khare, 2007). Roots are eaten as vegetable; dried powdered flowers and seeds are used to treat urine blockage, kidney stones and indigestion (Thakur et al., 2020). The roots contain two new stilbene glycosides, i.e., 4'-O-methylpiceid and rhapontin that exhibit moderate  $\alpha$ -glucosidase inhibitory activity. Anthraquinone glucoside (pulmatin), chrysophanein, and physcionin isolated from the roots exhibit cytotoxic activity against various cancer cells (Srinivas et al., 2007). Various polysaccharides are present in the roots and rhizomes of *R. webbianum* including lyxose, glucose, galactose, xylose, rhamnase, mannose, and ribose (Khare, 2007). This species is used for treating boils, wounds, and abdominal disorders including indigestion and flatulence (Chaurasia & Ballabh, 2009). It also acts as memory enhancer in senile patients (Tayade et al., 2012). *Rheum spiciforme* is rich in emodin, aloe-emodin, and rhein (Tabin et al., 2016a). Roots of *R. spiciforme* are used to treat wounds, inflammation, bone fracture, backache, stomachache, joint pain, rheumatic pain, intestinal infections and dysentery (Ganie et al., 2014). Leaves are cooked as vegetable (Miao, 2001; Khan et al., 2016).

## 6.5 ORIGIN AND DISTRIBUTION

*Rheum* species are herbaceous plants distributed in the Himalaya from Kashmir to Sikkim. In Himachal Pradesh, it grows in Chhota Bhangal and Bara Bhangal of Kangra district, Pangi-Bharmour of Chamba district, Parvati valley of Kullu district, Dodra Kwar, Khashadhar, and Rohru ranges of Shimla district, Kinnaur district, and in Lahaul and Spiti district. *Rheum australe* is distributed in the temperate and alpine zones of the Himalaya from Kashmir to Sikkim. The plant is a fleshy, branched, and erect herb with large petiolated leaves and bears dark purple flowers (Lee et al., 2017). Originally, the plant was cultivated for a long time in the mountainous region of North-West provinces of Tibet and China. In China, the therapeutic properties of *Rheum* are well-known since 2700 BC (Dymock et al., 1890), and its documentation was first of all done in the earliest global book on Materia Medica, '*Shen Nong Ben Cao Jing*' in 270 BC (Fang et al., 2011; Xiang et al., 2020). *Rheum australe* is presently reported endemic to the Himalayan region at elevations ranging from 3,300 to 5,200 m asl and covers the areas of India, Pakistan, Nepal, Bhutan, China, and Myanmar. The distribution of

*R. australe* varies widely due to its inhabitation in grassy or rocky slopes, forests areas, crevices, and moraines, between boulders and near streams of the specific regions.

The first record of *Rheum moorcroftianum* was found in the Himalayan region of Kashmir. It is widely distributed in Garhwal and Kumaon at altitudes of 3,000 to 5,200 m asl. *Rheum webbianum* is a perennial herb with 80 to 90 cm tall stem, large petiolated leaves and small light yellow flowers. It is widely distributed in the Himalayan region covering Nepal to Kashmir at an altitude of 3,000 to 5,000 m asl (Saggo & Farooq, 2011). *Rheum spiciforme* is distributed in Kashmir, Kumaon, and Sikkim Himalaya at an altitude of 1,700 m to 5,500 m asl (Tabin et al., 2016b).

## 6.6 BOTANY AND TAXONOMY

*Rheum* species are robust, perennial herbaceous plants with thick and long roots. The stem is stout, and is marked with green and brown colored streaks. Leaves are large, and shiny. The leaves are round in structure with diameter ranging from 20 to 60 cm. The flowering stem is quite distinctive, bearing red to purple colored numerous flowers on a single spike. The fruits are purple with narrow wings, a rounded heart-shaped base and notched apex.

*Rheum australe* is 1.5 to 3 m tall, robust, broad leaved perennial herb with fleshy rhizomes. The stem is hairless containing green and brown streaks with a shade of purple to red. Rhizomes are 6 to 12 inches long and their surface is dull orange to yellowish brown, less scented, coarser, and untrimmed. Roots and rhizomes are mainly used as raw material for drug preparation and are harvested between October and November. Leaves are round, heart-shaped, thick, rough, generally ovate, base cordate, subscaberulous from the above and papillose from the below, entire margin and sinuate with a flat apex. The roots are laxative, tonic, and astringent, while tuber is pungent and bitter. The upper leaves are small in size, while basal leaves are large (up to 60 cm). Flowering of *R. australe* occurs from June to August, while fruiting takes place from July to September (Li et al., 2003). Flowers are dark reddish-purple or yellowish arranged in dense branched clusters in 1 ft long inflorescence. The size of perianth is 3 to 3.5 mm with small oblong-elliptic outer parts. The filaments are subulate. The stigma is muricate and oblate, the ovary is rhomboid-obovoid. The fruit is ovoid-ellipsoid, large (0.5 to 1.5 cm), oblong with purple coloration and possess wings at its sides. Plants can be propagated either by seeds or by rootstock.

*Rheum moorcroftianum* is a fleshy, perennial herb that varies in height from 0.3 to 1.8 m. The stem bears radical leaves with diameter 10 to 60 cm. The leaves are thick, leathery, puberulous underneath with cordate base and undulate margins. The flowers are light yellow in color that arises in fleshy, glabrous racemes from the center of the large and stout radical leaves. The fruit is broadly oblong or orbicular in appearance and pink-purple in color (Chauhan, 1999).

*Rheum webbianum* possess basal and cauline leaves. Basal leaves are orbicular or broadly ovate, large (30 to 60 cm in length), pubescent abaxially, papilliferous or muriccate adaxially, with subcordate base, deeply palmately 5-lobed, central 3 lobes pinnatisect and narrow acute apex. The stem leaves are few and smaller as compared to the basal leaves which possess a large panicle and articulated pedicels and nine stamens. The ovary is broadly ovoid. The root is fleshy, straight, dark brownish from outside and yellowish or reddish-yellow from inside with 30 cm x 10 cm length and diameter, respectively. The stem is hollow, fleshy, finely sulcate, and non hairy. Leaves are large, triangular in shape, with long and thick petioles. The flowers are small, white to red, and grouped to form large compound leafy inflorescences (Tabin et al., 2016c).

Equally, *R. spiciforme* is a stout herb. Petiole of basal leaf 3 to 10 cm long, purplish red, subterete, stout, glabrous or papilliferous; leaf blade dark-green or yellow-green adaxially, purple-red abaxially, ovate or broadly ovate elliptic, coriaceous, papilliferous or glabrous abaxially and adaxially, rounded subcordate or base, margins slightly sinuate, and the apex obtuse. The leaves are radical (15 to 30 cm long), brownish-red in color with 7 to 15 cm long petiole, hard, glabrous, coriaceous, orbicular, broadly ovate or cordate. The inflorescence is pedunculate, glabrous, 10 to 30 cm long spike-like raceme. The flowers are small (2 to 3 mm), bracteate, ovate, and scarious with 2 to 7 mm long pedicel. The perianth segments are small, entire, obtuse, 2 to 3 mm long, yellowish or reddish in color. Fruit are ellipsoid or oblong with 0.5 to 1.5 cm length, rounded at the apex and contain membranous wings (Tabin et al., 2016c).

## 6.7 VARIETIES AND CULTIVARS

Various varieties of cultivated Rhubarb which are usually grown for food are recognized as *Rheum x hybridum* in the Royal Horticultural Society's list of recognized plant names (Clementi & Misiti, 2010). Figure 6.2 illustrates the *Rheum* species of Lahaul and Spiti (H.P.), India.





**FIGURE 6.2** *Rheum* species – (A) *Rheum australe*; and (B) *Rheum webbianum* of Lahaul and Spiti (H.P.), India.

## 6.8 SOIL AND CLIMATE

*Rheum* species are found abundantly in the western and central Himalaya, at altitudes ranging from 2,700 to 5,200 m asl, on well-drained, alpine slopes and on rocky outcrops. Generally, *Rheum* is found in moist type of climate

where there is no dearth of moisture or near water streams, on the banks of rivulets. However, in the two districts of Himachal Pradesh, it is found in different climatic conditions. In Spiti for instance, it is found in a comparatively dry type of climate, compared to Kinnaur where rain precipitation is more abundant with a soil type that is better and more suitable for cultivation.

## 6.9 PROPAGATION AND ROOTSTOCK

*Rheum* can be propagated through seeds and top rhizome segments from mother plants. In the months of September to October, collection of the seeds is done. The rate of seed germination is very high and requires no specific pretreatment. *Rheum australe* is prevalent to the Himalayan region and is distributed in grassy or rocky slopes and in forest areas at an altitude of 3,300 to 5,200 m asl (Li et al., 2003). Rootstocks or seeds are used for propagation. On planting in soil, the pieces of the rootstocks sprout successfully during May to June. Seeds get mature at the end of October and show successful germination when sown in their natural habitat or in cultivated land at the start of November (Nautiyal et al., 2002), or during February to April (Bhattarai & Ghimire, 2006). After sowing, germination starts after 7 to 10 days and continues for about one month. Better germination is achieved by soaking seeds in water for 10 to 12 hours prior to sowing (Bhattarai & Ghimire, 2006). Seedlings should be maintained in the same sown area for one year and transplanted to another place in March or April. Propagation is successful in well-drained, porous, sandy, and humus rich soil. Crop is ready for harvesting after a year in which one can get petioles rich in active ingredients. However, good rootstocks rich in bioactive constituents are harvested four to five years after germination (Nautiyal et al., 2002). *In vitro* techniques have also been developed for the mass propagation of *R. australe* from various parts including shoot tips, stem segments, leaves (Lal & Ahuja, 1993) or rhizome buds (Pandey et al., 2008; Malik et al., 2009).

## 6.10 PLANTING, IRRIGATION, AND NUTRIENT MANAGEMENT

1. **Raising Propagules:** In open sites, seedlings of *R. australe* are grown in March, whereas in sheltered places grown in February. Sowing of the seeds is done in lines with 50 cm spacing. In temperate regions, the sowing is done in the spring season, i.e., March to early April. Seeds take one month to germinate completely.

2. **Propagule Rate:** For raising a nursery in 1 hectare of land with a spacing of 50 cm x 50 cm, there is a requisite of approximately 600 g of seeds.
3. **Planting in the Field:**
  - i. **Preparation of Land and Application of Fertilizer:** The land is prepared by ploughing to get fine tilt and proper aeration. Basal dose of farmyard manure (FYM) at the rate of 10 tones/hectare may be applied for soil containing 1–1.5% of organic carbon.
  - ii. **Transplanting and Optimum Spacing:** Plants are transplanted in May at the age of three months. One hectare of land can accommodate a crop stand of 40,000 plants with the optimum spacing of 50 cm x 50 cm.
  - iii. **Intercropping System:** Intercropping is not possible with *Rheum australe* after second year as it occupies most of the soil surface. However, during the first year annual vegetable crops or other medicinal plants can be intercropped with *Rheum australe*. Intercropping is also successful with *R. moorcroftianum* which possess similar medicinal properties like *R. australe*.
  - iv. **Interculture and Maintenance Practices:** Before transplantation, half dose of nitrogen and full dose of potash and phosphorus are recommended along with the basal dose of FYM (10 tones/hectare). Remaining nitrogen is applied as top dressing six to eight weeks after transplanting *Rheum*.
  - v. **Irrigation Practices:** Irrigation is done immediately after transplanting the propagules followed by light irrigation at four-week intervals. During summers, light sprinkler irrigation is useful for the growth of the crop. However, excessive watering during winters may decay underground rhizomes.
  - vi. **Weed Control:** During the initial growth period of the crop, regular weeding should be done at an interval of 15 to 30 days. Weeding during monsoons has also proved to enhance plant growth.

### 6.11 DEADHEADING

Deadheading of spikes is done after flowering. Deadheading is done to remove flowers from plants when these are fading or dead. It is done to encourage more blooms on plants.

## 6.12 PEST AND DISEASE MANAGEMENT

The crop is often infected with *Fusarium* species. As a control measure, soil drenching is done with recommended dose of Carbendazim 50, i.e., at the rate of 2 g/liter of water. To prevent the attack of insects and aphids in early stage of the plant growth, spray with Ecalux at the rate of 0.5% is recommended twice at an interval of 10–15 days.

## 6.13 HARVESTING AND YIELD

1. **Crop Maturity and Harvesting Time:** Crop rose from seedlings get mature within four to five years. However, when grown from rhizome segments *Rheum* takes two to three years to get mature. After one year, flowering occurs in the months of May and June. The plants get ready for harvesting after the onset of fruiting in September and October. The plants reach maturity within four growing seasons.
2. **Post-Harvest Management Practices:** Cleaning of the root and rhizome is done followed by washing, chopping, and drying in shade. Packing of the dried crude drug material is done in airtight and moisture free containers.
3. **Yield and Cost of Cultivation:** After three years, the expected yield ranges from 37 quintals to 66 quintals/hectare. For 2016 and 2017, the cost of cultivation of *R. australe* was calculated at 1,18,592 INR per acre (Anonymous, 2021).

## 6.14 POST-HARVEST HANDLING AND STORAGE

To increase the shelf life of the plant material during storage, the essential guidelines are followed after harvesting the *Rheum* species. These are given as follows:

- i. Only mature parts are collected.
- ii. After collection, the material is immediately shade dried.
- iii. Plant parts are dried completely before packaging and storage.
- iv. The plant material is properly stored to minimize losses.

The following steps are involved in the post harvest handling and storage of *Rheum* species:

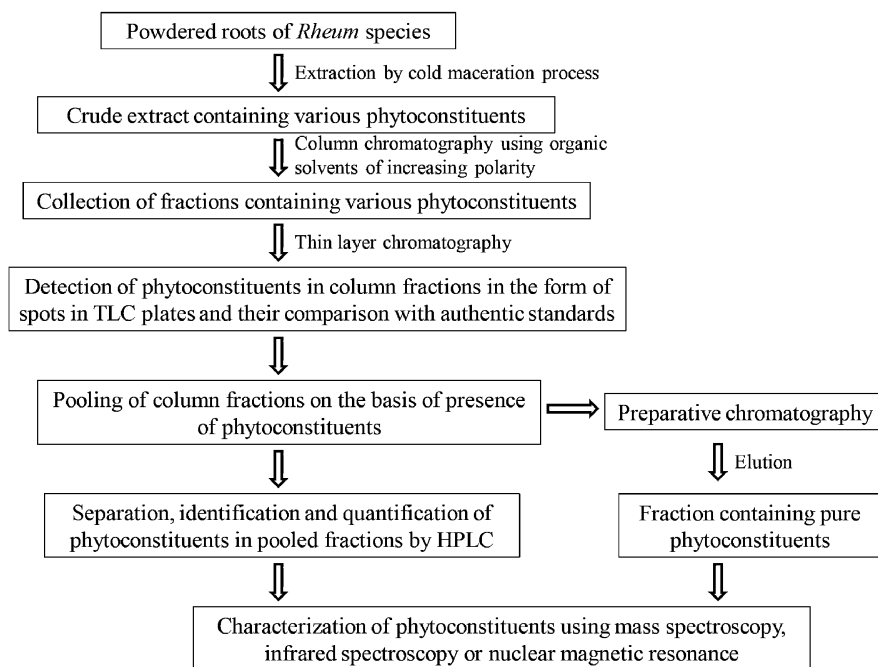
1. **Cleaning, Sorting, and Grading:** Cleaning and sorting is done to remove infested, immature, and undesirable matter such as dust, sand, stone, etc., from the plant material. Grading is done after

cleaning and sorting. The plant material is graded on the basis of its quality according to the market potential.

2. **Packaging:** To protect the plant material from extraneous matter or to prevent losses during storage, handling or shipment; the packaging is done in air tight containers.
3. **Storage:** The plant material is stored in cool and dry place to avoid contamination and deterioration. Low storage temperature is preferred to avoid breakdown of phytoconstituents or quality loss. Desiccant is used to maintain low humidity in the containers.

### 6.15 PROCESSING OF *RHEUM* SPECIES

Figure 6.3 depicts the schematic procedures for extraction, isolation, identification, and characterization of phytoconstituents in *Rheum* species. Roots of *Rheum* are first grounded to a fine powder. Powdered roots are then subjected to cold maceration process using various organic solvents of increasing polarity. Crude extract of *Rheum* roots is thus obtained containing



**FIGURE 6.3** Extraction isolation and identification of phytoconstituents from *Rheum* species.

various phytoconstituents. The extract is further fractionated using column chromatography. Elution of various fractions is done using various solvent mixtures. The fractions thus obtained are checked for various phytoconstituents using thin layer chromatography. Authentic standards are used to detect and confirm the presence of phytoconstituents in fractions of *Rheum* root extract. Column fractions are pooled on the basis of the presence of phytoconstituents. The collected fractions can further be subjected to HPLC for further separation, identification, and quantification of phytoconstituents. Preparative chromatography is employed to purify the individual phytoconstituent from the fractions. Further characterization of phytoconstituents can be done by mass spectroscopy (MS), infrared (IR) spectroscopy or nuclear magnetic resonance (NMR).

## 6.16 CHARACTERIZATION OF PHYTOCONSTITUENTS

More than 250 anthraquinones have been isolated from different parts of *Rheum* species by various researchers (Zargar et al., 2011; Rokayaa et al., 2012). Emodin is an important anthraquinone present in *Rheum*. Fang et al. (2011) reported five free anthraquinone derivatives (emodin, aloe-emodin, rhein, chrysophanol, and physcion) from *Rheum* species which account for their purgative (Sun, 1992), antimicrobial (Wang et al., 2010) and hepatoprotective (Ho, 1996; Wang et al., 2009; Zhao et al., 2009) properties. Among phenolic compounds, hydroxyanthraquinones, phenolic acids, stilbenes, flavonoids, and tannins are mainly present in *Rheum*. Table 6.3 illustrates a list of phytoconstituents isolated and characterized from various *Rheum* species.

## 6.17 VALUE ADDITION OF *RHEUM* SPECIES

Value addition of medicinal plants is essential for enhancing commercial and therapeutic value of the crude drugs. Value addition is important either due to low quality of the authentic plant material or their active constituents may not meet to the pharmacopeia standards or to the requirement of the industry or consumer. There may be the chance that the crude drug get rejected or accepted at a low price. This is likely to affect the cultivators or collectors who may lose economically and also undermine the potency and efficacy of the raw drug for therapeutic applications. Value addition of *Rheum* can be achieved by quality enhancement of the collected plant material by semi-processing that ensure that the plant material stands as a value added product. The following steps are essential to add value to *Rheum* species:

**TABLE 6.3** Phytoconstituents Isolated and Characterized from *Rheum* Species

Sl. No.	Plant Species	Plant Part	Isolated and Characterized Phytoconstituents	References
1.	<i>R. australe</i>	Roots	Emodin 8-O- $\beta$ -D-glucopyranosyl-6-O-sulfate, carpusin, maesopsin, 10-hydroxycascaroside C, 10-hydroxycascaroside D, 10R-chrysaloin 1-omicron- $\beta$ -D-glucopyranoside and 8-omicron- $\beta$ -D-(6'-omicron-acetyl) glucopyranosyl chrysophanol, flavonoids, chromones, anthrones, stilbenes, oxanthrone ethers and esters, lignans, carbohydrates, phenols, and sterols.	Krenn et al. (2003, 2004); Pandith et al. (2018)
		Rhizomes	Rheinal, rhein-11-O- $\beta$ -D-glucoside, 1,8-dihydroxy anthraquinone (6-methyl-rhein-1, 6-methyl-aloe-emodin)	Agarwal et al. (1999); Mohib & Shingare (2004); Singh et al. (2005)
2.	<i>R. moorcroftianum</i>	Rhizomes	Emodin, chrysophanol, emodin-8-O- $\beta$ -D-glucosides, chrysophanol-8-O- $\beta$ -D-glucosides, physcion	Rawat et al. (1989)
3.	<i>R. webbianum</i>	Whole plant	3',5'-Dihydroxy-4-methoxystilbene (desoxyrhapontigenin)	Chaudhari et al. (1983)
		Roots	1,8-dihydroxy-3-methyl-anthraquinone, 1,6,8-trihydroxy-3-methyl-anthraquinone and 1,8-dihydroxy-3-hydroxymethyl-anthraquinone.	Khetwal & Pathak (1988)
4.	<i>R. spiciforme</i>	Roots	Emodin, aloe-emodin, and rhein	Tabin et al. (2016a)

- 1. Collection in the Proper Seasons:** The plant material is collected in the appropriate season, because of the concentration of phytochemicals in plants varies according to the seasons. Accordingly, the efficacy and the potency of the crude drugs are affected as they do not contain the same phytochemicals all-year around or at the various stages of plant growth. This needs to be considered while harvesting.
- 2. Purity Assessment by Quality Testing:** Quality testing is done for the physico-chemical properties (proximate composition, secondary metabolites, etc.).

### 3. Semi-Processing of Rheum Species to Add Value to the Products:

Following value added products are formed from *Rheum* species:

- i. **Powder:** The plant material is cleaned thoroughly, dried, and finally pulverized to powdered form. The powder is sieved to get a homogenous powder.
- ii. **Tablets/Capsules:** The homogenous powder is converted into more compact form of a tablet or its desired dose is packed into a capsule by mixing with a suitable binding agent.
- iii. **Extracts:** The semi-processing of the medicinal plants in the form of extracts considerably enhance their value. Extracts can be prepared by extracting the dried and powdered plant material with suitable solvents of various polarities (hexane, petroleum ether, chloroform, ethyl acetate, acetone, methanol or water) via cold maceration process or hot extraction in a soxhlet extractor. The solvents are then distilled off under reduced pressure using rotary evaporator maintained at 40°C to obtain the crude extract. These crude extracts are then concentrated by lyophilization. Further standardization is done to achieve a desired concentration of the bioactive compounds present in the extracts.

## 6.18 BIO-PROSPECTION OF *RHEUM* SPECIES

*Rheum* species are potent in curing various diseases. *Rheum australe* is purgative, antioxidant (Yen et al., 2000; Kuo et al., 2002; Cai et al., 2004; Ganie et al., 2014), astringent, cytotoxic (Kubo et al., 1992), antiviral (Semple et al., 2001), nephroprotective (Kala, 2002; Rajkumar et al., 2010), antimicrobial, antitumor (Akhtar et al., 2009), anti-inflammatory (Malik et al., 2009), hepatoprotective (Ho et al., 2007; Radhika et al., 2010), antidiabetic (Alam et al., 2005), and effective for curing stomachache and skin diseases (Kapoor, 1990; Prasad & Purohit, 2001). Moreover, it is used in textile dyeing (Srivastava et al., 2015), in cosmetics and to impart color to the food (Kong et al., 2004). Rhizomes of *R. moorcroftianum* have purgative effect and are also used to dye wool. The long and fleshy petioles are consumed either raw or in cooked form (Peigen et al., 1984). *Rheum webbianum* is used to treat wounds, boils, and stomach disorders like indigestion and flatulence (Chaurasia & Ballabh, 2009). It is also helpful in treating cancers (Srinivas et al., 2007). *Rheum spiciforme* is used to treat rheumatic pain, bone fractures, backache, joints pain, boils, and wounds (Hesse, 1895).



## 6.19 COMMERCIAL/PHARMACEUTICAL PRODUCTS AVAILABLE

Various *Rheum* commercial products are available in market in the form of capsules, powder, oil, etc.

## 6.20 TECHNOLOGY TRANSFER/PATENTS

Some patents relating to the use of *Rheum* species as herbal drugs are available:

1. **DE102006015575A1:** Roots of *Rheum* species extracted with methanol followed by separation of lipophilic material and condensation of the fraction containing active ingredient which further used to prepare skin care cosmetics.
2. **US20110274635A1:** Extracts of *Oldenlandia diffusa*, *Rheum undulatum*, and *Broussonetia kazinoki* used to prepare whitening composition for applying in the external skin.

## KEYWORDS

- anthraquinones
- bio-prospection
- deadheading
- Himalaya
- nutrient management
- post-harvest handling
- *rheum*
- rhizome
- stilbenoids

## REFERENCES

Agarwal, S. K., Singh, S. S., & Vijai, L., (2001). Chemistry and pharmacology of rhubarb (*Rheum* species): A review. *J. Sci. Ind. Res.*, 60, 1–9.

- Agarwal, S. K., Singh, S. S., Verma, S., & Sushil, K., (1999). Two new anthraquinone derivatives from *Rheum emodi*. *Indian J. Chem.*, 38, 749–751. <https://nopr.niscpr.res.in/handle/123456789/16457> (accessed on 02 September 2023).
- Akhtar, M. S., Amin, M., Ahmad, M., & Alamgeer, A., (2009). Hepatoprotective effect of *Rheum emodi* roots (*Revand chini*) and Akseer-e-Jigar against paracetamol induced hepatotoxicity in rats. *Ethnobot. Leaflets*, 13, 310–315. <https://opensiuc.lib.siu.edu/ebl/vol2009/iss2/3> (accessed on 02 September 2023).
- Alam, M. M., Javed, K., & Jafri, M. A., (2005). Effect of *Rheum emodi* (*Revand chini*) on renal functions in rats. *J. Ethnopharmacol.*, 96, 121–125. <https://doi.org/10.1016/j.jep.2004.08.028>.
- Anjen, L., Bojian, B., Grabovskaya-Borodina, A. E., Hong, S. P., Mcneill, J., Mosyakin, S. L., Ohba, H., & Park, C. W., (2003). *Polygonaceae*. In: Wu, Z. Y., Raven, P. H., & Hong, D. Y., (eds.), *Flora of China* (Vol. 5, pp. 277–350). Science Press, Beijing, and Missouri Botanical Garden Press, St. Louis.
- Anonymous, (2020). <https://echarak.in/echarak/marketprice.do> (accessed on 02 September 2023).
- Anonymous, (2021). National Medicinal Plant Board, Ministry of Ayush, GOI, <https://nmpb.nic.in/content/marketing-trade-1> (accessed on 02 September 2023).
- Babu, K. S., Srinivas, P. V., Praveen, B., Kishore, K. S., Murty, U. S., & Rao, J. M., (2003). Antimicrobial constituents from the rhizomes of *Rheum emodi*. *Phytochemistry*, 62(2), 203–207. [https://doi.org/10.1016/s0031-9422\(02\)00571-x](https://doi.org/10.1016/s0031-9422(02)00571-x).
- Ballah, B., & Churasia, O. P., (2009). Medicinal plants of cold desert Ladakh used in the treatment of stomach disorders. *Indian J. Tradit. Know.*, 82, 185–192.
- Bhatia, A., Arora, S., Singh, B., Kaur, G., & Nagpal, A., (2011). Anticancer potential of Himalayan plants. *Phytochem. Rev.*, 10, 309–323. <https://doi.org/10.1007/s11101-010-9202-0>.
- Bhattarai, K. R., & Ghimire, M. D., (2006). *Cultivation and Sustainable Harvesting of Commercially Important Medicinal and Aromatic Plants of Nepal* (p 393). In Heritage Research and Development Forum, Nepal.
- Cai, Y. Z., Sun, M., Xing, J., & Corke, H., (2004). Antioxidant phenolic constituents in roots of *Rheum officinale* and *Rubia cordifolia*: Structure-radical scavenging activity relationships. *J. Agric. Food Chem.*, 52, 7884–7890. <https://doi.org/10.1021/jf0489116>.
- Cao, Y. J., Pu, Z. J., Tang, Y. P., Shen, J., Chen, Y. Y., Kang, A., Zhou, G. S., & Duan, J. A., (2017). Advances in bio-active constituents, pharmacology, and clinical applications of rhubarb. *Chin. Med.*, 12(1), 36–47. <https://doi.org/10.1186/s13020-017-0158-5>.
- Chaudhari, M., Jain, G. K., Sarin, J. P., & Khanna, N. M., (1983). Spasmolytic principle from *Rheum webbianum* Royle. *Indian J. Chem.*, 22, 1163, 1164.
- Chauhan, N. S., (1999). *Medicinal and Aromatic Plants of Himachal Pradesh* (pp. 346–350). Indus Publishing Company, New Delhi.
- Churasia, O. P., & Ballabh, B., (2009). Medicinal plants of cold desert Ladakh used in treatment of stomach disorders. *Indian J. Tradit. Know.*, 82, 185–192.
- Clementi, E. M., & Misiti, F., (2010). Potential health benefits of rhubarb. In *Bioactive Foods in Promoting Health* (pp 407–423).
- Dymock, W., Warden, C. J. H., & Hopper, D., (1890). *Pharmacographia Indica, A History of the Principal Drugs of Vegetable Origin (Part III)* (pp. 152–157). M/S Bishen Singh Mahendra Pal Singh, Dehradun & M/S Periodical Expert, Delhi.

- Fang, F., Wang, J. B., Zhao, Y. L., Jin, C., Kong, W. J., Zhao, H. P., Wang, H. J., & Xiao, X. H., (2011). A comparative study on the tissue distributions of rhubarb anthraquinones in normal and CCl<sub>4</sub>-injured rats orally administered rhubarb extract. *J. Ethnopharmacol.*, *137*, 1492–1497. <https://doi.org/10.1016/j.jep.2011.08.028>.
- Ganie, A. H., Tali, B. A., Khuroo, A. A., Nawchoo, I. A., & Rather, A. M., (2014). *Rheum spiciforme* Royle (*Polygonaceae*): A new record to the flora of Kashmir valley, India. *Natl. Acad. Sci. Lett.*, *37*(6), 561–565. <https://doi.org/10.1007/s40009-014-0279-7>.
- Hesse, O., (1895). The chemistry of Rhubarb. *Pharmaceutical J.*, *55*, 325–327.
- Ho, N. K., (1996). Traditional Chinese medicine and treatment of neonatal jaundice. *Singapore Med. J.*, *37*(6), 645–651.
- Ho, T. Y., Wu, S. L., Chen, J. C., Li, C. C., & Hsiang, C. Y., (2007). Emodin blocks the SARS coronavirus spike protein and angiotensin-converting enzyme 2 interaction. *Antiviral Res.*, *74*, 92–101. <https://doi.org/10.1016/j.antiviral.2006.04.014>.
- Kabir, D. A., Siddiqui, M. A. A., Wahid-ul, H., Lone, A. H., Manzoor, N., et al., (2015). Threat status of *Rheum emodi* - a study in selected cis-Himalayan regions of Kashmir valley Jammu & Kashmir India. *Med. Aromat. Plants*, *4*, 183. <https://doi.org/10.4172/2167-0412.1000183>.
- Kala, C. P., (2002). Indigenous knowledge of Bhotiya tribal community on wool dyeing and its present status in the Garhwal Himalaya, India. *Current Sci.*, *83*, 814–817. <https://www.jstor.org/stable/24107081>.
- Kala, C. P., Dhyani, P. P., & Sajwan, B. S., (2006). Developing the medicinal plant sector in northern India: Challenges and opportunities. *J. Ethnobot. Ethnomed.*, *2*, 32. <https://doi.org/10.1186/1746-4269-2-32>.
- Kapoor, L. D., (1990). *Handbook of Ayurvedic Medicinal Plants* (p. 487). CRC Press, Boca Raton, FL, and London.
- Katiyar, C., Gupta, A., Kanjilal, S., & Katiyar, S., (2012). Drug discovery from plant sources: An integrated approach. *AYU*, *33*(1), 10–19. <https://doi.org/10.4103/0974-8520.100295>.
- Kaul, M. K., (1997). *Medicinal Plants of Kashmir and Ladakh*. Indus Publishing Company F-5, Tagore Garden, New Delhi.
- Keser, S., Keser, F., Karatepe, M., Kaygili, O., Tekin, S., Turkoglu, I., Demir, E., et al., (2019). Bioactive contents, *in vitro* antiradical, antimicrobial, and cytotoxic properties of rhubarb (*Rheum ribes* L.) extracts. *Nat. Prod. Res.*, *1*, 5.
- Khan, S., Kamili, A., & Gupta, R. C., (2016). Economic and medicinal properties of some medicinal plants found in Kashmir Himalaya. *J. Med. Plants Studies*, *4*(3), 38–44.
- Khare, C. P., (2007). *Indian Medicinal Plants: An Illustrated Dictionary* (p 544). Springer Publishers.
- Khetwal, K. S., & Pathak, R. P., (1988). Active anthraquinones from *Rheum webbianum* royle. *Indian J. Chem. Soc.*, *65*(3), 227, 228.
- Kong, L. D., Cheng, C. H., & Tan, R. X., (2004). Inhibition of MAO A and B by some plant derived alkaloids, phenols, and anthraquinones. *J. Ethnopharmacol.*, *91*, 351–355. <https://doi.org/10.1016/j.jep.2004.01.013>.
- Krenn, L., Pradhan, R., Presser, A., Reznicek, G., & Kopp, B., (2004). Anthrone C-glucosides from *Rheum emodi*. *Chem. Pharm. Bull.*, *52*, 391–393. <https://doi.org/10.1248/cpb.52.391>.
- Krenn, L., Presser, A., Pradhan, R., Bhar, B., Paper, D. H., Mayer, K. K., & Kopp, B., (2003). Sulfemodin 8-O-β-D-glucoside, a new sulfated anthraquinone glycoside and antioxidant phenolic compounds from *Rheum emodi*. *J. Nat. Prod.*, *66*, 1107–1109. <https://doi.org/10.1021/np0301442>.

- Kubo, I., Murai, Y., Soediro, I., Soetarno, S., & Sastrodihardjo, S., (1992). Cytotoxic anthraquinones from *Rheum palmatum*. *Phytochemistry*, *31*, 1063–1065.
- Kuo, P. L., Lin, T. C., & Lin, C. C., (2002). The antiproliferative activity of aloe-emodin is through p53-dependent and p21-dependent apoptotic pathway in human hepatoma cell lines. *Life Sci.*, *71*, 1879–1892. [https://doi.org/10.1016/s0024-3205\(02\)01900-8](https://doi.org/10.1016/s0024-3205(02)01900-8).
- Lal, N., & Ahuja, P. S., (1993). Assessment of liquid culture procedures for *in vitro* propagation of *Rheum emodi*. *Plant Cell Tissue Organ Culture*, *34*, 223–226. <https://doi.org/10.1007/BF00036106>.
- Lee, M. R., Hutcheon, J., Dukan, E., & Milne, I., (2017). Rhubarb (*Rheum* species): The role of Edinburgh in its cultivation and development. *J. R. Coll. Phys. Edinburgh*, *47*(1), 102–109. <https://doi.org/10.4997/JRCPE.2017.121>.
- Li, A. R., (1998). *Flora Republicatae popularis sinicae*. Beijing Science Press.
- Li, A., Bao, B., Grabovskaya-Borodina, A. E., Hong, S. P., McNeill, J., Mosyakin, S. L., Ohba, H., & Park, C. W., (2003). *Rheum*. In: Wu, Z. Y., Raven, P. H., & Hong, D. Y., (eds.), *Flora of China* (Vol. 5, pp. 341–350). Science Press, Beijing, and Missouri Botanical Garden Press, St. Louis.
- Malik, S., Kumar, R., Vats, S. K., Bhushan, S., Sharma, M., & Ahuja, P. S., (2009). Regeneration in *Rheum emodi* Wall.: A step towards conservation of an endangered medicinal plant species. *Eng. Life Sci.*, *9*(2), 130–134. <https://doi.org/10.1002/elsc.200800071>.
- Matsuda, H., Morikawa, T., Toguchida, I., Park, J., Harima, S., & Yoshikawa, M., (2001). Antioxidant constituents from Rhubarb: Structural requirements of stilbenes for the activity and structures of two new anthraquinone glycosides. *Bioorg. Med. Chem.*, *9*, 41. [https://doi.org/10.1016/S0968-0896\(00\)00215-7](https://doi.org/10.1016/S0968-0896(00)00215-7).
- Miao, M. S., (2001). *Therapeutic Medicine Pharmacology* (p. 673). Science Press, Beijing: China.
- Mohib, K., & Shingare, M. S., (2004). TLC-colourimetric estimation of free and combined forms of chrysophanol, emodin, and physcione in Indian Rhubarb. *Indian J. Pharmaceut. Sci.*, *65*, 552–553.
- Nautiyal, B. P., Prakash, V., Maithani, U. C., Chauhan, R. S., Purohit, H., & Nautiyal, M. C., (2002). Germinability, productivity, and economic viability of *Rheum emodi* Wall. ex Meissn. cultivated at lower altitude. *Current Sci.*, *84*, 143–148.
- Pandey, S., Malik, S., Sharma, S., & Sharma, M., (2008). Studies on differential growth behavior of two alpine herbs of western Himalaya from different altitudes under *in vitro* conditions. *Indian J. Biotech.*, *7*, 137–140.
- Pandith, S. A., Dar, R. A., Lattoo, S. K., Shah, M. A., & Reshi, Z. A., (2018). *Rheum australe*, an endangered high-value medicinal herb of North Western Himalayas: A review of its botany, ethnomedical uses, phytochemistry, and pharmacology. *Phytochem. Rev.*, *17*, 573–609. <https://doi.org/10.1007/s11101-018-9551-7>.
- Pandith, S. A., Hussain, A., Bhat, W. W., Dhar, N., Qazi, A. K., Rana, S., Razdan, S., et al., (2014). Evaluation of anthraquinones from Himalayan rhubarb (*Rheum emodi* Wall. ex Meissn.) as antiproliferative agents. *South Afr. J. Bot.*, *95*, 1–8. <http://dx.doi.org/10.1016/j.sajb.2014.07.012>.
- Peigen, X., Liyi, H., & Liwei, W., (1984). Ethnopharmacologic study of Chinese rhubarb. *J. Ethnopharmacol.*, *10*(3), 275–293. [https://doi.org/10.1016/0378-8741\(84\)90016-3](https://doi.org/10.1016/0378-8741(84)90016-3).
- Prasad, P., & Purohit, M. C., (2001). Altitude acclimatization and concentration of active constituents and calorific value of two medicinal plant species *Rheum emodi* and *R.*

- nobile* (Rhubarb) in Sikkim Himalaya. *Current Sci.*, 80, 734–736. <https://www.jstor.org/stable/24105657>.
- Radhika, R., Kumari, D. K., & Sudarsanam, D., (2010). Antidiabetic activity of *R. emodi* in Alloxan induced diabetic rats. *Int. J. Pharmaceut Sci. Res.*, 1, 296–300.
- Rajkumar, V., Guha, G., & Kumar, R. A., (2010). Antioxidant, and anti-cancer potentials of *Rheum emodi* rhizome extracts. *eCAM*, 2010, 1–9. <http://dx.doi.org/10.1093/ecam/nejq048>.
- Rawat, M. S., Negi, D. S., Panwar, M. S., Pant, G., Shibata, S., Okada, Y., Oshima, Y., & Okuyama, T., (1989). Anthraquinone glycosides from *Rheum moorcroftianum* Royle. *Pharmazie*, 44, 509, 510.
- Rehman, H., Begum, W., Anjum, F., & Tabasum, H., (2014). *Rheum emodi* (Rhubarb): A fascinating herb. *J. Pharm. Phytochem.*, 3(2), 89–94.
- Rokayaa, M. B., Munzbergova, Z., Timsina, B., & Bhattaraid, K. R., (2012). *Rheum australe* D. Don: A review of its botany, ethnobotany, phytochemistry, and pharmacology. *J. Ethnopharmacol.*, 141, 761–774. <https://doi.org/10.1016/j.jep.2012.03.048>.
- Saggo, M. I. S., & Farooq, U., (2011). Cytology of *Rheum*, a vulnerable medicinal plant from Kashmir Himalaya. *Chromosome Bot.*, 6, 41–44. <https://doi.org/10.3199/iscb.6.41>.
- Semple, S. J., Pyke, S. M., Reynolds, G. D., & Flower, R. L., (2001). *In vitro* antiviral activity of the anthraquinone chrysophanic acid against poliovirus. *Antiviral Res.*, 49, 169–178. [https://doi.org/10.1016/s0166-3542\(01\)00125-5](https://doi.org/10.1016/s0166-3542(01)00125-5).
- Singh, P., Negi, J. S., Rawat, M. S. M., & Pant, G. J., (2010). Quantification of mineral elements of *Rheum emodi* (Wallr.). *Biol. Trace Elem. Res.*, 138(1–3), 364–371. <https://doi.org/10.1007/s12011-009-8603-7>.
- Singh, S. S., Pandey, S. C., Singh, R., & Agarwal, S. K., (2005). 1,8-dihydroxyanthraquinone derivatives from rhizomes of *Rheum emodi* Wall. *Indian J. Chem.*, 44, 1494–1496. <http://hdl.handle.net/123456789/9126>.
- Srinivas, G., Babykutty, S., Sathiadevan, P. P., & Srinivas, P., (2007). Molecular mechanism of emodin action: Transition from laxative ingredient to an antitumor agent. *Med. Res. Rev.*, 27, 591–608. <https://doi.org/10.1002/med.20095>.
- Srivastava, M., Mogra, D., & Gupta, P., (2015). Dye extraction from *Rheum emodi* for coloring silk using natural mordants. *J. App. Nat. Sci.*, 7(1), 182–186.
- Sun, X., (1992). Can purgation therapy be adjunct to SDD? *Intensive Care Med.*, 18, 252, 253. <https://doi.org/10.1007/BF01709845>.
- Tabin, S., Gupta, R. C., Kamili, A. N., & Bansal, G., (2016a). Phytochemical analysis of wild and *in vitro* raised plants of *Rheum* species using HPLC. *Biochem. Pharmacol. (Los Angel)*, 5, 4. <https://doi.org/10.4172/2167-0501.1000215>.
- Tabin, S., Kamili, A. N., & Gupta, R. C., (2016b). Novel study on *in vitro* culture of *Rheum spiciforme* Royle: An endangered medicinal plant of Gurez valley. *Int. J. Curr. Res.*, 8(4), 28971–28979.
- Tabin, S., Kamili, A. N., & Gupta, R. C., (2016c). Morphological studies, and development of *ex-situ* protocol for rehabilitation of threatened *Rheum* species under nursery conditions. *Curr. Bot.*, 7, 17–26. <https://doi.org/10.19071/cb.2016.v7.3045>.
- Tayade, A., Dhar, P., Ballabh, B., Kumar, R., Chaurasia, O. P., Bhatt, R. P., & Srivastava, R. B., (2012). *Rheum webbianum* Royle: A potential medicinal plant from trans-Himalayan cold deserts of Ladakh, India. *Plant Arch.*, 12, 603–606.
- Thakur, M., Sharma, P. K., Asrani, R. K., Patil, R. D., & Gautam, H., (2020). Traditional therapeutic uses of some important medicinal and aromatic plants of the tribal area of Lahaul valley of Himachal Pradesh, India. *Indian J. Tradit. Know.*, 19(4), 761–775.

- Wang, C., Wu, X., Chen, M., Duan, W., Sun, L., Yan, M., & Zhang, L., (2007). Emodin induces apoptosis through caspase 3-dependent pathway in HK-2 cells. *Toxicology*, *231*, 120–128. <https://doi.org/10.1016/j.tox.2006.11.064>.
- Wang, J. B., Zhao, Y. L., & Xiao, X. H., (2009). Assessment of the renal protection and hepatotoxicity of rhubarb extract in rats. *J. Ethnopharmacol.*, *121*, 18–25. <https://doi.org/10.1016/j.jep.2009.04.018>.
- Wang, J., Zhao, H., Kong, W., et al., (2010). Microcalorimetric assay on the antimicrobial property of five hydroxyanthraquinone derivatives in rhubarb (*Rheum palmatum* L.) to *Bifidobacterium adolescentis*. *Phytomedicine*, *17*, 684–689. <https://doi.org/10.1016/j.phymed.2009.10.009>.
- Xiang, H., Zuo, J., Guo, F., et al., (2020). What we already know about rhubarb: A comprehensive review. *Chin. Med.*, *15*, 88. <https://doi.org/10.1186/s13020-020-00370-6>.
- Yen, G. C., Duh, P. D., & Chuang, D. Y., (2000). Antioxidant activity of anthraquinones and anthrone. *Food Chem.*, *70*, 437–441. [https://doi.org/10.1016/S0308-8146\(00\)00108-4](https://doi.org/10.1016/S0308-8146(00)00108-4).
- Zargar, B. A., Masoodi, M. H., Ahmed, B., & Ganie, S. A., (2011). Phytoconstituents and therapeutic uses of *Rheum emodi* wall. ex Meissn. *Food Chem.*, *128*, 585–589. <https://doi.org/10.1016/j.foodchem.2011.03.083>.
- Zhao, Y. L., Wang, J. B., Zhou, G. D., et al., (2009). Investigations of free anthraquinones from rhubarb against alpha-naphthyl isothiocyanate-induced cholestatic liver injury in rats. *Basic Clinic Pharmacol. Toxicol.*, *104*, 463–469. <https://doi.org/10.1111/j.1742-7843.2009.00389.x>.

## CHAPTER 7

---

# Rose (*Rosa* sp.) More Than Just Beautiful: Exploring the Therapeutic Properties of the Rose Species

NAOKO TAKAHASHI

*United Nations Staff, Rome, Italy*

---

### ABSTRACT

Rose is one of the most ancient and popular flowers grown around the world over millions of years, embedded in the long history of human development and traditional practices. Rose, a well-known symbolic representation of love and beauty are found in various traditional cultures. According to fossil evidence, rose is at least 35 million years old with historical use dating back to ancient Persia. Genus *Rosa*, belonging to the Rosaceae family, contains approximately 200–350 recognized species and 18,000–30,000 cultivars acknowledged in ‘The Plant List’ of the Royal Botanic Gardens, Kew, and the Missouri Botanical Garden. In nature, rose species are grown widely in the Northern hemisphere, in places like Asia, Europe, North America, and northern Africa. The beauty of roses and their fragrance have led to its enormous production as ornamentals in various countries; rose flowers are currently one of the most important global commodity. Both rose flowers and fruit are harvested and have been used medicinally around the world for thousands of years. While the horticulture industry has developed numerous species and cultivars for the beauty aspect of rose, so far, rose natural and medicinal products with high medicinal potency are made according to traditional practices and traditional medicinal products are made from the same species which were used in ancient time. However, in recent years, rose medicinal products (rose flower water, rose essential oils, rose concrete

(solvent extraction of fresh rose flower, non-steamed, and external moisture free), rose absolute (solvent extracted rose essential oil) have become popular and the demand for different rose cultivars has grown exponentially. In addition, the trade of rose hip, and rose tea has increased because of the rich pharmacological and therapeutic properties. Curative properties include: anti-inflammatory, pain-relief, anti-HIV, antioxidant, antibacterial, antitussive, anti-diabetic, hypnotic, and a relaxant effect on tracheal chains. Moreover, the symbolic feature of rose is embedded in love, romance, motherhood, and beauty, while the rich compounds support widely people's health. Rose thus is portrayed as one of the most essential plants in the world.

## 7.1 GENERAL INTRODUCTION

Roses, important species of the Rosaceae family, and are popular as ornamental plants, commonly called “king or queen of flowers” (Nikbakht, Kafi, Mirmasoumi, & Babalar, 2005; Cai, Xing, Sun, Zhan, & Corke, 2005). The existence of roses have been found in fossils in Oregon, Colorado, Montana, and China (Haghighi, Tehranifar, Nikbakht, & Kafi, 2006; Becker, 1963). Dating back to 30–35 million years ago. The literature on the fragrance of roses is mentioned in ancient Sanskrit, Chinese, and the Assyrian records. Rose and petrified rose wreaths have been preserved in Ancient Egyptian tombs (Yaniv & Dudai, 2014; Shakywar, Tomar, & Patidar, 2016). Moreover, Cleopatra, the famous Egyptian beauty queen was well-known for her love for roses and their fragrances (Yaniv & Dudai, 2014).

In ancient lore, the Greek and Roman mythologies also described roses as the symbol of ‘Venus,’ referring to a deity of love and peace (Shakywar, Tomar, & Patidar, 2016). Rose oil and rose water were used in their religious ceremonies. Around 1,000 years ago, Avicenna (AD 980 to 1037) described the medicinal benefits of the damask rose, for cosmetic, gastrointestinal, and cardiac tonic use, and as an astringent on mucosal lesions, and for its anti-nociceptive and anti-inflammatory effects (Nayebi, Khalili, Kamalinejad, & Emtiazy, 2017). In ancient times, rose water was extracted by immersing flowers of the roses in warm water or macerated with olive oil (Yaniv & Dudai, 2014). Although distillation is a modern technique, the earliest record referring with rose oil is found in the works of Ibn Haldun (1332 to 1406). In the eighth and ninth centuries of India and China, Hardun further mentions that distilling rose flowers to produce rose oil was traded (Yaniv & Dudai, 2014).

Records show that the distillation of rose was already practiced in the Ottoman era. In the Ottoman palace and hospital in Edirne, Turkey, 15<sup>th</sup> century Gülhane rose works or rose distillation facilities were found. Gülhane



(Giilhane) was also built in Istanbul between 1460 and 1478, where over 300 shops sold rose water in the 17<sup>th</sup> century (Yaniv & Dudai, 2014). In the mid-1600s, Culpeper wrote in his book ‘The Complete Herbal’ (1653) that roses were used in water or wine to cure headaches, eyes, ears, throat, heart, and stomach pains, and gums, and regulated menstruation (Potterton, 1983). Aghili Shrazi (AD 1670 to 1747) described how the medicinal properties of roses were used as a brain tonic and analgesic for various diseases (Nayebi, Khalili, Kamalinejad, & Emtiazy, 2017). In the 18<sup>th</sup> century, Bulgaria was highly productive in cultivating rose for producing rose oil and water, as the main supplier for the Ottomans (Yaniv & Dudai, 2014). Thus, the extended history between rose and humans shows that rose was one of the most attractive flowers for human beings, symbolizing love, passion, and romance for many (Shakywar, Tomar, & Patidar, 2016) (Figure 7.1).



**FIGURE 7.1** *Rosa* spp., Japan (© Naoko Takahashi).

## 7.2 AREA AND PRODUCTION

Roses are one of the most produced and traded plants globally. The vast volume of the plant is traded as ornamental crops. The production of rose cut stems is estimated at 60 to 80 million per year and 220 million grown for landscape purposes (Debener & Byrne, 2014).

### 7.2.1 ROSE PRODUCTION

In 2012–2013, the main countries in the world producing cut roses were India, China, Ecuador, Colombia, Kenya, Mexico, Italy, Thailand, Japan, and the Netherlands (Bhagat, Badgular, Bhosale, & Supe, 2019). India alone contributed 47% of the global share of cut flowers between 2012 and 2013 (Table 7.1).

**TABLE 7.1** Cut Rose Production per Country between 2012 and 2013 (Bhagat et al., 2019)

Exporting Countries	Area (ha)	Share (%)
India	28,130	46.54
China	14,316	23.68
Ecuador	4,073	6.74
Columbia	2,588	4.28
Kenya	2,164	3.58
Mexico	1,421	2.35
Italy	1,221	2.02
Thailand	439	0.73
Japan	409	0.68
Netherlands	384	0.64

### 7.2.2 ROSE EXPORT

According to the Agri Exchange of the Agricultural and Processed Food Products Export Development Authority of the Government of India (APEDA, 2019), Royal Flora Holland was the key global trader in importing and re-exporting 40% of rose flowers globally. However, over time, countries like Kenya and India have led. The global exporters depend on the export destination (Table 7.2).

**TABLE 7.2** Export Destinations of Rose Cut Flowers in 2018 (APEDA, 2019)

Exporting Countries	Export Destination Countries			
	USA	Germany	UK	France
1.	Columbia	Netherlands	Netherlands	Kenya
2.	Ecuador	Kenya	Kenya	Ethiopia
3.	Netherlands	Italy	Italy	Ecuador
4.	Canada	Ecuador	Ecuador	Belgium

### 7.2.3 ROSE IMPORT

According to the Agri Exchange of the Agricultural and Processed Food Products Export Development Authority of the Government of India (Agri-Exchange 2020), the USA was the largest importer in 2018 with a market valued at USD 636.54 million, followed by the Netherlands (USD 562.83 million), UK (USD 229.53 million), Russia (USD 192.34 million), Belarus (USD 177.15 million), and France (USD 157.26 million) (Table 7.3).

**TABLE 7.3** Value of Rose Import per Country

Importing Countries	2016		2017		2018	
	Qty (kg)	Value	Qty (kg)	Value	Qty (kg)	Value
USA	0	569.57	0	580.86	74,819,045	636.54
Netherlands	2,88,805,645	656.83	2,39,477,361	635.85	1,80,940,572	562.83
United Kingdom	29,663,580	215.97	29,013,201	210.04	51,608,703	229.53
Russia	24,684,406	180.68	28,929,348	179.83	41,851,469	192.34
Belarus	5,953,710	43.85	16,549,862	107.02	22,315,875	177.15
France	23,495,333	156.53	23,023,682	155.54	18,484,896	157.26
Belgium	0	41.66	40,852,254	42.93	21,818,271	103.55
Italy	11,733,055	77.52	11,410,699	75.33	12,538,894	83.03
Poland	4,868,452	29.64	8,839,399	48.19	13,220,414	75.82
Canada	0	54.16	0	58.68	0	59.64

Source: APEDA Agri-Exchange – March 2020.

However, the regions for rose oil production are more limited compared to the countries producing garden roses. It is mainly produced in Turkey, Bulgaria, Iran, Russia, Morocco, India, and China (Yaniv & Dudai, 2014). In Turkey for instance, 80% of rose cultivation for the rose oil production is located in the region of Isparta (Yaniv & Dudai, 2014). In Bulgaria, roses are mainly produced in the region of Kazanlik.

## 7.3 MARKETING AND TRADE

Roses are the largest traded flowers in the world (Bhattacharjee & Banerji, 2010), and among the most important economically viable genus of horticultural, aromatic, and medicinal plants. Roses are cultivated globally for ornamental purposes, perfumery industries, and medicinal properties (Hassanein, 2010). The flowers are largely traded for ornamental plants for parks, houses, and gardens. Rose medicinal products are also largely traded, as rose essential oils, rose waters and dried petals (Bhattacharjee & Banerji, 2010; Boskabady, Shafei, Saberi, & Amini, 2011; Jabbarzadeh & Khosh-Khui, 2005).

### 7.3.1 CUT FLOWERS

In the 1990s, the global cut and garden rose market was estimated to value approximately 11.7 billion USD per year; however, in 2008, the global rose

market production grew to approximately USD 28 billion (Jabbarzadeh & Khosh-Khui, 2005). The trade of rose cut flowers has grown exponentially in the world, and currently stands as the main trade on the European market (Center for the Promotion of Imports from Developing Countries (CBI), 2017a). Between 2011 and 2015, fresh cut rose imports increased from 588€ to 718€ million and are expected to further increase (CBI, 2017b). The market for Dutch rose cut flowers in 2018 was estimated at 10 billion USD (Ahmad, Dole, Khan, Qasim, Ahmad, & Khan, 2010) and the North American market was estimated at 1 billion USD (Debener & Byrne, 2014) in 2013. This reveals that the rose industry is a lucrative business worldwide worth 10 billions of dollars (Debener & Byrne, 2014). The main importers in Europe are the Netherlands, Germany, and the UK, which together constitutes approximately 70% of cut rose imports in the EU (CBI, 2017b). Furthermore, according to the CBI Market International Database 2017 (2017b), Germany was the largest importer of rose cut flowers in the world, increasing its import from €272 million to €309 million (approximately 322 to 365 million USD) between 2011 and 2015. The consumption of cut flowers per capita in Western and Southern European countries ranges from €20 to €50 annually, compared with Central and Eastern European countries and Spain which are relatively lower ranging from €10 and €20 per capita annually (CBI, 2017c). However, the highest consumption of rose cut flowers per capita are in Norway and Switzerland, over €80 per capita annually (CBI, 2017a).

Imports of cut roses within EU countries are mainly distributed from the Netherlands (40%) (CBI, 2017a). Other supplying countries of rose cut flowers out of Europe are Kenya, Ethiopia, and Ecuador, €343 million, €157 million, €132 million, respectively. Zimbabwe, Israel, and Columbia follows. The growing market demand is leading to the development of new rose industries, such as those produced in India, Malawi, Nigeria, Swaziland, Uganda, and Tanzania, which also export to Europe. Previously, the Netherlands was the primary producer of rose cut flowers; however, the export volume has gradually fallen due to the emergence of competitive countries; in particular, the sweetheart rose production has largely shifted to East Africa. The Dutch production therefore decreased from 932 hectares in 2000 to 280 hectares in 2015 (CBI, 2017a). However, the Dutch roses still maintain a prime position on the world market of rose cut flowers because of the high quality and freshness of the flowers, and the producers' ability to provide various varieties.

However, with the recent increased supply of cut flowers from developing countries, the sustainability and the ethical aspects of flower production have

come to the forefront. Scientists have pointed to numerous unethical practices, such as environmental exploitation, basic rights violation especially of the vulnerable producers, and growing inequality between the Global North and South (Gichure, 2010; Raynolds, 2012). While the Southern countries provide the scarce land and water for the business, cheap labor is often exposed to toxic chemicals (Maharaj, 1995). In line with European legislation, EU retailers are therefore increasingly demanding responsible and environmental friendly certificates. They require that the suppliers comply with production standards-MPS-ABC, Global G.A.P., and Fairtrade and Ethical Trading Initiative (ETI) (CBI, 2017a). Thus, Southern countries are compelled to develop new standards and codes of practices; for instance, the Kenya Flower Council (KFC) has adopted the 'KFC Code of Practice,' and 'the Code of Practice for Sustainable Flower Production,' certificates which the Ethiopian Horticulture Producer and Exporters Association (EHPEA) (Rikken, 2010) deliver.

### **7.3.2 COSMETIC, MEDICINAL, AND PERFUMERY INDUSTRIES**

Turkey and Bulgaria are well known for their rose essential oil production which supplies mainly the cosmetic and perfumery industries and largely destined for export (Kovacheva, Rusanov, & Atanassov, 2010). Bulgaria and Turkey supply 80 to 90% of the global rose oil market (Gunes, 2005; Ucar, Kazaz, Eraslan, & Baydar, 2016); however, Bulgarian rose oil is mainly exported to France, Germany, the USA and Japan (Kovacheva, Rusanov, & Atanassov, 2010; Chalova, Manolov, & Manolova, 2017). The annual production of rose oil in 2014 was estimated at 15,000 kg worldwide, out of which Bulgaria and Turkey accounted for 85% of the rose oil demand worldwide (Kovacheva, Rusanov, & Atanassov, 2010; Ucar, Kazaz, Eraslan, & Baydar, 2016). The average price also increased from 3,217 Euros/kg in 2001 to 4,600 Euros/kg in 2008 for Bulgarian rose oil (Kovacheva, Rusanov, & Atanassov, 2010). Overall, the global rose oil market is forecasted to increase to USD 442.0 million by 2025, compared to USD 278.7 million in 2018. According to Grand View Research, Inc. (2019), this represents an increase of 6.8% for the period 2019–2025. Per usage, the fragrance and cosmetics application dominates with an overall share of 71% in 2018 for the global rose oil market. Furthermore, organic farming is generating additional benefits, and pushes the price of rose oil to approx 20% higher compared to rose grown in regular agricultural practices (Kovacheva, Rusanov, & Atanassov, 2010). Besides Bulgaria and Turkey, roses for producing rose oil are also cultivated in Iran, Morocco, India, Afghanistan, Pakistan, France,

Saudi Arabia, and China. While the production of rose oils from Turkey and Bulgaria is mainly for export purposes, rose oils from other countries are mainly sold for domestic use.

Iran has grown roses for medicinal and perfumery products throughout history. The flowers are cultivated on approximately 1,610 ha, and produces 5,483 tons of flowers, with an average yield of 3,410 kg/ha. Roses are mainly produced in the Isfahan and Azerbaijan western regions and in eastern Azerbaijan, Horasan, Kashan, Semnan, Gilan, Merkezi, and Yazd provinces. In Iran, Isfahan, and western Azerbaijan regions hold 90% of the rose farms and 92% of the production. While Iran produce rose flower as almost as high as Turkey and Bulgaria, its global trade is limited; rose water is more common in the country and mainly used for domestic purpose. In Morocco, French companies like *L'Oreal* and *Beyond Beauty* cultivate rose flowers which are processed in the factories and finally exported to France. In India, China, and Saudi Arabia, most of the rose oils are produced for domestic use (Yaniv & Dudai, 2014).

## 7.4 COMPOSITION AND USES

Numerous species in the genus *Rosa* have medicinal properties, and a wide spectrum of identified phyto-chemicals; these include sugars, organic acids, terpenoids, flavonoids, cyanogenic glycosides, phloretin, tannins, vitamin A, B, C, E, K, and minerals, and particularly potassium and iron. The phyto-chemicals holds diverse medicinal properties: astringent, antiseptic, diuretic, anti-hemorrhoidal, anti-inflammatory, relaxation, and anti-anxiety, antidepressant, anti-phlogistic, antispasmodic, anti-viral, aphrodisiac, and tonic properties (Grand View Research Inc., 2019; Alamgir, 2017). Edible use of rose hips has also been featured for its antioxidant activity and anti-inflammatory properties (Uggla, Gao, & Werlemark, 2003). The dominant species globally used for rose oil and water production are: *Rosa damascena* Herrm., *Rosa gallica* L., *Rosa centifolia* L., *Rosa alba* L., *Rosa moschata* Mill., and *Rosa bourboniana* L. (Edward rose) (Yaniv & Dudai, 2014). *Rose damascena* is known as the preferred species for essential oil distillation among other rose species, particularly for its yield and oil quality (Yaniv & Dudai, 2014; Pati, Sharma, Sood, & Ahuja, 2005; Baydar, 2006).

### 7.4.1 WIDESPREAD USES OF ROSE

Humans have been using rose for multiple purposes; due to the rich chemical composition of roses and other attractive features and scent, they are used for decoration; medicinal purpose, essential oil, rose flower water, and herbal

tea, food, and cooking; and for perfume and cosmetic use. For instance, rose oil relaxes the mind and depression, stress, and tension (Haghighi, Tehranifar, Nikbakht, & Kafi, 2006; Boskabady, Shafei, Saberi, & Amini, 2011). In herbal medicine, it relieves digestive system problems, reduces thirst, relieves colds and supports the respiratory system (healing old cough), supports women's health, skin health and wound healing (Haghighi, Tehranifar, Nikbakht, & Kafi, 2006). Rose oil vapor thermal therapy relieves some allergies, headaches, migraine (Zargari, 1982). Rose oil (*Rosa damascena*) has been reported to exert anti-HIV properties which binds various proteins and inhibit HIV-infections (Mahmood et al., 1996).

The consumption of roses is also common and traditional in many countries; it is drunk as a tea for medicinal purposes, and consumed as jam and fruit juice (Uggla, Gao, & Werlemark, 2003). For instance, in Turkey, several traditional products – rose hip jam, rose hip pestil (a Turkish traditional sweet), rose hip syrup, and rose hip tea made with both fruit and roots – are widely available (Ercisli, 2007). Rose hips with their high content of vitamin C (300–4,000 mg/100 g) are well known (Uggla, Gao, & Werlemark, 2003; Ercisli, 2007). Moreover, rose hips contains other rich vitamins and minerals, and various phyto-chemicals (Ercisli, 2007).

#### **7.4.2 TRADITIONAL THERAPEUTIC AND NUTRACEUTICAL VALUE**

The nutritional and therapeutic effects of rose are relatively safe and used traditionally worldwide. In *Traditional Chinese Medicine* (TCM), roses are warming and bitter, supporting the stomach, liver, and spleen channels, balancing blood coagulation and moving the Qi, to break stagnation, relieve breast tenderness, premenstrual syndrome (PMS), balance emotions, belching, and poor appetite (He et al., 2018; <https://yinyanghouse.com/>). In *Ayurvedic medicine*, rose is considered to be sweet, bitter, pungent, astringent, and cooling. It balances the three doshas (namely, kapha, pitta, and vata); however, it increases kapha if taken excessively. Similarly to TCM, Ayurvedic practitioners and western herbalism also use rose for female reproductive system, the circulatory system and for the nervous system (Frawley & Lad, 2001).

### **7.5 ORIGIN AND DISTRIBUTION**

Rose primarily originates from Iran and the Middle East region (Boskabady, Shafei, Saberi, & Amini, 2011; Bricchet, 2003). Fossil records suggest that rose already existed in the last 35 million years (Yaniv & Dudai, 2014).

Due to popular human use and its resilience to various climate conditions, rose species spread across the northern hemisphere (Brichet, 2003). Globally, a large number of native rose species are found in China: 48 endemic species; 42 endemic species in the rest of Asia; 32 native species in Europe; six endemic species in the Middle East; seven in North Africa; and 26 endemic species in North America (Harkness, 2003). Nowadays, it is widely distributed across the Middle East, North Africa, Mediterranean, Europe, Asia, and North America. In Europe, it spreads down to the Arctic Circle; in North America, it is mainly located in Canada, the USA and Mexico; in the Mediterranean basin, its location occurs in the coastline; in Asia, it spreads widely west-to-east as far as India and Japan excluding desert and tropical areas (Brichet, 2003).

## 7.6 BOTANY AND TAXONOMY

According to the Plant List (2013), 366 species are recognized under the genus *Rosa* (The Plant List Version 1.1, 2013); however, due to its widespread, the genus *Rosa* species differs largely. Scientists estimate of the number of rose species varies from 100 species (Ercisli, 2007; Guner, Ozhatay, Ekim, Husnu, & Base, 2001; Rehder, 1940), 150 species (Takeuchi, Nomura, Uchiyama, & Yoneda, 2000), and up to 200–250 species (Yaniv & Dudai, 2014; Mahboubi, 2016). Furthermore, there are more than 18,000–30,000 cultivars (Cai, Xing, Sun, Zhan, & Corke, 2005; Shakywar, Tomar, & Patidar, 2016; Boskabady, Shafei, Saber, & Amini, 2011) in the world which vary in form, shape, size, color, fragrance, and flowering habit in cultivation.

Rose grows as a perennial bush, spreading for ground cover and vertical for ornament. The stems are typically covered with thorns, and compound leaf composed of five to seven leaflets. Inflorescences are determinant, varying in panicle, corymb, or solitary. Typical flowers have five sepals and at least one five-petal layer, and numerous stamens (Mierow & Shetha, 1987). Color of the flower ranges from pink, red, white, yellow, orange, and combinations of these; however, most herbalists use red and pink flowers. The fruit of the flowers are termed ‘hip’ and contain high amount of vitamin A, B, and C (Shakywar, Tomar, & Patidar, 2016). Key Characteristics for *rosa* identification, are the prickly stems, alternate leaf arrangement, odd pinnate compound leaves, and the presence of hips (Harkness, 2003).

John Lindley (1799–1865), a pioneer of rose classification mostly classified the members of the genus *Rosa* (Harkness, 2003). At a later date, Alfred Rehder (1949) from the Arnold Arboretum in Boston (Rehder, 1940) divided



the botanical order of rose species. He grouped the species into four sub-families (subgenera), three of which were monotypic (Takeuchi, Nomura, Uchiyama, & Yoneda, 2000). The four subgenera are *Hulthemose* (Harkness, 2003) or *Hulthemia* (Dumort) (Yaniv & Dudai, 2014) (also known as *Simplicifolia*) which means single leaves, *Hesperhodos* meaning ‘western roses’ in Greek, *Platyrhodon* referring to ‘flaky roses’ due to their bark peels, *Eurosa* (Harkness, 2003) derived from the Latin *ura* meaning east also found in wide areas of the northern hemisphere from Japan to North America (Harkness, 2003). All of the subgenus are monotypic, and composed of to one or two species except *Eurosa*; however Rehder (Takeuchi, Nomura, Uchiyama, & Yoneda, 2000) further divided into 10 sections. Detailed species names of each section are shown in Table 7.4 (Yaniv & Dudai, 2014; Matsumoto, Kouchi, Yabuki, & Kusunoki, 1998). Scientists have conducted molecular classification of the genus *Rosa*, which conformed to the traditional botanical classifications, and limited number of species were reported to belong to another large clade (Matsumoto, Kouchi, Yabuki, & Kusunoki, 1998). Popular rose species for a range of uses are shown in Table 7.5.

**TABLE 7.4** Commonly Used Species of the Genus *Rosa* and Subgenera

Subgenus	Section	Species
<i>Eurosa</i>	Pimpinellifoliae	<i>R. hugonis</i> Hemsl., <i>R. spinosissima</i> L. var. <i>lutea</i> Bean, <i>R. fetida</i> Herrm. var. <i>bicolor</i> (Jacq.) Willmott.
	Gallicanae	<i>R. gallica</i> L., <i>R. centifolia</i> L., <i>R. damascena</i> Herrm.
	Caninae	<i>R. canina</i> L., <i>R. pomifera</i> Herm., <i>R. rubrifolia</i> Vill., <i>R. eglanteria</i> L., <i>R. glauca</i> Pourr.
	Carolinae	<i>R. Carolina</i> L., <i>R. foliorosa</i> Nutt., <i>R. nitida</i> Willd., <i>R. virginiana</i> Mill.
	Cinnamomeae ( <i>Rosa</i> )	<i>R. rugosa</i> Thumb., <i>R. willmottiae</i> Hemsl.
	Synstylae	<i>R. moschata</i> Herm., <i>R. multiflora</i> Thumb.
	Indicae	<i>R. chinensis</i> Jacq., <i>R. gigantea</i> Collett.
	Banksianae	<i>R. banksiae</i> Ait.
	Laevigatae	<i>R. laevigata</i> Michx.
	Bracteae	<i>R. bracteata</i> Wendl.
<i>Platyrhodon</i>	–	<i>R. roxburghii</i> Tratt.
<i>Hulthemia</i>	–	<i>R. persica</i> Michx.
<i>Hesperhodos</i>	–	<i>R. stellata</i> Woot. var. <i>mirifica</i> Cockerell

Source: Takeuchi, Nomura, Uchiyama, & Yoneda (2000); Matsumoto, Kouchi, Yabuki, & Kusunoki (1998)

**TABLE 7.5** Commonly Used Rose Species for Each Use

Uses	Commonly Used Species
Essential oil (Özel, Göğüş, & Lewis, 2006)	<i>Rosa damascena</i> Herrm, <i>Rosa gallica</i> L., <i>Rosa centifolia</i> L., and <i>Rosa moshata</i> Herrm. (The main rose oil producer Turkey uses <i>Rosa damascena</i> Herrm.)
Flower water (Haghighi, Tehranifar, Nikbakht, & Kafi, 2006)	<i>Rosa damascena</i> Herrm.
Food and tea (Rosehip) (Uggla, Gao, & Werlemark, 2003)	<i>Rosa moschata</i> Herm., <i>Rosa rubiginosa</i> L., and <i>Rosa canina</i> L.

## 7.7 VARIETIES AND CULTIVARS

Although wild roses extend throughout the northern hemisphere, the development of the species into cultivated forms was mainly confined to two regions divided along East and West lines. In the rose evolutionary history, East takes garden practices from China, Korea, Japan, and nearby regions, while the West embraces practices from the Himalayas to the Atlantic, including the shoreline of North Africa (Harkness, 2003). With gardening practices for instance, the popularity of *Rosa* species promulgated the development of numerous cultivations from diverse origins (Bhattacharjee & Banerji, 2010; Brichet, 2003). Given the wide spread of rose cultivation throughout the world, it is hardly possible to define the number of cultivars (European Medicines Agency, 2013); however, scientists estimate there are more than 18,000–30,000 rose cultivars worldwide (Cai, Xing, Sun, Zhan, & Corke, 2005; Yaniv & Dudai, 2014; Shakywar, Tomar, & Patidar, 2016; Boskabady, Shafei, Saberi, & Amini, 2011; Nazari, Khosh-Khui, & Salehi, 2008). Thousands of cultivars were extensively hybridized among Chinese, European, and Middle-Eastern roses mainly and limited wild species, and shaped the genetic basis of “modern rose cultivars,” namely *Rosa hybrida* L. (Nazari, Khosh-Khui, & Salehi, 2008; Qi et al., 2018). *Rosa hybrida* L. refers up to 30,000 to 35,000 rose cultivars (Qi et al., 2018). *Rosa hybrida* includes various valuable species cultivated as ornamental, food, and medicinal crop worldwide. Given the popularity of rose cultivation, many rose amateur growers cultivate roses from diverse origin of the world (Bhattacharjee & Banerji, 2010; Brichet, 2003).

The most renowned European rose collections are the *L’HayÈ* – les-Roses in France, *Cavriglia* in Italy, and *Sangerhausen* in Germany (Brichet, 2003). North America has also numerous collections, while the Southern hemisphere (e.g., Australia) has been relatively slow in developing rose collections. In the Southern hemisphere, native wild roses have been removed

by humans in recent years and have not been found so far (Harkness, 2003; Kogan, Schaefer, Erdman, & Schoenfeld-Tacher, 2016). However, Southern Australia, South Africa, New Zealand and Uruguay have rich collections despite dissimilar climate conditions. In addition, Chile, Zimbabwe, and East African countries grow large amount of commercial cut-flower varieties to provide the rose flowers of northern markets during the winter season (Brichet, 2003). In the Middle-Eastern region, the *Flora of Turkey and the East Aegean Islands* identifies 24 *rosa* cultivars which exist in the region, including eight as native (Yaniv & Dudai, 2014; Guner, Ozhatay, Ekim, Husnu, & Base, 2001).

Rose cultivars which are used for essential oil distillation and flower water do not equal the garden cultivars, as the industry still use the traditional species, such as *Rosa damascena* Herrm., *Rosa gallica* L., for these purposes.

## **7.8 SOIL AND CLIMATE**

### **7.8.1 SOIL REQUIREMENTS**

Roses grow in all types of garden soils. Nevertheless, they thrive better in sticky, well drained, fresh, loamy, and salt-free soil rich in organic matter with an ideal pH of six to eight. Because of their highly sensitive root systems, extreme soil conditions are not suitable for growing rose, i.e., clayish, sandy or extremely calcareous (Yaniv & Dudai, 2014). However, roses grow well in slight sandy soil, deep, and soft soils with rich organic matters, that benefit from slight amount of iron salts and moisture. In ideal soil conditions, a rose plantation can produce flowers for 20 to 25 years, especially with regular pruning every 7 to 12 years.

### **7.8.2 CLIMATE REQUIREMENTS**

The wide spread distribution of roses indicates their adaptability to various climates except in areas with harsh unsuitable climatic conditions. Roses can be found in the chilly conditions of the Arctic tundra, in the dry arid mountains of New Mexico, in wetlands of Indian marshlands and in the high-altitude regions of Yemen highlands, and in the humid Burmese forests and windy Hebridean islands. Most rose species prefer a temperate climate, adequate water supply, frequent morning dew, especially during drought and

spring frost season, flowering period, and are often found in upland areas where other plants do not block the sunlight (Yaniv & Dudai, 2014; Harkness, 2003). However, this does not mean that the distribution is limited; rather, the tolerance of rose species to various climate conditions enable the spread from sea level to altitudes as high as 3,000 m (Ercisli, 2007).

While roses are resilient to various climatic conditions, the temperature and moisture largely determines the flowering period. Climate conditions during the flowering period, such as high temperature and droughts, result in the decreased concentration of rose oils in the petals. To maximize the oil yields, a temperature between 10°C and 15°C during the flowering period is preferred. Night temperature under 5°C and day temperature above 20°C decrease the oil yield and 60–70% of humidity is ideal, as it promotes the accumulation of oil in flowers during the spring time. However, heavy rain and storms damage the buds and flowers which affect negatively the yield (Yaniv & Dudai, 2014).

## 7.9 PROPAGATION AND ROOTSTOCK

The common propagation for rose is performed by using asexual methods, such as cuttings, layering, sucker, budding, grafting, and cutting-grafting (stenting) (Jabbarzadeh & Khosh-Khui, 2005; Pati, Sharma, Sood, & Ahuja, 2005; Nazari, Khosh-Khui, & Salehi, 2008). Seeds are occasionally used for new cultivar propagation and rootstock production (Pati, Sharma, Sood, & Ahuja, 2005).

Traditionally, cutting is the most common propagation technique. Rose pruning are usually conducted during 7 to 12 years old rose plants for rejuvenation. For instance, to cultivate 1,000 m (Cai, Xing, Sun, Zhan, & Corke, 2005) rose plantations, 400 kg (1,200–1,400 cuttings) rose cuttings are required. Ideally, these should be cut at four to five cm from the soil level and pruned to 100–150 cm long. The propagation rate of this technique is 1:8–1:10. Processing the cutting is important to avoid the risk of transferring diseases. Layering is also a common technique following cutting and involves burying one branch of the stand in the soil to initiate rooting. However, the propagation rate of this layering method is lower than if cutting at 1:10–1:15. Grafting is also used to generate rose rootstocks, particularly for *Rosa canina* L. The propagation rate for grafting is high, which also enables the maintenance of high-grade roses. Additionally, green cuttings and rooted wood are also practiced for propagation but to a lesser extent (Yaniv & Dudai, 2014).

Previous research conducted on rose propagation shows that stenting offers the quickest propagation (Nazari, Khosh-Khui, & Salehi, 2008; Van De, & Breukelaar, 1982; Ohkawa, 1980). The stenting method is a quick propagation technique that involves cutting and grafting in just one step: it involves simultaneously grafting a cut scion onto a non-rooted rootstock. The method was developed in the Netherlands and further improved by grafting a scion onto an internode without buds onto the rootstock (Van De, & Breukelaar, 1982). This method decreased the wild suckering issue, and improved the simultaneous occurrence of the graft union and the adventitious roots formation which can be performed all year around (Van De, & Breukelaar, 1982). Recent research reported that grafting scion onto the rootstock rather than onto the plant's own roots improved both the quality and quantity of the production (Nazari, Khosh-Khui, & Salehi, 2008). Production parameters include the fresh weight and diameters of the flowering stem, the flowers' weight (both fresh and dry), diameter, and length of the flower, number of petals, and the chlorophyll content of the leaf. The quality index was also reported higher in grafted roses compared to the cutting technique (Nazari, Khosh-Khui, & Salehi, 2008). Other research reported that regardless of rootstock type, the three *Rosa hybrida* cultivars, namely First Red, Versilia, and Virginia rootstock combinations, are reported superior to the own-rooted roses for both re-blooming time and yield (Safi, 2005).

In addition, the propagation method differs from one country to another. In the Netherlands, cutting, and cutting-grafting (stenting) are the most common technique. In Iran however, rose growers prefer propagating plants with stenting rather than cutting (Nazari, Khosh-Khui, & Salehi, 2008). For rose micro-propagation, agar-gelled medium is the most common technique (Pati, Sharma, Sood, & Ahuja, 2005). Research also reported that the use of liquid media demonstrated successful multiplication for *Rosa damascena* and *Rosa bourboniana* which introduces *in vitro* propagation and improves the tissue culture protocols. Furthermore, the value of osmotic potential was reported to improve rooting development and growth compared to agar-gelled cultures (Pati, Sharma, Sood, & Ahuja, 2005).

## **7.10 PLANTING, IRRIGATION, AND NUTRIENT MANAGEMENT**

### **7.10.1 PLANTING SYSTEM**

In the Middle-East region, common rose species such as *Rosa damascena* is generally planted in autumn. Around 15 to 20 days prior to planning ditches of width and depth 40 cm and 50 cm respectively, deep are dug out parallel

to each other. The ditches are made perpendicular to the untidy fields' slope, and facing North-South side on a flat surface. Occasionally, top soil of 10 to 15 cm is added to fill the ditches. Rose cuttings are then placed in the ditches and covered with 10 cm of soil combined with organic manures. Following the germination in the spring time, weeds are removed and extra top soil is added until the filled ditches level with the ground (Yaniv & Dudai, 2014).

### **7.10.2 IRRIGATION AND NUTRIENT MANAGEMENT**

In Turkey, Ucar et al. (2016) studied the irrigated water and nitrogen impacts on *Rosa damascena*. The results showed that increasing the amount of irrigation water and doses of nitrogen significantly increases the flower yield. However, the results also showed a strong correlation between water irrigation and flower yield compared to the nitrogen application in semi-arid climate characteristics. In Turkey, the most adequate amount of irrigation water and nitrogen doses for growing the highest flower yield was obtained from the 113.3 mm, 160 kg/ha and 113.3 mm, 240 kg/ha treatment, respectively (Ucar, Kazaz, Eraslan, & Baydar, 2016).

### **7.11 TRAINING AND PRUNING**

Conventional training methods for rose plants are pruning and bending in June and July (Nimura, Yamaguchi, & Itoh, 1997). However, autumn pruning is also commonly practiced for winter flowers to improve the quantity and quality of flowers (Hassanein, 2010; Zieslin, Hurwitz, & Halevy, 1975). Research has further shown that pruning promotes a higher light photosynthetic impact, and stimulates Nitrate reductase activity and reduce  $\text{NH}_4^+$  concentration, a phenomenon that relates to a high turnover to amino acids (Calatayud, Roca, Gorbe, & Martínez, 2008). Further research (Zieslin, Hurwitz, & Halevy, 1975) has also shown that pruning in spring decreased the starch content, and delays the time of maximum accumulation. Pruning is therefore useful to program the production cycles of rose flowers, and also to obtain a high photosynthetic activity by removing the old parts. In Egypt, pruning at the beginning of the end of September or in the following three weeks produced the fastest and longest winter flowering (Hassanein, 2010). Pruning of the plants in the autumn is believed to increase two to three more flowers per plant and to maintain the good root condition (Larson, 1992). Training roses with bending is also a common practice. Tjosvold (2001)

tested the effectiveness of the bending method on five cultivars; he concluded that bending alone increased the production and the quality for many of the rose cultivars (Tjosvold, 2001).

## 7.12 PEST AND DISEASE MANAGEMENT

Various biotic, meso-biotic, and abiotic factors, such as pathogenic fungi and bacteria, viruses, nematodes, and pests often attack roses, which are vulnerable to major diseases and pests (Chalova, Manolov, & Manolova, 2017; Kovatcheva, Zheljazkov, & Astatkie, 2011). In conventional systems of production, chemical treatments are used to control diseases and pests; however, rose pathogens negatively impact the flower yield and the quality which are crucial for rose producers who may otherwise encounter financial loss. However, this differs for rose essential oil producers who prefer organic farming, for instance in Bulgaria. The general cost for controlling diseases and pest either with organic or conventional means costs 32,000 USD/ha per year (Debener & Byrne, 2014). Beside minor pathogens that attack the roots systems of rose plants, the main expenditure is linked to the treatment of pathogens that invade the flowers and leaves of the plants; however, if left untreated, the income of growers is jeopardized. As the appearance of the flower is key to the economic viability, higher levels of disease/pest control are required.

### 7.12.1 MAJOR FUNGAL AND BACTERIAL DISEASES

Fungal diseases typically seen on roses include black spots, powdery mildew, botrytis, and downy mildew (Debener & Byrne, 2014; Chalova, Manolov, & Manolova, 2017). Black spots (*Diplocarpon rosae* Wolf) are the most common rose fungi pathogens characterized by leaf spotting and defoliation. Rust (*Phragmidium* spp.), cercospora (*Cercospora puderii* B.H. Davis and *Cercospora rosicola* Pass.), and anthracnose (*Sphaceloma rosarum* (Pass.) Jenkins) also affect the leaves in a similar way (Debener & Byrne, 2014). Black spots spread the disease widely and reach an epidemic level during the rainy and warm spring season (Chalova, Manolov, & Manolova, 2017). The initial symptoms of black spots eventually lead to the loss of leaves during the summer season. In addition, powdery mildew (*Podosphaera pannosa* (Wallr.) de Bary) and downy mildew (*Peronospora sparsa* Berk.) may spread more widely on the roses in the greenhouse than when in the field;

rose powdery mildew is the most serious disease for the rose cut-flower producers (Kakade, Gurav, Singh, & Nimbalkar, 2006; Nicetic, Watson, & Beattie, 2002). Research shows that controlling powdery mildew under commercial greenhouse conditions requires using more than 20 fungicide sprays per year, increasing the high economic cost for the producers in order to prevent the occurrence (Nicetic, Watson, & Beattie, 2002).

Furthermore, cool, and humid conditions facilitate the spread of the pathogen. Mild temperatures (15°C) and high humidity (90–99%) at night time and high temperatures (26–27°C) with low humidity (35–70%) favor spore maturation and release (Chalova, Manolov, & Manolova, 2017; Larson, 1992). The affected bud formation which in turn affects the low development of roses impacts the quality of the flowers which requires an additional input of approx 40% of pesticides to address this particular pathogen (Debener & Byrne, 2014).

Fungus botrytis (*Botrytis cinerea* Pers. Ex Nocca and Balb.) is a major rose post harvest pathogen, commonly affecting stored plants and flowers (Larson, 1992). Spore germination requires continuous 12 hours of independent water on the plant surfaces (Larson, 1992). For the production of cut roses, the costs of controlling this particular disease are similar to those spent on controlling powdery mildew; however, the resistance of the rose plant to botrytis is still unknown (Debener & Byrne, 2014). Symptoms display small and light-colored spots surrounded by red colored holes on the petals, which may develop into a major blotches (Chalova, Manolov, & Manolova, 2017).

Other common rose pathogens are crown galls (*Agrobacterium tumefaciens* Conn.), a bacterial disease which sometimes promotes the production of aerial galls on the stem where flowers have been removed. According to Smith and Townsend (Boelema, 1969), *Agrobacterium tumefaciens* Conn. is responsible for this occurrence, which was reported as early as 1892 (Boelema, 1969). Colonies generally vary, from white, convex, circular, to glistening and translucent features. The bacteria's optimum temperature of 27°C spreads through the infected plants and the contaminated soils. It survives many years in the soil and can be transported with water and the infected plant parts (Shakywar, Tomar, & Patidar, 2016). Effective control of Crown galls often involves heating the soil at 60°C for 30 minutes, washing, and disinfecting the tools, cutting out the galls and dipping the roots and lower stem for two hours in 500 ppm of Streptomycin before planting.

Overall, the mentioned bacterial and fungal diseases are generally managed by applying preventive fungicidal and bactericidal treatments, coupled with environmental management (i.e., greenhouse production),



sanitation (potential sources of inoculum reduction), and exclusion which involves to limit using the clean stocks and resistant cultivars (Debener & Byrne, 2014). In addition, new roses with improved resistance to diseases such as black spots are being developed; however, this practice is still limited.

### **7.12.2 VIRAL DISEASES**

Various viruses for roses have been reported and include – prunus necrotic ring spot virus (PNRS), arabis mosaic virus (ArMV), apple mosaic virus (ApMV), tobacco streak virus (TSM), tobacco ring spot virus (TRSV), strawberry latent ring spot (SLRS), tomato ring spot virus (TomRSV), rose yellow vein virus, rose cryptic virus-1 (RCV-1), and rose rosette virus (Debener & Byrne, 2014). The frequency and the symptoms vary with each virus and the area of production. The rate of virus infection varies largely from 1% of the cut rose plants in Europe, up to 65% of the tested roses in New Zealand (Debener & Byrne, 2014). Most viruses are not lethal; however, they negatively influence the production of flowers and their quality. Yet, some viruses like the rose rosette virus can kill the plants. The symptoms vary by the cultivar, and commonly include shoot proliferation, unusual thorniness, reddening shoots, and distorted flowers leading to stunting, defoliation, and occasionally eventually plant deaths.

The management of rose viral diseases is crucial, the main approach is to avoid the virus from spreading; certification programs that guarantee that all materials for planting are virus indexed. Recent research conducted at the Foundation Plant Services at the University of California provides thermotherapy which has the capability of eliminating the viruses altogether (Debener & Byrne, 2014).

### **7.12.3 ORGANIC FARMING**

While conventional farming system is more common, some countries have banned the use of chemical treatments in rose organic farming. Due to the lack of resistance of many rose species, rose organic farming is still a challenge. In Bulgaria, rose disease and pest control are not sufficiently researched to produce organic commercial goods, but rather use the products available (Chalova, Manolov, & Manolova, 2017). Trifolio S-forte, Botrysec, and products based from copper and sulfur are examples of commercial products which organic rose oil growers currently used in Bulgaria.

In addition, green manure application including animal manure and compost is a typical organic practice that increases soil fertility and disease control. Mixtures of cereals and legumes (pea with barley, vetch with rye/wheat) are also sown in the autumn between rows of the rose plants and plowed in the spring; this adds natural nitrogen and other nutrients (Chalova, Manolov, & Manolova, 2017). Moreover, intercropping is also a successful organic farming approach as it stimulates biodiversity and promotes the health of the agro-ecosystem. Some farmers plant *Rosa damascena* with potato and maize, cowpea, and maize, and geranium and maize, and which were reported to have increased the economic profit (Yaseen, Kothari, Singh, Singh, & Sattar, 2001).

## **7.13 HARVESTING AND YIELD**

### **7.13.1 HARVESTING**

The general common practice to harvest roses is to cut above the five-leaflet leaf, second from the base (Zieslin, Hurwitz, & Halevy, 1975). In a dry morning, roses is cut with shears or a sharp knife; the flowers are at the pick of fragrance after blooming. The best harvest stages vary largely with each cultivar; however, generally, it is cut at a stage that allow the flowers to develop further for the final consumer (Larson, 1992). The rose is usually cut when still tight in the bud, so that it readily opens in plain water (Larson, 1992). The cutting position on the shoot varies by the height of the plant and the needs of the markets. Generally, it is cut on the first five-leaflets leaf just above the flowering origin of the stem. Rose hips can be harvested in autumn when their color turns to red or orange.

### **7.13.2 YIELD**

In Turkey and Bulgaria, most of the harvested rose are used for rose essential oil largely destined for export. Turkey cultivated roses on 1,900 ha with a flower yield of 3,430 kg/ha in 2012 (Yaniv & Dudai, 2014) . However, the yield of rose flowers varied largely in 2010 and 2011, and ranged from 2,339–3,046 kg/ha and 2,215–6,373 kg/ha respectively (Ucar, Kazaz, Eraslan, & Baydar, 2016). Gunes (2005) reported that the production of 10 g of rose essential oil, required approx 100 kg of fresh rose flowers. On average, one kg of rose oil is extracted from three to five tons of rose flowers (Gunes,

2005). In Turkey, the yield of rose essential oil was approx 1.10–1.66 kg/ha in 2010, 1.13–3.42 kg/ha in 2011, and 0.72–2.89 kg/ha in 2012 (Ucar, Kazaz, Eraslan, & Baydar, 2016). Annual rose products, such as rose essential oil, rose concrete, rose absolute production in Turkey represents 1.2–1.8 tons for rose essential oil, 6–9 tons for rose concrete, and 2–2.5 tons for rose absolute production, with high exporting qualities (Baydar & Baydar, 2013).

In Bulgaria, the total area cultivated for rose oil in 2013 was 3,800 ha, of which 1,588 ha (42%) were grown organically (Chalova, Manolov, & Manolova, 2017). Approximately 90% of the rose flowers were processed for rose oil, and 5 to 6% for rose concrete and 3 to 4% of rose water, and remaining were used to make edible products like jams and liqueurs (Kovacheva, Rusanov, & Atanassov, 2010).

#### **7.14 POST-HARVEST HANDLING AND STORAGE**

Post harvesting techniques are generally required in the cut flower industry. To avoid the wilting of flowers and to prevent a high intake of water, cut flowers are usually hydrated in a deep, acidified water to solve these issues. A traditional common acidifier is citric acid and is administered around 350 ppm (Larson, 1992). Following the hydration, cut rose flowers are preserved using clean containers and clean water to which chlorine compounds are added or just simply replacing the water frequently. Sugar containing preservatives are not ideal at this stage, while preservatives are recommended when the storage temperatures exceed 3–5°C.

The cut flowers are graded to different lengths ranging from 30–75 cm, depending on the market requirements (Larson, 1992). Grading is usually done with machinery, and the roses are packed in bundles of 20–25 flowers. These are loosely wrapped so that they can be cut again when delivered. The bunches of cut flowers are then deposited in boxes that usually accommodate 400 to 600 flowers ready to be dispatched to market without delay. Some shippers use sealed ice or thermal gels. The lifespan of the flowers significantly improve when they are stored in dry storage for several days, by which time they may have fully opened. Dried stored roses are more difficult to re-hydrate; however, this can be restored by placing the flowers under water and removing the old stem base. When the stems are already cut, they should be immersed with warm water of 25–30 cm (40°C) containing citric acid (Larson, 1992).

## 7.15 PROCESSING OF MEDICINAL AND AROMATIC PLANTS

Most rose flowers (97%) are processed for medicinal and aromatic purposes (Gunes, 2005). Historical account has shown that humans have developed various techniques to extract rose essential oils for aromatic purpose; these include: hydro distillation (water distillation), steam distillation, solvent extraction, super critical fluid extraction, high-pressure CO<sub>2</sub> extraction, cold, and hot pressing (Özel, Göğüş, & Lewis, 2006; Younis, Riaz, Khan, Khan, & Pervez, 2008). Traditionally, rose oil production was made from rose flowers water distillation, and was then followed by cohobation, a practice of returning the distillate water to the still after separation of the oil so that it can be re-boiled (repeated distillation process), thereby minimizing the loss of oxygenated components like phenols. The final product of the process is called Rose Otto or Attar (Kovacheva, Rusanov, & Atanassov, 2010). Otto or Attar is one of the most renowned scents among the perfume industry (Younis, Riaz, Khan, Khan, & Pervez, 2008). Attar processing needs to unfold in remote places as the flowers are treated quickly after collection.

In the largest producing country Turkey, two method of rose oil distillation are prevalent: traditional distillations type using long-fired crude copper within the village called *Imbeks*, and the modern distillation type using hydro-steam called *Kanas*. Both extraction methods provide similar quality of rose oil; however the traditional method is slowly disappearing (Gunes, 2005). Common species to extract rose essential oils are *Rosa damascena* Herrm., *Rosa gallica* L. and *Rosa centifolia* L., while producers in Turkey and Bulgaria usually grows *Rosa damascena* Herrm.

Nowadays, solvent extraction and steam distillation (Younis, Riaz, Khan, Khan, & Pervez, 2008) are commonly used for the extraction of rose oils. Steam distillation uses the fresh or occasionally dried rose flowers to set into the distillation chamber, and steam generated with pressure from an another chamber is circulated through the flowers. The heated steam opens up the intercellular spaces containing the essential oils and the compounds will be captured in the steam. The heat is then cooled down and the essential oil and flower water extracted. Alongside distillation, rose scent can be extracted by using solvent extraction producing a wax-like mass known as Concrete which is re-extracted with alcohol, the final product known as Rose Absolute (Kovacheva, Rusanov, & Atanassov, 2010).

Younis et al. (2008) compared the different methods of extraction and examined the differences in the oil contents using four common rose species (*Rosa damascena*, *Rosa centifolia*, *Rosa borboniana* and *Rosa 'Gruss an*

*Teplitz*'). They concluded that the yield of solvent extraction produced more absolute oil (0.11%) compared to the steam distillation (0.075%) (Younis, Riaz, Khan, Khan, & Pervez, 2008). Among the extraction methods, hexane had the highest dissolve ability of the odoriferous principles, and able to distil without treating in higher temperature (Younis, Riaz, Khan, Khan, & Pervez, 2008). However, hexane has relatively high solvent loss in the process.

## 7.16 CHARACTERIZATION OF PHYTOCONSTITUENTS

Various secondary metabolites are contained in the genus *Rosa* plants, such as phenolic acids (e.g., acid, gallic acid, and chlorogenic), fatty acids, flavonoids (e.g., quercetin, flavonols, anthocyanins), fragrant components (volatile oils, e.g., sesquiterpenes, monoterpenes), hydrolyzable, and tannins condensed (e.g., procyanidins, rugosins), vitamin C, and bitter principles (Cai, Xing, Sun, Zhan, & Corke, 2005; Boskabady, Shafei, Saberi, & Amini, 2011).

Characteristic components of rose oil, one of the major distillation product, are acyclic monoterpene primary alcohol, including geraniol (75%), citronellol (20%), linalool, nerol (20%) and up to 10% of long-chain hydrocarbons like nonadecane or heneicosane (Gunes, 2005; Özel, Göğüş, & Lewis, 2006). These components contribute mainly to the rich fragrance of roses. The rose oil's dominant trace mineral is  $\beta$ -damascenone regardless of its lower concentration (0.01%). The pleasant fragrance of rose water is attributed to the 2-phenylethanol which accumulates in the water (Gunes, 2005). In addition, small amounts of hydrocarbons are also found in rose, mainly: dodecane, tridecane, tetradecane, 1-nonadecene, nonadecane, heneicosane, docasane, and octacosine (Özel, Göğüş, & Lewis, 2006).

## 7.17 VALUE ADDITIONS OF MEDICINAL AND AROMATIC PLANTS

Various rose flowers and rosehips products are currently commercialized. These products include:

### 7.17.1 ROSE ESSENTIAL OIL

Rose oil production is believed that the crude distillation process originated in the Persia era in the late AD seventh century, which eventually extended

to the Ottoman Empire in the 14<sup>th</sup> century (Boskabady, Shafei, Saberi, & Amini, 2011). Rose essential oil is a yellow pale essential oil, usually more expensive compared to other essential oils, mainly used for medicinal and cosmetic purposes. Morocco also produces rose essential oil; however, Bulgaria, Turkey are the main producers (Mahboubi, 2016). Out of the genus *Rosa* species 100 to 200, only few of them are suitable for essential oil distillation. *Rosadamascena* Herrm. is considered to have a superior quality of the distilled rose essential oil (Kovacheva, Rusanov, & Atanassov, 2010; Mahboubi, 2016), with a weight varying from 0.032 to 0.049% (w/w).

### **7.17.2 ROSE WATER**

Rose water is usually transparent which can be collected from the distillation process of the rose essential oil production. It contains approx. 0.075% of essential oil and 3.81% of ethyl alcohol (Haghighi, Tehranifar, Nikbakht, & Kafi, 2006). Rose water can be used as a toning product and for gentle cleansing for all types of skin. It balances the pH of the skin, stimulates the reparative processes, and calms the acne and sunburns (Haghighi, Tehranifar, Nikbakht, & Kafi, 2006). The calming and relaxing properties of rose water is also traditionally used in various religious ceremonies, such as the washing of wash God House (Kaaba) in Mecca, Saudi Arabia (Mahboubi, 2016). This is done yearly using a special rose water produced in Kashan, Iran (Haghighi, Tehranifar, Nikbakht, & Kafi, 2006). In Iran, rose water is produced from *Rosa damascena* Herrm. and a product commonly used for religious ceremonies for its calming and relaxing properties. It is also used to flavor certain food dishes in Iran.

### **7.17.3 DRIED FLOWERS**

Dried rose flowers are commonly used and exported when fresh plants are scarce or in poor condition, especially during the winter period. Dried rose flowers are used in arrangements, bouquets, for decoration purposes, potpourris, and dried rose petals are edible as and used as herbal tea. Several methods for drying the flowers are used, and the dried flowers can be stored in a damp free atmosphere for several months, or even years if dried correctly. Drying methods include: air drying method, glycol preservation, solvent dehydration and freeze-drying (Kumari & Peiris, 2000). In Iran, rose flowers, buds, and petals are dried and sold as a flavoring agent and in laxative

formulae (Mahboubi, 2016). Iranian people also consume dried rose petals daily mixed with yogurt, a combination known to solve digestive problems. In North Africa, the traditional spice mixture *Ras El Hanout* contains dried flower buds and petals (Nasery, Hassanzadeh, Najaran, & Emami, 2016).

#### **7.17.4 ROSEHIPS**

Rosehips are traditionally used as a vitamin supplement, herbal tea, and as a food product in various European and middle-east countries (Gao, Bjork, Trajkovski, & Ugglä, 2000). Rosehips, berry-like fruit of rose flowers, are formed after the success of flower pollination. The process starts in late spring or early summer, and ripens between later summer and autumn. Rosehips are known for their high content of vitamins, minerals, and fatty acids, in particular its content of vitamin C which is higher than other citrus fruits (300–4,000 mg/100 g (Leahu, Damian, Oroian, Ropciuc, & Rotaru, 2014)). Vitamin C supplements which can be found widely in health food stores throughout European countries (Strålsjö, Alklint, Olsson, & Sjöhol, 2003). The hips are usually collected from *Rosa canina* L. and *Rosa damascena* Herrm. They are usually consumed in the dried form rather than fresh. Many European countries use the dried rosehips to make tea. Recent studies show that rosehips are also rich in other compounds, and have high anti-oxidative and anti-mutagenic properties (Strålsjö, Alklint, Olsson, & Sjöhol, 2003). Traditionally, rosehips are used for the common cold and various infections, and is used as a diuretic agent and for treating inflammatory diseases (Leahu, Damian, Oroian, Ropciuc, & Rotaru, 2014). In Iran, rosehips are used daily, both dried and fresh, processed, and raw (Haghighi, Tehranifar, Nikbakht, & Kafi, 2006). In Turkey, rosehips are also used as a traditional remedy to treat diabetes (Orhan, Aslan, Hoşbaş, & Deliorman, 2009).

#### **7.17.5 ROSE CONCRETE**

Rose concrete is obtained from the solvent extraction, and looks similar to Vaseline cream with a red orange tint (Mahboubi, 2016). Rose concrete is made by shaking the rose flowers in a vat containing an hexane solvent for instance, which then extracts the aromatic compounds of the flowers, and evaporating the solvent in vacuum (Kurkcuoglu & Baser, 2003). In Bulgaria, petroleum ether is used as a solvent for rose concrete (Kurkcuoglu & Baser, 2003). Rose concrete has soft texture as wax, with scent of rose-like and a

pink/red rose color (Aydinli & Tutaş, 2003). Rose concrete is used as a raw material for rose absolute production, produced by dissolving the concrete in hot ethanol. Approximately 375 to 400 kg rose petals are needed to obtain one kg of rose concrete (Baydar, 2006).

### **7.17.6 ROSE ABSOLUTE**

Rose absolute is product processed from the rose concrete; it is first dissolved with ethanol (to reach 96% purity) with approx. 10 times of its own respective weight (Aydinli & Tutaş, 2003). The alcoholic treated compound containing undissolved stearoptens is then chilled at  $-25^{\circ}\text{C}$  and the crystalized stearoptens filtered latterly in vacuum by black band strainer paper. The separated stearoptens are washed with ethanol to collect the liquid filtrates ready for chilling. The obtained alcoholic extracts are then further concentrated with rotary evaporation to extracted the water and alcohol. The remaining concentrate from the distillation is known as the rose absolute in a liquid form (Aydinli & Tutaş, 2003). The rose absolute has an orange-red liquid with rose aroma (Mahboubi, 2016). The benefits of producing the rose absolute is that it extracts the phenylethyl alcohol (60 to 75%), the dominant constituent of rose absolute. Because phenylethyl alcohol is only dissolved in water, its extraction by distillation using steam or heat is difficult as it renders the phenylethyl alcohol content in rose oil generally low (1.2–2.2%) (Kurkcuoğlu & Baser, 2003). The perfume industry uses rose absolute more than the essential oils due to its high constituent of phenylethyl, while rose essential oil is more common for aromatherapeutic usage.

## **7.18 BIO-PROSPECTION OF MEDICINAL AND AROMATIC PLANTS**

Much of the research done on rose species is still in the pre-clinical phase (Boskabady, Shafei, Saberi, & Amini, 2011; Mahboubi, 2016; Schriener et al., 2012); *Rosa damascena* has been largely studied for its traditional therapeutic uses and its high-value essential oils, recognized for its antioxidant and antibacterial effect (Özcan, 2002). Boskabady (2011) reported the rich pharmacological effects of *Rosa damoscena*, i.e., antibacterial, anti-HIV, antitussive, antioxidant, antidiabetic, hypnotic, and a calming effect on the tracheal chains (Boskabady, Shafei, Saberi, & Amini, 2011). Schriener et al. (2012) reported the action of *Rosa damoscena* on fruit flies (*Drosophila melanogaster*) and the decreased mortality without impairing the reproductive



fitness or metabolic rate (Schriner et al., 2012). Nayebi et al. (2017) who conducted a systematic review on *Rosa damascene* of its efficacy and safety, confirmed its positive effects on depression, sexual function, relaxation, and respiration (Nayebi, Khalili, Kamalinejad, & Emtiazy, 2017). Recent studies demonstrated the significant pain relief, anti-inflammatory, and analgesic effects of *Rosa damascene* (Nayebi, Khalili, Kamalinejad, & Emtiazy, 2017; Bani et al., 2014; Christensen, Bartels, Altman, Astrup, & Bliddal, 2008).

Several researchers have conducted clinical tests on the pharmacological effects of *Rosa damascena*. To study its anti-inflammatory and pain-relief constitutes, Hoseinpour et al. (2011) conducted double-blind, randomized, placebo-controlled investigation with 50 patients; they concluded that an aqueous extract of rose containing mouthwash was more effective than the placebo used in the treatment of recurrent aphthous stomatitis (Hoseinpour et al., 2011). For anti-oxidative effect, Kalim et al. (2010) evaluated the effects of 10 herbs (*Rosa damascena*, *Gardenia gummifera*, *Cleome icosandra*, *Abies pindrow*, *Cyperus scariosus*, *Valeriana wallichii*, *Anacyclus pyrethrum*, *Holarrhena antidysenterica*, *Asphodelus tenuifolius* and *Cyperus scariosus*) commonly used in the Unani (traditional medicinal system of the Middle East and South Asia); they concluded that *Rosa damascena* has remarkable potential for decreasing oxidative DNA damage and radical scavenging activity (Kalim, Bhattacharyya, Banerjee, & Chattopadhyay, 2010). For primary dysmenorrhea (menstrual cramps without organic diseases), Bani et al. (2014) conducted a cross-over clinical trial on dysmenorrheal pain intensity of *Rosa damascena* with 92 women aged between 18 and 24 in Iran. They compared the effect of *Rosa damascena* extract capsule (200 mg every 6 hours) with Mefenamic acid (conventional prescription) on primary dysmenorrhea; they concluded that Mefenamic acid and *Rosa damascena* had alike effects on primary dysmenorrhea pain intensity. Therefore, *Rosa damascena*, which does not have the chemical side effects of conventional medicine, can be treated for patients with primary dysmenorrhea (Bani et al., 2014).

Rose hips are also investigated on their pharmacological activities. *Rosa canina* L. contains high sources of polyphenols and vitamin C (Fan, Pacier, & Martirosyan, 2014; Winther, Campbell-Tofte, & Vinther, 2016). Rose hips are high in vitamin C, and contain nearly 200% of the daily value per ounce (28 grams) of fresh wild rose hips. The vitamin C content of rose hips within the *Rosa* genus ranges from 140–1,100 mg/100 ml, while *Rosa canina* contained one of the highest, 880 mg/100 ml (Ercisli, 2007; Gao, Bjork, Trajkovski, & Uggl, 2000; Fan, Pacier, & Martirosyan, 2014). In

addition, studies demonstrated that these particular rose hips exhibited anti-inflammatory, antioxidant, and anti-obesogenic activities (Fan, Pacier, & Martirosyan, 2014). Andersson et al. (2012) conducted clinical test on 31 obese individuals over six weeks to investigate the effect of rose hip drunk daily (a drink made out of 40 g of powdered rose hips) for its metabolic effects. They concluded that the cardiovascular risk was significantly reduced because the systolic blood pressure and plasma cholesterol levels decreased (Andersson et al., 2012). For pain reducing effects, three studies of meta-analysis were conducted with 287 patients and a median trial-duration of three months to observe the activity of *Rosa canina* powder from to reduce osteo-arthritic pain. Although the clinical data were limited, the analysis concluded that rosehip powder had reduced the pain considerably (Christensen, Bartels, Altman, Astrup, & Bliddal, 2008). Other Species like *Rosa centifolia* L. are also used for rose essential oil distillation, and *Rosa gallica* L. is mostly used for its astringent effect on the skin, while *Rosa chinensis* Jacq. flowers are commonly used in traditional Chinese medicine and exhibit radical scavenging and antioxidant activities (Cai, Xing, Sun, Zhan, & Corke, 2005; Alamgir, 2017; Özcan, 2002; Winther, Campbell-Tofte, & Vinther, 2016; Foster, 2012).

## 7.19 AVAILABLE COMMERCIAL AND PHARMACEUTICAL PRODUCTS

The fragrance component of rose oil is used essentially in pharmaceutical purposes, and also substantially as an astringent and fragrance component in creams, perfumes, and soaps (Nayebi, Khalili, Kamalinejad, & Emtiazy, 2017; Younis, Riaz, Khan, Khan, & Pervez, 2008). In addition, the pharmaceutical industry has shown an increasing interest in natural products with bioactive substances. This is mainly due to the potential adverse effects that synthetic antioxidants can cause, and the increasing facilities for screening plants and their antioxidant properties worldwide. Vinokur et al. (2006) conducted research on the antiradical and antioxidant properties of roses. They analyzed the hot water infusion of dried rose petals (rose tea) and demonstrated that the tea had high antioxidant activity, similar with green tea. They further reported that *Rosa damascena* showed the highest antioxidant activity, and concluded that antioxidant-rich caffeine-free beverages could be prepared from dried rose petals (Vinokur, Rodov, Reznick et al., 2006). Other researchers reported that rose essential contains a high

content of citronellol (34.2%), the main compound of rose oil showing high antioxidant activity. Thus, the result showed the high antioxidant capacity (50%), which was also found at the low concentration of 50 g/ml (Wei & Shibamoto, 2007).

Additionally, rose essential oil is recognized for its high antioxidant, analgesic, antimicrobial, anti-inflammatory, anti-depressant, and anti-diabetic properties. However, the lack of clinical studies and relatively high cost of rose oil are limiting its usage for therapeutic applications. Furthermore, rose essential oil and its therapeutic applications are not listed in the Pharmacopeia of most countries. Beside the 1983 British Herbal Pharmacopoeia that acknowledges rosehips for gastritis, polydipsia, and avitaminosis C (Tobyn, Denham, & Whitelegg, 2011), rose oil does not have an entry in the pharmacopeia.

However, two countries have registered rose within their Pharmacopoeia: The French Pharmacopoeia contains two monographs of *Rosa gallica* L. (Rose Rouge, 1989) and *Rosa centifolia* L. (Rose Pâle, 1989; European Medicines Agency, 2014). The US Pharmacopoeia also registered *Rosa gallica* L., *Rosa damascena*, and *Rosa centifolia* L. These official registration initiatives contribute to the expanding pharmaceutical health products industry on rose, enhancing the role of roses as efficient alternatives to synthetic medication. In addition to the pharmaceutical industry, rose is also commonly used in food, in the perfume and cosmetic industries. A wide range of products is available worldwide, as essential oil, rose concrete, rose water (rose hydrosol), rose syrup, rose jam, rose buds dried, and cosmetics made from rose essential oil.

## 7.20 TECHNOLOGY TRANSFER/PATENTS

Rose has the large record of plant patents in the world. The first U.S. Plant Patent Number 1 was issued to a climbing rose “New Dawn” in 1931, for its everblooming characteristics (Bosenberg, 1931). Since then, thousands of rose patents worldwide have been registered on every step, i.e., seedling generation, planting method, processing, extraction, preparation methods for unique products, product composition. Currently, there are over hundreds of patents registered each year, a testimony to the popularity of rose species, embedded in many societies and cultures, traditionally, and also in modern days. Recent examples of rose patents in 2019 relate to cosmetics (extraction method and mixture for face whitening, moisturizing, and anti-aging) (符春丽, 田伟兰, 汪垠明 et al., 2020; 石毛, 林志隆., 2020); tea (decoction

method, particular tea formula for particular effect), food, and beverage (processing for beverage (Furusho & Hiramoto, 2016), rose wine, and health food) and other compositions (hand disinfection sanitizer (Mehmet, 2019), and new *Rosa damascena* cultivar (Majed, 2017)). Growing number of patents have shown that various technologies are increasingly available worldwide for rose products, the high market value of roses.

## KEYWORDS

- **patents**
- **pharmacological properties**
- **post-harvest handling**
- ***Rosa canina***
- ***Rosa damascene***
- **rose**
- **rose essential oil**
- **rose products**
- **technology transfer**

## REFERENCES

- Ahmad, I., Dole, J. M., Khan, M. A., Qasim, M., Ahmad, T., & Khan, A. S., (2010). Present status and future prospects of cut rose production in Punjab, Pakistan. *Hort Technol.*, 20(6), 1010–1015. doi: <https://doi.org/10.21273/HORTSCI.20.6.1010>.
- Alamgir, A. N. M., (2017). In: Rainsford, K. D., (ed.), *Therapeutic Use of Medicinal Plants and Their Extracts* (Vol. 1). Cham, Switzerland: Springer. doi: <https://doi.org/10.1007/978-3-319-63862-1>.
- Andersson, U., Berger, K., Högberg, A., Landin-Olsson, M., & Holm, C., (2012). Effects of rose hip intake on risk markers of type 2 diabetes and cardiovascular disease: A randomized, double-blind, cross-over investigation in obese persons. *Eur. J. Clin. Nutr.*, 66(5), 585–590. doi: 10.1038/ejcn.2011.203.
- APEDA, (2019). *Market Intelligence Report: Cut Flowers – Roses*. New Delhi. [https://agriexchange.apeda.gov.in/Weekly\\_eReport/Flowers\\_Report.pdf](https://agriexchange.apeda.gov.in/Weekly_eReport/Flowers_Report.pdf) (accessed on 02 September 2023).
- Aydinli, M., & Tutaş, M., (2003). Production of rose absolute from rose concrete. *Flavor Fragr. J.*, 18(1), 26–31. doi: 10.1002/ffj.1138.

- Bani, S., Hasanpour, S., Mousavi, Z., Mostafa, G. P., & Gojazadeh, M., (2014). The effect of *Rosa damascena* extract on primary dysmenorrhea: A double-blind cross-over clinical trial. *Iran Red Crescent Med J.*, 16(1), 1–6. doi: 10.5812/ircmj.14643.
- Baydar, H., (2006). Oil-bearing rose (*Rosa damascena* Mill.) cultivation and rose oil industry in Turkey. *Euro Cosmet.*, 14(6), 13–17.
- Baydar, N. G., & Baydar, H., (2013). Phenolic compounds, antiradical activity and antioxidant capacity of oil-bearing rose (*Rosa damascena* Mill.) extracts. *Ind Crops Prod.*, 41(1), 375–380. doi: 10.1016/j.indcrop.2012.04.045.
- Becker, H. F., (1963). The fossil record of the genus *Rosa*. *Bull. Torrey Bot. Club.*, 90(2), 99–110. <http://www.jstor.org/stable/2483008> (accessed on 02 September 2023).
- Bhagat, A. A., Badgajar, C. D., Bhosale, S., & Supe, V. S., (2019). An economics analysis for export of fresh cut rose flowers from India. *J. Pharmacogn. Phytochem.*, SP2, 291–298.
- Bhattacharjee, S. K., & Banerji, B. K., (2010). *The Complete Book of Roses*. Jaipur: Aavishkar Publishers, Distributors.
- Boelema, B. H., (1969). Resistance of rose rootstocks to crown gall (*Agrobacterium tumefaciens*). *Netherlands J. Plant Pathol.*, 75(1, 2), 147–150. doi: 10.1007/BF02137209.
- Bosenberg, H., (1931). *United States Patent Office: Climbing or Trailing Rose*, 410, 473.
- Boskabady, M. H., Shafei, M. N., Saberi, Z., & Amini, S., (2011). Pharmacological effects of *Rosa Damascena*. *Iran J. Basic Med Sci.*, 14(4), 295–307.
- Brichet, H., (2003). Distribution and ecology. *Encycl Rose Sci.*, 199–200. doi: 10.1016/b0-12-227620-5/00209-3.
- Cai, Y. Z., Xing, J., Sun, M., Zhan, Z. Q., & Corke, H., (2005). Anthocyanins identified by LC-ESI-MS and MALDI-QIT-TOF MS from *Rosa chinensis* flowers. *J. Agric. Food Chem.*, 53, 9940–9948. doi: 10.1021/jf052137k.
- Calatayud, Á., Roca, D., Gorbe, E., & Martínez, P. F., (2008). Physiological effects of pruning in rose plants cv. grand gala. *Sci Hort. (Amsterdam)*, 116(1), 73–79. doi: 10.1016/j.scienta.2007.10.028.
- Center for the Promotion of Imports from Developing Countries (CBI), (2017a). *Exporting Roses to Europe*.
- Center for the Promotion of Imports from developing countries (CBI), (2017b). *Exporting Roses to Germany*.
- Center for the Promotion of Imports from developing countries (CBI) (2017c). *Exporting Carnations to Europe*.
- Chalova, V. I., Manolov, I. G., & Manolova, V. S., (2017). Challenges for commercial organic production of oil-bearing rose in Bulgaria. *Biol. Agric. Hortic.*, 183–194. doi: 10.1080/01448765.2017.1315613.
- Christensen, R., Bartels, E. M., Altman, R. D., Astrup, A., & Bliddal, H., (2008). Does the hip powder of *Rosa canina* (rosehip) reduce pain in osteoarthritis patients? - a meta-analysis of randomized controlled trials. *Osteoarthritis Cartilage*, 16, 965–972. doi: 10.1016/j.joca.2008.03.001.
- Debener, T., & Byrne, D. H., (2014). Disease resistance breeding in rose: Current status and potential of biotechnological tools. *Plant Sci.*, 228, 107–117. doi: 10.1016/j.plantsci.2014.04.005.
- Ercisli, S., (2007). Chemical composition of fruits in some rose (*Rosa* spp.) species. *Food Chem.*, 104(4), 1379–1384. doi: 10.1016/j.foodchem.2007.01.053.
- European Medicines Agency, (2013). *Assessment Report on Rosa gallica L. Rosa Centifolia L., Rosa Damascena Mill., Flos.*, 44, 1–20. [http://www.ema.europa.eu/docs/en\\_GB/](http://www.ema.europa.eu/docs/en_GB/)

- document\_library/Herbal\_-\_HMPC\_assessment\_report/2013/12/WC500158837.pdf (accessed on 02 September 2023).
- European Medicines Agency, (2014). *Assessment Report on Rosa Gallica L. Rosa Centifolia L., Rosa Damascena Mill., Flos.* London. [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Herbal\\_-\\_HMPC\\_assessment\\_report/2013/12/WC500158837.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Herbal_-_HMPC_assessment_report/2013/12/WC500158837.pdf) (accessed on 02 September 2023).
- Fan, C., Pacier, C., & Martirosyan, D. M., (2014). Rose hip (*Rosa canina* L): A functional food perspective. *Funct. Foods Heal Dis.*, 4(11), 493–509. doi: 10.31989/ffhd.v4i12.159.
- Foster, A., (2012). The medicinal plant collection at the University of Oxford Botanic Garden. *Planta Med.* doi: 10.1055/s-0032-1321356.
- Frawley, D., & Lad, V., (2001). *The Yoga of Herbs: An Ayurvedic Guide to Herbal Medicine.* (2<sup>nd</sup> edn.). Wisconsin, United States: Lotus Press.
- Furusho, T., & Hiramoto, T., (2016). *Roasted Mixture and Method for Producing a Beverage Using Same.* Patent Application Publication. US20160262415 A1.
- Gao, X., Bjork, L., Trajkovski, V., & Uggla, M., (2000). Evaluation of antioxidant activities of rosehip ethanol extracts in different test systems. *J. Sci. Food Agric.*, 80, 2021–2027. doi: 10.1002/1097-0010(200011)80,14<2021::AID-JSFA745>3.0.CO;2-2.
- Gichure, C. W., (2010). Ethical sourcing and moral responsibility in global business: Is ‘the common good’ the missing factor? The case of the cut flower industry in Kenya. In: Moore, G., (ed.), *Fairness in International Trade* (pp. 66–96). The Intern. Dordrecht: Springer. doi: 10.1007/978-90-481-8840-6\_5.
- Grand View Research Inc., (2019). *Rose Oil Market Size, Share & Trends Analysis Report by Application (Fragrance & Cosmetics, Pharmaceuticals, Food & Beverages), By Product (Organic, Conventional), And Segment Forecasts, 2019 – 2025.* San Francisco.
- Guner, A., Ozhatay, N., Ekim, T., Husnu, K., & Base, C., (2001). *Flora of Turkey and the East Aegean Islands* (Vol. 11). Edinburgh: Edinburgh University Press.
- Gunes, E., (2005). Turkey rose oil production and marketing: A review on problem and opportunities. *J. Appl. Sci.*, 5(10), 1871–1875. doi: 10.3923/jas.2005.1871.1875.
- Haghighi, M., Tehranifar, A., Nikbakht, A., & Kafi, M., (2006). Research and current profile of Iranian production of damask rose (*Rosa damascena* Mill.). In: *XVII International Horticultural Congress-IHC2006: International Symposium on Asian Plants with Unique Horticultural*, 769, 449–456.
- Harkness, P., (2003). In: Black, A., (ed.), *The Rose.* London: Scriptum Editions, Royal Horticultural Society.
- Hassanein, A. M. A., (2010). Improved quality and quantity of winter flowering in rose (*Rosa* spp.) by controlling the timing and type of pruning applied in autumn. *World J. Agric. Sci.*, 6(3), 260–267.
- He, F., Chen, J., Dong, K., et al., (2018). Multi-technical analysis on the antioxidative capacity and total phenol contents of 94 traditional Chinese dietary medicinal herbs. *Food Sci. Nutr.*, 6, 1358–1369. doi: 10.1002/fsn3.689.
- Hoseinpour, H., Peel, S. A. F., Rakhshandeh, H., et al., (2011). Evaluation of *Rosa damascena* mouthwash in the treatment of recurrent aphthous stomatitis: A randomized, double-blinded, placebo-controlled clinical trial. *Quintessence Int (Berl)*, 42(6), 483–491.
- Jabbarzadeh, Z., & Khosh-Khui, M., (2005). Factors affecting tissue culture of damask rose (*Rosa damascena* Mill.). *Sci Hortic (Amsterdam)*, 105, 475–482. doi: 10.1016/j.scienta.2005.02.014.

- Kakade, D. S., Gurav, S. B., Singh, B. R., & Nimbalker, C. A., (2006). Management of powdery mildew in rose under polyhouse condition. *J. Ornament. Horticult.*, 9(4), 293–295.
- Kalim, M. D., Bhattacharyya, D., Banerjee, A., & Chattopadhyay, S., (2010). Oxidative DNA damage preventive activity and antioxidant potential of plants used in Unani system of medicine. *BMC Complement Altern. Med.*, 10(77), 1–11. doi: 10.1186/1472-6882-10-77.
- Kogan, L. R., Schaefer, K., Erdman, P., & Schoenfeld-Tacher, R., (2016). University counseling centers' perceptions and experiences pertaining to emotional support animals. *J. College Stud. Psychother.*, 30(4), 268–283. doi: 10.1080/87568225.2016.1219612.
- Kovacheva, N., Rusanov, K., & Atanassov, I., (2010). Industrial cultivation of oil bearing rose and rose oil production in Bulgaria during 21st century, directions, and challenges. *Biotechnol. Biotechnol. Equip.*, 24(2), 1793–1798. doi: 10.2478/V10133-010-0032-4.
- Kovacheva, N., Zheljazkov, V. D., & Astatkie, T., (2011). Productivity, oil content, composition, and bioactivity of oil-bearing rose accessions. *HortScience*, 46(5), 710–714. doi: 10.21273/HORTSCI.46.5.710.
- Kumari, D. L. C., & Peiris, S. E., (2000). Preliminary investigation of preservation methods to produce dried flowers of rose and statice. *Trop Agric Res.*, 12, 416–422.
- Kurkcuoglu, M., & Baser, K. H. C., (2003). Studies on Turkish rose concrete, absolute, and hydrosol. *Chem. Nat. Compd.*, 39(5), 457–464. doi: 10.1023/B:CONC.0000011120.71479.7f.
- Larson, R., (1992). *Introduction to Floriculture* (2<sup>nd</sup> edn.). Academic Press.
- Leahu, A., Damian, C., Oroian, M., Ropciuc, S., & Rotaru, R., (2014). Influence of processing on vitamin C content of rosehip fruits. *Anim. Sci. Biotechnol.*, 47(1), 116–120. <http://spasb.ro/index.php/spasb/article/view/1812> (accessed on 02 September 2023).
- Maharaj, N., (1995). *The Game of the Rose: The Third World in the Global Flower Trade*. Utrecht: International Books for the Institute for Development Research Amsterdam.
- Mahboubi, M., (2016). *Rosa damascena* as holy ancient herb with novel applications. *J. Tradit. Complement Med.*, 6(1), 10–16. doi: 10.1016/j.jtcm.2015.09.005.
- Mahmood, N., Piacente, S., Pizza, C., et al., (1996). The anti-HIV activity and mechanisms of action of pure compounds isolated from *Rosa damascena*. *Biochem Biophys Res Commun.*, 229, 73–79.
- Majed, A., (2017). *Shrub Rose Plant Named 'KASCT491-1'*.
- Matsumoto, S., Kouchi, M., Yabuki, J., & Kusunoki, M., (1998). Phylogenetic analyses of the genus *Rosa* using the mat K sequence: Molecular evidence for the narrow genetic background of modern roses. *Sci. Hortic. (Amsterdam)*, 77, 73–82.
- Mehmet, E. Y., (2019). *Floral Compositions for Hand Disinfection*.
- Mierow, D., & Shetha, T. B., (1987). *Himalayan Flowers and Trees*. Kathmandu, Nepal: Sahayogi Press.
- Mohebitabar, S., Shirazi, M., Bioos, S., Rahimi, R., Malekshahi, F., & Nejatbakhsh, F., (2017). Therapeutic efficacy of rose oil: A comprehensive review of clinical evidence. *Avicenna J. Phytomedicine*, 7(3), 206–213. doi: 10.22038/ajp.2016.7760.
- Nasery, M., Hassanzadeh, M. K., Najaran, Z. T., & Emami, S. A., (2016). *Rose (Rosa × Damascena Mill.) Essential Oils*. Elsevier. doi: 10.1016/B978-0-12-416641-7.00075-4.
- Nayebi, N., Khalili, N., Kamalinejad, M., & Emtiazy, M., (2017). A systematic review of the efficacy and safety of *Rosa damascena* Mill. with an overview on its phytopharmacological properties. *Complement Ther Med.*, 34, 129–140. doi: 10.1016/j.ctim.2017.08.014.

- Nazari, F., Khosh-Khui, M., & Salehi, H., (2008). Growth and flower quality of four *Rosa hybrida* L. cultivars in response to propagation by stenting or cutting in soilless culture. *Sci Hortic. (Amsterdam)*, 4. doi: 10.1016/j.scienta.2008.08.004.
- Nicetic, O., Watson, D. M., & Beattie, G. A. C., (2002). A horticultural mineral oil-based program for control of two-spotted mite and powdery mildew on roses in greenhouses. In: Beattie, G., Watson, D., Stevens, M., Rae, D., & RN, S. H., (eds.), *Spray Oils Beyond 2000 - Sustainable Pest and Disease Management* (pp. 387–395). Sidney: University of Western Sidney.
- Nikbakht, A., Kafi, M., Mirmasoumi, M., & Babalar, M., (2005). Micropropagation of damask rose (*Rosa damascena* Mill.) cvs Azaran and Ghamsar. *Int. J. Agric Biol.*, 7(4), 535–538.
- Nimura, M., Yamaguchi, N., & Itoh, K., (1997). Effects of training methods and flower cutting methods on the yield and quality of a rose crop. *Res. Bull. Aichi. Agric. Cntr.*, 20, 185–192.
- Ohkawa, K., (1980). Cutting grafts as a means to propagate greenhouse roses. *Sci. Hortic. (Amsterdam)*, 13, 191–199. doi: 10.1016/0304-4238(80)90084-9.
- Orhan, N., Aslan, M., Hoşbaş, S., & Deliorman, O. D., (2009). Antidiabetic effect and antioxidant potential of *Rosa canina* fruits. *Pharmacogn Mag.*, 5(20). doi: 10.4103/0973-1296.58151.
- Özcan, M., (2002). Nutrient composition of rose (*Rosa canina* L.) seed and oils. *J. Med. Food*, 5(3), 137–140. doi: 10.1089/10966200260398161.
- Özel, M. Z., Göğüş, F., & Lewis, A. C., (2006). Comparison of direct thermal desorption with water distillation and superheated water extraction for the analysis of volatile components of *Rosa damascena* Mill. using GCxGC-TOF/MS. *Anal Chim. Acta*, 566(2), 172–177. doi: 10.1016/j.aca.2006.03.014.
- Pati, P. K., Sharma, M., Sood, A., & Ahuja, P. S., (2005). Micropropagation of *Rosa damascena* and *R. bourboniana* in liquid cultures. In: *Liquid Culture Systems for in Vitro Plant Propagation* (pp. 373–385). Netherlands: Springer. doi: 10.1007/1-4020-3200-5\_29.
- Potterton, D., (1983). *Culpeper's Color Herbal* (pp. 61–158). Foulsham & Company Ltd.
- Qi, W., Chen, X., Fang, P., et al., (2018). Genomic and transcriptomic sequencing of *Rosa hybrida* provides microsatellite markers for breeding, flower trait improvement and taxonomy studies. *BMC Plant Biol.*, 18(119), 1–11. doi: 10.1186/s12870-018-1322-5.
- Raynolds, L. T., (2012). Fair trade flowers: Global certification, environmental sustainability, and labor standards. *Rural Sociol.*, 77(4), 493–519. doi: 10.1111/j.1549-0831.2012.00090.x.
- Rehder, A., (1940). *Manual of Cultivated Trees and Shrubs* (2<sup>nd</sup> edn.). New York: MacMillan; 1940.
- Rikken, M., (2010). *The European Market for Fair and Sustainable Flowers and Plants*. Brussels.
- Safi, M., (2005). Flower production related to re-blooming time of three *Rosa hybrida* cultivars in response to rootstock type. *Science Asia*, 31, 179–181. doi: 10.2306/scienceasia1513-1874.2005.31.179.
- Schriner, S. E., Katoosi, N. S., Pham, K. Q., Gazarian, M., Zarban, A., & Jafari, M., (2012). Extension of *Drosophila* lifespan by *Rosa damascena* associated with an increased sensitivity to heat. *Biogerontology*, 13(2), 105–117. doi: 10.1007/s10522-011-9357-0.
- Shakywar, R. C., Tomar, K. S., & Patidar, R. K., (2016). Diseases of rose crop and their management. *Crop Diseases and Their Management*, 267.
- Short, K. C., & Roberts, A. V., (1991). *Rosa* spp. (roses): *In vitro* culture, micropropagation, and the production of secondary products. *Med Aromat Plants III*, 15, 376–397. doi: 10.1007/978-3-642-84071-5\_23.



- Strålsjö, L., Alklint, C., Olsson, M. E., & Sjöhol, I., (2003). Total folate content and retention in rosehips (*Rosa* ssp.) after drying. *J. Agric. Food Chem.*, *51*(15), 4291–4295. doi: 10.1021/jf034208q.
- Takeuchi, S., Nomura, K., Uchiyama, H., & Yoneda, K., (2000). Phylogenetic relationship in the genus *Rosa* based on the restriction enzyme analysis of the chloroplast DNA. *J. Japanese Soc. Hortic. Sci.*, *69*(5), 598–604. doi: <https://doi.org/10.2503/jjshs.69.598>.
- The Plant List Version 1.1*, (2013). Published on the Internet. <http://www.theplantlist.org/> (accessed on 02 September 2023).
- Tjosvold, S. A., (2001). Effect of bending on production and quality of commercial greenhouse roses in field soil. *Acta Hortic.*, *547*, 299–302. doi: 10.17660/ActaHortic.2001.547.35.
- Tobyn, G., Denham, A., & Whitelegg, M., (2011). *Rosa damascena*, damask rose. In: *The Western Herbal Tradition: 2000 Years of Medicinal Plant Knowledge* (p. 392). London: Elsevier.
- Ucar, Y., Kazaz, S., Eraslan, F., & Baydar, H., (2016). Effects of different irrigation water and nitrogen levels on the water use, rose flower yield and oil yield of *Rosa damascena*. *Agric Water Manag.*, *182*, 94–102. doi: 10.1016/j.agwat.2016.12.004.
- Uggla, M., Gao, X., & Werlemark, G., (2003). Variation among and within dogrose taxa (*Rosa* sect. *caninae*) in fruit weight, percentages of fruit flesh and dry matter, and vitamin C content. *Acta Agric Scand Sect B Soil Plant Sci.*, *53*(3), 147–155. doi: 10.1080/09064710310011746.
- Van De, P. P. A., & Breukelaar, A., (1982). Stenting of roses; a method for quick propagation by simultaneously cutting and grafting. *Sci. Hortic. (Amsterdam)*, *17*(2), 187–196. doi: 10.1016/0304-4238(82)90012-7.
- Vinokur, Y., Rodov, V., Reznick, N., et al., (2006). Rose petal tea as an antioxidant-rich beverage: Cultivar effects. *J. Food Sci.*, *71*(1). doi: 10.1111/j.1365-2621.2006.tb12404.x.
- Wei, A., & Shibamoto, T., (2007). Antioxidant activities and volatile constituents of various essential oils. *J. Agric. Food Chem.*, *55*, 1737–1742. doi: 10.1021/jf062959x.
- Winther, K., Campbell-Tofte, J., & Vinther, H. A. S., (2016). Bioactive ingredients of rose hips (*Rosa canina* L) with special reference to antioxidative and anti-inflammatory properties: *In vitro* studies. *Bot. Targets Ther.*, *6*, 11–23. doi: 10.2147/btat.s91385.
- Yaniv, Z., & Dudai, N., (2014). In: Mathe, A., (ed.), *Medicinal, and Aromatic Plants of the Middle-East*. Medicinal. Dordrecht Heidelberg New York London: Springer. doi: 10.1007/978-94-017-9276-9\_16.
- Yaseen, M., Kothari, S. K., Singh, U. B., Singh, K., & Sattar, A. R. S., (2001). Bio-economic evaluation of scented rose (*Rosa damascena*) based intercropping systems in north Indian plains. *J. Med. Aromat. Plant Sci.*, *23*(2), 69–74.
- Yin Yang House. <https://yinyanghouse.com/> (accessed on 02 September 2023).
- Younis, A., Riaz, A., Khan, M. A., Khan, A. A., & Pervez, M. A., (2008). Extraction and identification of chemical constituents of the essential oil of *Rosa* species. *Acta Hortic.*, *766*, 485–492. doi: 10.17660/ActaHortic.2008.766.65.
- Zargari, A., (1982). *Medicinal Plants* (Vol. 1). Tehran. Iran: Tehran University publications.
- Zieslin, N., Hurwitz, A., & Halevy, A. H., (1975). Distribution of carbohydrates in different parts of baccara rose plants as influenced by various pruning and pinching treatments. *J. Hortic. Sci.*, *50*(4), 339–348. doi: 10.1080/00221589.1975.11514643.
- 石毛, 林志隆., (2020). *Anti-Wrinkle Firming Composition*, 21. CN 110812262 A.
- 符春丽, 田伟兰, 汪垠明, et al., (2020). *Compound Essential oil for Skin Brightening, Moisturizing, Soothing, and Anti-aging, and Preparation Method and Application Thereof*, 11(CN 110772454 A).



Taylor & Francis

Taylor & Francis Group

<http://taylorandfrancis.com>

## CHAPTER 8

---

# Safed Musli: A Critical Review on its Bioactive Compounds, Medicinal Properties, and Biological Activity

SABYASACHI BANERJEE,<sup>1</sup> UTSAB CHAKRABORTY,<sup>2</sup> and SANKHADIP BOSE<sup>3</sup>

<sup>1</sup>*Department of Phytochemistry, Gupta College of Technological Sciences, Asansol, West Bengal, India*

<sup>2</sup>*School Pharmacy, YBN University, Rajaulatu, Namkum, Ranchi, Jharkhand, India*

<sup>3</sup>*School of Pharmacy, The Neotia University, Sarisa, Diamond Harbor Road, South 24 Parganas, West Bengal, India*

---

### ABSTRACT

*Chlorophytum borivilianum* belongs to Liliaceae or Asparagaceae family is a conventional scarce Indian therapeutic herb generally utilized for treating numerous clinical states. It's a significant medication usually versed as 'Safed Musli.' It offers extremely broad spectrum of medicinal properties in the systems of Homeopath, Ayurveda, Unani, and Allopathy. Within the Ayurvedic erudition, *C. borivilianum* is commended as a Divya Aushadhi with incomparable therapeutic benefits. It's a main element for preparing over 100 Ayurvedic preparations. *Chlorophytum borivilianum* is broadly propagated all through India. Significant phytoconstituents revealed from *C. borivilianum* roots incorporate essentially fructans and fructoligosaccharides (FOS), steroidal saponins, phenolics, proteins, and acetylated mannans. In this chapter, the botanical descriptions, ethno-medicinal uses, phytoconstituents, and biologic activities of the different plant parts, along with the

molecular targets of *C. borivilianum* are included which may play a suitable base for additional research on this plant.

## 8.1 INTRODUCTION

Nature has offered us with an enormous number of various kinds of herbs, which appear as wild in various portions of India. It's assessed that around 3.6 lakh herb species over on globe and from which 40% is attainable in the Indian subcontinent. Mentioning of around 67 plants, 81 plants and 290 plants have been indicated in Rigveda, Yajurveda, and Atharvaveda respectively. Correspondingly, Charak Samhita and Sushrut Samhita depicted the qualities and functions of 1,100 and 1,270 trees, respectively. In pursuance of the World Health Organization, >80% of the world's demography in developing nations relies essentially upon herbal medication for basic healthcare needs (Banerjee et al., 2020). The utilization of herbal medications in developed nations is additionally rising regularly.

*Chlorophytum borivilianum* also called safed musli is a herb, belonging to the Liliaceae/Asparagaceae family, was basically propagated in Indian thick timberlands. Around 300 species are dispersed all through the sub-tropical and tropical places in the globe. Sub-tropical as well as tropical regions of Africa are the possible spots where this genus originated. There're 17 kinds of Chlorophytum species had been present in India (Oudhia, 2001). All vary in therapeutic actions however because of absence of relevant data, all of those are designated as safed musli. It's deliberated as a significant therapeutic herb in India, while in different portions of the earth it's being utilized for ornamented herb. The tuberous roots are plentiful in saponins, minerals, alkaloids, proteins, steroids, carbohydrates, vitamins as well as polysaccharides. It's having different therapeutical actions like total rejuvenator, immunomodulator, and antioxidant. It's being utilized as an anticancer and antiarthritic agent. Because of the aphrodisial properties, it is frequently known to as 'Herbal viagra.' It's located in the tropical wet as well as dry deciduous timberlands (Thakur et al., 2009a). It's broadly dispersed in India predominantly in North Gujarat, Western Madhya Pradesh, Southern Rajasthan, and several portions of Karnataka. However, ceaseless investigation has diminished its distribution, frequency as well as the quality. The complex of 'Safed Musli' is usually presumed to comprise of *C. borivilianum*, *C. tuberosum*, *C. arundinaceum*, and *Asparagus adscendens*. Among these variants, *C. borivilianum* is growing at a larger scale in numerous portions

of the region since it delivers the maximal production and most noteworthy saponins, is utilized as Safed Musli. Albeit timberlands are affluent in 'Safed musli' in India, and its demands are expanding quickly in India as well as worldwide medicine markets. As per a statement in 2005–2006, the requirement for dried Safed musli is in the range of 35,000 tons/year, with a supply of 5,000 tons/annum (Singh et al., 2012). Henceforth there's a solid requirement to comprehend the present situation of its propagation, depiction, and its new therapeutic benefits.

## 8.2 AREA AND PRODUCTION

In India, it's propagated in portions of Rajasthan, Gujarat, Uttar Pradesh, Madhya Pradesh, Maharashtra, Chhattisgarh, Karnataka, and Haryana into subtropical as well as tropical weathers with altitude up to 1,500 m. It's being developed on a territory in excess of 400 hectare for its root tubers and furthermore naturally grown in utmost timberlands of central India with suitable climate (Kothari et al., 2003). Safed musli grows in both tropical and sub-tropical areas around the globe. It's discovered basically in the India, Australia, and America. It's found naturally in the woodlands of Rajasthan, Gujarat, Maharashtra, and Madhya Pradesh in India. It's habitant in wider extent of territories from the open, stony lands to shadowy and exceptionally humus richer soils of the forest. Commercially propagation of safed musli began in Central India and has now spread throughout the nation. Its propagation has become exoteric within the cultivators of Madhya Pradesh, Maharashtra, Gujarat, Rajasthan, West Bengal, Bihar, Uttar Pradesh, Andhra Pradesh, Kerala, and Tamil Nadu.

## 8.3 MARKETING AND TRADE

As of now, the assessed worldwide marketed demands and productions respectively is around 35,000 and 5,000 tons per year that meet under 15% of the requisite demands. Another statistic puts the global demands for root is near 50,000 tons/year (Somanath, 2008). Over 95% of the attainable quantity of safed musli comes from wild reaping, which is specifically forbidden by the different governments of the states. The present worldwide trading in therapeutic spices is >60 billion dollar, that's expected to grow by about five trillion dollar by 2050 with outgrowth rates of 7% per year. India's present potency in worldwide trading is ₹4.36 billion which is desired to uprising to ₹222 billion by 2050.

The investigation of previously reported data shows the higher economical significance of *C. borivilianum* both in domestically and abroad markets; thus, its trading might be elevated by the governments to bring higher foreign profits. There's a requirement of wider acknowledgment within the cultivators, producers, traders, and medication specialists who may work in congruity to realize the entire mercantile benefits.

#### 8.4 COMPOSITION AND USES

The key bio-chemical components of safed musli are carbohydrates (42%), fibers (20–30%), alkaloids (15–25%), protein (10%), and saponins (2–17%). Mainly alkaloids and saponins exhibit therapeutic values. It's a richer well-spring of more than 25 kinds of saponins, alkaloids, carbohydrates, vitamins, proteins, steroids, potassium, magnesium, resins, phenol, polysaccharides, mucilage, and calcium, and additionally comprises of higher amount of sugars, essentially galactose, fructose, sucrose, glucose, xylose, and mannose.

Genus *Chlorophytum* shows extensive decent variety in leaves, roots, inflorescence length, flower size and shape. Four kinds of roots are seen in the Indian *Chlorophytum* viz., *C. arundinaceum* kind where roots are fibrous with ellipsoid tubers; *C. malabaricum* kind of fasciculated uniformly thick small non tuberous roots; *C. borivilianum* kind of short, fasciculated, sessile, large, and thick roots and *C. bharuchae* kind where roots are long, uniformly thick and fleshy. Similarly, tuber size and shape are additionally variable and relies upon the age and size of the plants. *Chlorophytum laxum* R. Br. is the species with small plants in the genus while *C. nimmonii* Dalzell has largest plants. *Chlorophytum glaucum* Dalzell and *C. nepalense* (Lind.) Baker likewise have large plants when contrasted with other species in India. It has been perceived 3 kinds of leaves in the genus Viz. Canna like (distinctly petiolate, elliptic leaves), Anthericum like (sessile, linear lanceolate leaves) and *Juncus* like (narrow linear, leaves). Third type of leaves (*Juncus* type) are not announced in any Indian species. The smallest scapes were found in *C. laxum* followed by *C. heynei* while biggest in *C. nepalense* followed by *C. nimmonii*. Largest flowers were seen in *C. nepalense* followed by *C. gothanense* while smallest flowers in *C. laxum* followed by *C. kolhapurensis*. Stamen filament texture is found to be species specific in Indian *Chlorophytums*. There are 3 kinds of filament textures Viz., *C. laxum* type (smooth filaments, no ornamentation); *C. heynei* (papillose filament) and *C. bharuchae* type (warty or wrinkled filaments). Comparative chart of taxonomically significant morphological characters is reported in Table 8.1.

**TABLE 8.1** Significant Morphological Characters and Somatic Chromosome Number (2n) in Chlorophytum Species Found in India

SL. No.	Morphological Characters	<i>C. attenuatum</i>	<i>C. bharrachae</i>	<i>C. arundinaceum</i>	<i>C. belgannense</i>	<i>C. borivilianum</i>	<i>C. breviscapum</i>	<i>C. glaucum</i>	<i>C. glaucoides</i>	<i>C. indicum</i>	<i>C. heynei</i>	<i>C. gohanense</i>	<i>C. kohlhapurense</i>	<i>C. malabaricum</i>	<i>C. laxum</i>	<i>C. nepalense</i>	<i>C. nimmonii</i>	<i>C. sharmae</i>	<i>C. tuberosum</i>	<i>C. comosum</i>	<i>C. filipendulum</i> <i>subsp. amaniiense</i>	
1.	Root fibrous, tuberous			✓	✓		✓	✓	✓	✓		✓			✓				✓	✓		
2.	Roots fasciculated	✓									✓			✓		✓	✓	✓				✓
3.	Roots long or short, uniformly thickened		✓			✓							✓									
4.	Leaves sessile, linear to lanceolate	✓	✓		✓	✓	✓			✓		✓	✓	✓	✓	✓		✓	✓	✓		
5.	Leaves pseudo-petiolate, lanceolate to elliptic			✓				✓	✓	✓	✓						✓					✓
6.	Scape branched		✓										✓			✓	✓			✓		
7.	Scape not branched or rarely branched	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓			✓	✓	✓		✓
8.	Scape without sterile bract	✓	✓	✓	✓	✓	✓			✓	✓	✓		✓	✓	✓	✓		✓	✓		✓
9.	Scape with sterile bracts							✓	✓				✓					✓				
10.	Pedicle other than white, usually brown, cylindrical		✓										✓		✓							
11.	Pedicle white, greenish white, cylindrical to trigonous	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓		✓		✓	✓	✓	✓	✓		✓
12.	Pedicle articulation at base of flower		✓						✓		✓		✓	✓								✓
13.	Pedicle articulation at the middle or below middle	✓		✓	✓	✓	✓	✓		✓					✓	✓	✓	✓	✓	✓		
14.	Perianth lobes greenish white throughout or at least at the middle		✓								✓		✓		✓					✓		✓

TABLE 8.1 (Continued)

SL. No.	Morphological Characters	<i>C. filipendulum</i> subsp. <i>amanianse</i>	<i>C. comosum</i>	<i>C. tuberosum</i>	<i>C. sharnae</i>	<i>C. nimmonii</i>	<i>C. nepalense</i>	<i>C. laxum</i>	<i>C. malabaricum</i>	<i>C. kohlapurense</i>	<i>C. gohanense</i>	<i>C. heynei</i>	<i>C. indicum</i>	<i>C. glaucoides</i>	<i>C. glaucum</i>	<i>C. breviscapum</i>	<i>C. borvitanum</i>	<i>C. belgamenense</i>	<i>C. arundinaceum</i>	<i>C. bharrachae</i>	<i>C. attenuatum</i>		
15.	Anther up to 3 mm long, very short as compared to filament length	✓	✓					✓	✓	✓		✓		✓							✓		
16.	Anthers longer or at least half the length of the filament			✓	✓	✓	✓				✓		✓		✓	✓	✓	✓	✓				
17.	Filament smooth		✓	✓	✓		✓			✓							✓						
18.	Filament Warty									✓									✓				
19.	Filament papillose	✓				✓			✓			✓	✓	✓	✓	✓		✓					
20.	Style declinate			✓		✓	✓				✓		✓		✓	✓	✓	✓					
21.	Style straight	✓	✓					✓	✓	✓		✓		✓						✓	✓		
22.	Capsule triquetrous and elongated							✓				✓									✓		
23.	Vessels element with spiral thickening							✓													✓		
24.	Amphistomatic							✓													✓		
25.	Intraseptal nectaries absent																				✓		
26.	Flowers sweet scented																				✓		
27.	Chromosome number	42	16	42	42	28	42	42	42	84	14	42	16	42	16	42	16	56	42	42	16	28	14



In India the *C. borivilianum* tuberous root are utilized as indigenous medication for various disorders and hygiene related issues from 11<sup>th</sup> century A. D. The ancient Indian medicinal system, Ayurveda retains an extremely eminent rank for *C. borivilianum* and related with 'Caitha' as one of the providential herb. It's additionally deliberated 'divya aushadhi' in Ayurvedic medicinal systems. Ayurveda depicts the characteristics of *C. borivilianum* as sweet, unctuous (Guna), bitter (Rasa), moist, sweet post-digestive effects (Vipaka) and cold (heavy Virya) (Toth et al., 1994; Paques et al., 1987).

The *C. borivilianum* has been used for approximately 4,000 years, as per the Hindu epic "Srimad Bhagawatam." It's part of the "Vajikaran Rasayana" group of Ayurvedic herbs, which are used for rejuvenating and renewing characteristics in order to improve sexual aspects and alleviate sexual dysfunctions (Puri, 2003; Triveni, 1977). This's additionally the premise of medications suggested in Kamasutra (Hooper, 2002). According to Hindu scripture, a celestial physician Ashwini Kumar, made the 'chyawanprash' from safed musli for Chyavanrishi, who wedded at 80, to improve sexual wellness. Safed musli was portrayed as 'Vajikaran,' likewise in different antiquated Ayurveda treatise, for example, Rasendra Sarsangrah, Bhavaprakash, and Raja Ballabh Nighantu. The distinctive Siddha and Ayurvedic treatise referenced 30 to 35 therapeutic herbs having 'Rasayana' benefits inclusive of *C. borivilianum*. Shushruta characterized 'Rasayana' as a treatment which captures aging (Vayasthapam), increment lifespan (Ayushkaram), strength (Bala) and intelligence (Medha) (Pushpangadan et al., 2012).

Conventionally, roots of *C. borivilianum* are notable to treat oligospermia, male impotency, and are an especial kind of immunomodulator (Kirtikar et al., 1956; Mishra, 2005; Kothari et al., 2004; Puri, 2003; Singh et al., 2012; Sharma et al., 1999; Tandon et al., 1995; Triveni, 1977). They've anti-pyretic, carminative, astringent, and diuretic actions (Kirtikar et al., 1975). Tuberous roots are likewise utilized as galactagogue as well as stomachic agent (Chetty et al., 1989; Bhandary et al., 1995). In certain locales of Mewar, India, tuberous roots have been utilized for treating erectile dysfunctionality (Deshwal et al., 2011). The activity of *C. borivilianum* tuberous roots over central nervous system is alike Ginseng and is typically called 'Indian Ginseng' because of the exceptional therapeutical potency (Singhania, 2003). It not just revitalizes the reproductive systems, however that additionally prevents prematurely ejaculations and improves the overall immune system of the body. It's known for promoting strengths and endurance while countering general body weakness, increasing muscular mass, and assisting in the recovery from physical stress and lethargy. The roots

are also utilized for energy boosting in asthma patients. The powdered root alongside other natural ingredients have been used in formulation of a few Unani as well as Ayurvedic health tonic (Haque et al., 2011).

In West-India, particularly Gujrat, expending a spatula of *C. borivilianum* along with milk two times a day is an element of a daily healthcare regimen. The leaves are chewed as an expectorant in the homespun people of India's West Ghats (Sebastian et al., 1988). During pregnancy, roots are applied as a nutritional excitant for both the pregnant woman and the fetus, and they are also utilized to replace body fluid during postpartum period (Singh et al., 2013). The corpulent tuber of *C. borivilianum* is one of the components in formulation of a unique kind of laddoo (ball-formed sweet) that women consume as an invigorating meal latterly giving birth. The arid roots powder additionally elevates lactations in nursing moms and breastfeeding garget, and is utilized for manage a wide range of gynecological problems, including leucorrhea, gonorrhoea, and post- and pre-natal symptoms (Deshwal et al., 2011). Furthermore, safed musli tuberous root are utilized to treat rheumatism, arthritis, and joint pains (Singh et al., 2013). It's perceived to remove the knee torment inside 7 days whenever devoured everyday with milk (Singhania, 2003; Elizabeth, 2001; Singh et al., 2003a). In India the *C. borivilianum* tubers have efficiently been utilized by Meena society of Rajasthan, to treat bone fractures, leukorrhoea, and male tonic (Meena et al., 2010). Rai et al. (2011) recently introduced an investigation of 302 herbs of 96 families utilized for medication by local Mizo and other societies in North-Eastern India more than a decennial ago. Within those herbs, safed musli has been identified as a primary resource of metabolic enhancing and aphrodisiac properties. The Bharia along with other societies of Pataalkot valley adjacent Madhya Pradesh's district Chindwara utilize *C. borivilianum* for a regional therapy in medical purposes, particularly to boost immunity. The indigenous healers namely Bhumkas or certain older individuals are familiar with the healing system. According to an ethnobotanical investigation done in Korku-dominated forest areas of Madhya Pradesh, the Korku community utilized 38 plant species for food, feed, oil, and medication inclusive of *C. borivilianum*. The conventional utilizations of tubers of *C. borivilianum* against different ailments like dysuria, diabetes mellitus, dysentery, and diarrhea are all around recorded in the literatures (Dabur et al., 2007; Purohit et al., 2003; Negi, 1993; Oudhia, 2001a). In the event of throat and mouth aphthae, the powdered root roasted in ghee is consumed; it is also used orally as a subsidiary treatment for blood cleansing and abeyance in aging process. It's additionally deliberated as a viable medication for controlling and preventing

obeseness and its adverse impacts. The roots have likewise been reported for cosmetic uses. A root's paste combined of goat milk or honey might be implemented topically to the face for brightening the dermal tone (Singh et al., 2013). Despite the fact that safed musli exhibits no side impacts however in case of overdosing it might result in gastrointestinal ailments. Aside from folklore, *C. borivilianum* leaves are utilized as vegetable in several culinary formulations in Goa and Maharashtra (Patil, 2000; Vartak, 1981).

## 8.5 ORIGIN AND DISTRIBUTION

The genus Chlorophytum is said to have originated in tropical and sub-tropical Africa, thereafter it has transported to India. The *C. borivilianum* herb appeared in the noticeable quality about late 1980's. The Chlorophytum genus is illustrated by roughly 300 rhizomatous plant species, dispersed mostly in tropical and sub-tropical timberlands in the nature up to 1,500 meters altitude (Nayar et al., 1988; Chakraborty et al., 2009; Raghavendra et al., 2005; Oudhia, 2001a). According to Genera Plantarum it's been described that 40 Chlorophytum species are dispersed in tropical Africa, Asia, Australia, and America (Bentham et al., 1880). Around 13 chlorophytum species have been described to present in India, between which 6 to 7 species are utilized in local medicinal systems (Sheriff et al., 1972; Nair, 1974). Whilst a few types of Chlorophytum species are propagated for exhibiting attractive benefits (Bordia et al., 1995).

## 8.6 BOTANY AND TAXONOMY

*C. borivilianum* Santapau and Fernandes is member of Liliaceae or Asparagaceae family, and Anthericoideae subfamily (Santapau et al., 1955; Govaerts, 1999) and having 6 to 16 radical of (13 to 23 × 1 to 2.5) cm sized, sessile, imbricated spirally at base, lineal ovate leaves; smaller, whitish, bracteate, pedicellate with joint, zygomorphic blooms placed in alternative fascicles; brownish to blackish barked, whitish after scrapping, tasteless, characteristic odor, fleshy, 3 to 20 in number, 8 to 25 cm longer roots; greenish-yellow colored, triquetrous, loculicidal capsule, bears 3 to 12 seeds inside every fruits and black, smaller, angular shaped, endospermical seeds (Mandal et al., 2012; Singh et al., 2004a, b, 2012; Paturde et al., 2000).

The herbaceous plant *C. borivilianum* has a compact stem disc from where a leaf whorl originates. Sessile leaves are of 10 to 40 cm long and 0.6 to 4.0 cm wide. The blooms are pendicellate with having joints, smaller,

whitish, bracteate, and zygomorphical, and the inflorescence is racemes. The perianth comprises of 6 tepals organized into 2 heteromorphous series each with three tepals. The 6 stamens are arranged opposite the tepals in the androecium. Filaments are shorter than anthers. Stigma is placed off from the stamens, and the pistil appears larger than the stamen. On the upper portion of the scape, the flower clusters are dense, the purple bracts are papery, linear, and 10–105 mm length, as well as the whiter pedicel measures 6–10 mm longer. It produces greenish to yellowish fruits whose length and width is identical. Endospermic seeds are onion-alike in appearance, blackish in color, and angular shaped. The fruit is a trilobed capsule with 3 to 12 seeds. The black seeds are flat. The plant's roots (fibrous) are transformed in the fleshy roots (fascicular roots), which are the financially valuable component. Its tuberous fleshy root is fascicle-like and originating direct from the disc of the stems without any fibrous structures. They're tubular and 5 to 20 in numeral. It's having 6 to 13 leaves which is radical, spirally imbricated at base, sessile natured, ovate or linear shaped with acute apex and somewhat constricted at the base. Smooth surfaces, wavy borders, and parallel venation characterize the leaves, which spread horizontally.

Safed musli is a little annual plant, grown enough in subtropical and tropical weathers with altitude up to 1,500 m. It grown up to a maximal of 1.5 feet height. Tubers could grown up to a depth of 10 inches.

### **8.6.1 ROOT**

The light brown to whitish colored root has a characteristic odor and have no taste. Tuberous fleshy root is fascicle-like and originating direct from the disc of the stems without having fibrous structures and separated it from Chlorophytum genus's different species. Tubers are tubular in shape, with an average length of eight centimeters with 0.9 cm diameter. The quantity of tubers alters according on the herb, but on average there are 5–30 tubers per herb, slightly tapering towards the lower side and like a pestle.

### **8.6.2 LEAVES**

It is having 6 to 13 basal leaves that are spirally imbricated at base, sessile, lanceolate, and ovate or linear with sharp apex and somewhat constricted at base and < 30 cm longer. The horizontally spread leaves are having smoother surfaces, wavy margins as well as paralleled venation.

### 8.6.3 FLOWERS AND FRUIT

Tiny, white, pedicillate, bracteate, zygomorphical *C. borivilianum* flowers are organized in alternative clusters, every cluster containing three flowers. The above portion of the scape flower clusters, are thick; purple bracts are papery, linear, and 1.0 to 10.5 cm longer; pedicle is whitish and 6 to 10 mm longer. It produces greenish to yellowish fruits that is about identical in width and length. The seed is tiny, blackish, and completely encased in the perforations. There are around 10 to 12 seeds in each hole. Endospermic seeds are onion-like in appearance, black in color, and angular in shape.

*C. borivilianum* has a variety of common names relying on the language spoken in a particular locality. Table 8.2 lists the names utilized in several languages in India and other countries.

**TABLE 8.2** *C. borivilianum*'s Vernacular Names (Khanam et al., 2013)

Country	Vernacular Names (Language)
India	Swetha musli (Sanskrit); Hazarmuli, Safed musli, Satmuli (Hindi); Dholi musali, Ujlimusli (Gujrati); Shedheveli, Shedeveli (Malyalam); Kuli, Sufed musli (Marathi); Tannirvittan-Kizhangu, Tannirvittang, Taniravi thang, Vipurutti (Tamil); Tsallogadda (Telgu); Mushali, Hirtha-wariya (Sinhalese); Jhirna (Garhwali); Khairuwa (Bhojपुरi).
Saudia Arabia	Shaqaqule-hindi, Shaqqale (Arabic).
England, USA	Spider plant, Indian spider plant, White musale (English).
France	Chlorophytum medicinal (French).

The taxonomic data of *C. borivilianum* includes:

- Kingdom: Plantae.
- Phylum: Tracheophyta.
- Class: Liliopsida.
- Order: Asparagales.
- Family: Liliaceae/Asparagaceae.
- Genus: Chlorophytum.
- Species: *Chlorophytum borivilianum*.

## 8.7 VARIETIES AND CULTIVARS

Some global crop varieties are there which includes:

1. *Chlorophytum arundinaceum* **Baker**: Portions of central India, districts of Chhota Nagpur, foothills of north-east Himalayan in

- Assam, Bihar, and West Bengal (Singh, 1974; Haines, 1961; Chadha et al., 1980).
2. *C. attentuatum* **Baker**: From Karnataka to Coimbatore, the Western Ghats stretch southward (Hooker, 1894).
  3. *C. breviscapum* **Dalz.**: Sikkim Himalaya, West Penninsula and Belgaum (Verma et al., 2020).
  4. *C. borivilianum* **Sant and Fern.**: Timberlands of north Gujarat, west Madhya Pradesh, subtropical Himalayas, south Rajasthan, from Khasia hills to Kanyakumari, Kumaon, Assam, Bengal, Kokan, West peninsula, Kanara, and Chennai (Sriram et al., 2012; Santapau et al., 1955; Purohit et al., 1994).
  5. *C. glaucum* **Dalz.**, *C. orbidastrum* **Lindley**: Western India's Sahyadris mountain ranges (Verma et al., 2020).
  6. *C. undulatum* **Wall. Syn.**, *C. kbasianum* **Hooker**, *C. nepalense* (**Lindley**) **Baker**: India's eastern regions (Verma et al., 2020).
  7. *C. laxum* **R.Br.**: Deccan Peninsula, Kakti Hills, Dharwar, Belgaum (Verma et al., 2020).
  8. *C. malabaricum* **Baker**: Western Ghats as well as Nilgiris (Verma et al., 2020).
  9. *C. tuberosum* **Baker**: Travancore to Konkan regions of Kerla, the East Himalayan, West Bengal and Bihar (Verma et al., 2020).
  10. *C. kolhapurensis*: Sutagatti ghat, Karnataka (Verma et al., 2020).
  11. *C. glaucoides*: Tillari, Kolhapur (Verma et al., 2020).
  12. *C. bharuchae*: Adi chikkodi, Karnataka (Verma et al., 2020).
  13. *C. heynei*: Anamalai Hills, Tamilnadu (Verma et al., 2020).
  14. *C. indicum*: Nandi hills, Sultanpeth, Karnataka (Verma et al., 2020).
  15. *C. gothanense* (**Gothane plateau**): Sangali, Gothane Plateau (Verma et al., 2020).
  16. *C. tuberosum*: Ratnagir, Maharashtra (Verma et al., 2020).
  17. *C. gothanense* (**Kondushi plateau**): Kondushi Gargoti (Verma et al., 2020).
  18. *C. sharmae*: Munnar, Kerala (Verma et al., 2020).

## 8.8 SOIL AND CLIMATE

For optimal plant growths and tuber developments, *C. borivilianum* requires a warm, humid weather. Areas with annual rainfall of 50 to 150 cm (July to October) are deemed appropriate for cultivations (Kharif crops). Temperatures above 35°C are not conducive to growth, and a permeable soil with

a higher organic material contents aids in the formation of mushy tubers (Singh et al., 2003). The pH of 5 to 8 is excellent for safed musli, according to Paturde et al. (2000). The availability of macro- and micro-nutrients in *C. borivillianum* is greatly influenced by soil pH over 8 (Singh et al., 2001b; Bordia et al., 1995).

## 8.9 PROPAGATION

*C. Borivillianum* is mainly produced by vegetative methods rather than seed germination since seeds have a low germination rate (5 to 13%), although strongly linked species *C. tuberosum* germinating was found to be between 28% and 62% (Jat, 1993; Trivedi et al., 1989; Satyabrata et al., 2005; Shrivastava et al., 2001; Dalal et al., 1987). The germination rate of seeds procured from nature has been predicted should be between 11% and 24% (Bordia et al., 1990). Every seedling generates just 1 unit of plantation material and sprouts and establishes faster than tubers (95–100%). *C. borivillianum* is vegetatively propagated by separating discs from past year's output, every disc or sprout having 1 to 3 mushy tubers and weighing around five grams (Bordia et al., 1995). Because tuber cultivation is expensive and time-consuming, Kaur et al. (2009) predicted that steroidal hormones (cholesterol, testosterone) and plant growing regulators (kinetin, 24-epibrassinolide and indole butyric acid) would have a positive effect on the *C. borivillianum* seed's germinating rate. During some other study, rather than employing costlier hormones, tuberous roots of propagule have been pre-treated using K<sup>+</sup> salts to boost tuber's productivity (Tyagi et al., 2011).

## 8.10 PLANTING, IRRIGATION, AND NUTRIENT MANAGEMENT

Safed musli is a kharif crop that is sown in June following the first monsoon rainfall. About 400–500 kg seed tubers or nearly 30,000–35,000 fingers are required per acre (wet tuber with crown). *C. borivillianum* usually cultivated either earlier or afterwards the raining season has started, and the optimal time to sow differs depending on location. Chandra et al. (2007); Dalal et al. (1987); and Bordia et al. (1995) uncovered that depending on the soil quality and amount of rainfall, various kinds of beds (flat, furrow, and ridge, double, and triple rows raising beds) plus plants spacing effectively contributes to *C. borivillianum* productivity. For maximal fresh root productivity (3.46 tons/ha), Chandra et al. used a spacing 10 x 30 cm by means of 3,33,000 plants population per hector in a hot semi-arid ecoregion (Chandra et al.,

2007). The other workers recommended planting 15 x 30 cm or 10 x 30 cm apart (Dalal, 1987; Bordia et al., 1995). One gram (350-kilogram tubers per hectare) and 12.5 gram per unit were identified as the ideal planting material weights (Kothari et al., 2003, 2001; Paturde et al., 2000). Using 75% PAR (photosynthetically active radiation), the maximum arid root production of safed musli was reported by Yaseen et al. (2013). The musli tubers are properly cleansed in fresh water after getting pulled out from the ground. The tubers are divided into large and healthy fingers, with the little tubers being set aside for planting material the following seasons. The larger fingers are considered for processing. With a stainless-steel knife, the outer brownish skin is carefully peeled off then aired with in sunlight over 3–4 days. Those dried fingers are wrapped and sold in plastic bags.

Cow peas, pigeon pea, black gram, lablab bean, maize, sweet basil, bottle gourd, okra, mustard, and sacred basil are some of the intercrop's varieties of *C. borivilianum* (Chouhan et al., 2000; Bordia et al., 1995). Bottle gourd and Pigeon pea intercropping with safed musli offers high cumulative yield, financial profit, land equivalent ratio (LER), and economical returns. Those combinations increased bottle gourd and pigeon pea yields by 49.82 and 6.51 ton/ha, respectively, without lowering *C. borivilianum* root yields appreciably (Singh et al., 2011).

Rainy season grasses are the most common invaders of *C. borivilianum*, with *Cyperus rotundus* L. accounting for 62% of the overall weed populations, following by 33.9% of another kinds. The significant grass species inclusive of *Digitaria sanguinalis* (L.) Scop, *Dactyloctenium aegyptium* (L.) Beauv., *Eleusine indica* (L.) Gaertn, and *Phyllanthus amarus* Schum and Thonn, the only dicot species available by monsoon season. The wintery seasons weed includes *Gnaphalium indicum* L. and *Elitolus indica*, comprises of 17.4% and 82.6% of the weed growth, respectively. *Argemone maximana* L. (Satyanasi), *Parthenium hysterophorous* L. (Parthenium), *C. scariosus* (Nagarmotha), and Lantanas are immensely competitive and common weeds of the musli (Oudhia, 1996; Singh et al., 2003). After 15 to 20, 25 to 30, and 50 to 55 days following planting, manually weeding is particularly successful in lowering the weeds populations (Singh et al., 2001b).

The nutrient needs to grow safed musli, especially potassium (K), phosphorus (P), and nitrogen (N), are quite lower, according to research directed at Central Institute of Medicinal and Aromatic Plants. For increased tuber yields, multiple researchers suggested applying N, P<sub>2</sub>O<sub>5</sub>, and K<sub>2</sub>O at rates of 25 to 75, 60 to 65, and 2 to 30 kg/ha, respectively (Wankhade et al., 2004; Kothari et al., 2003; Singh et al., 2004a; Paturde et al., 2000). According



to the studies, applying NPK in ratios of 25:25:25, 45:60:60, and 50:50:50 kilogram per hectore, or farmyard manure (FYM) (10 to 40 tons/hectore) alone or in conjunction with NPK, considerably increases fresh tuber output (Chouhan et al., 2002; Ingle et al., 2004; Paturde et al., 2002; Kothari et al., 2003; Singh et al., 2001a; Chauhan et al., 2005; Wankhade et al., 2004). The intake of primary nutrients (NPK), the secondary nutrients (Fe, S, Mg, Ca), and the micro-nutrients (Mn, Zn, Cu) in safed musli is also influenced by the presence of water within the fields (Vijaya et al., 2009a).

### 8.11 PRUNINGS

Unnecessary branches, leaves, and stems must be eliminated to allow for air penetration within the crop.

### 8.12 PEST AND DISEASE MANAGEMENT

Safed musli is generally invaded by leaf blight, leaf spots, tuber rot, collar rot, and rust disorders (Table 8.3). Application of tridemorph (0.1%), propiconazole (0.1%), dithane M-45 (0.25%), Zineb + hexaconazole (0.2%) exhibited higher inhibitions in *Alternaria alternate* and *Colletotrichum dematium* growths (Tekade et al., 2009).

**TABLE 8.3** Diseases in *C. borivilianum*

Diseases	Causative Agents	References
Rust	<i>Uromyces clignii</i> and <i>U. loculiformis</i>	Mukherji et al. (1986)
Leaf spots	<i>Colletotrichum dematium</i> , <i>C. chlorophyti</i>	Mukherji et al. (1986)
Tuber rot	<i>Rhizoctonia bataticola</i> , <i>Fusarium solani</i>	Tekade et al. (2009); Raghavendra et al. (2005)
Collar rot	<i>Corticium rolfsii</i>	Singh et al. (2001a)
Leaf blights	<i>Colletotrichum dematium</i> , <i>C. capsici</i> , <i>Alternaria alternate</i>	Tekade et al. (2009); Sattar et al. (2006)
Tuber infections by roundworms	<i>Tylenchorhynchus brevilineatus</i> , <i>Helicotylenchus indicus</i> , and <i>Meloidogyne incognita</i>	Singh et al. (2004a)
Tuber infections by insecta	<i>Zonabris pustulata</i>	Oudhia (2000c)
Spoilage of tubers when storing	<i>Fusarium</i> spp., <i>Aspergillus</i> spp.	Bordia et al. (1995)

In brief, attempts should be made to standardize safed musli farming procedures. There's a wide opportunity to investigate the various growing parameters, based on the geographic region; in order to optimize maximal yield. The use of hormones in propagating might be a cause of concernment; as there might be probability of hormone accumulation in roots and examination may be essential prior to utilizing it as a medication. There's a call for broad exploration to discover economic and environment friendly substitute to promote cultivation by seeds. According to the literature, FYM can also considerably boost tuber yield, thus organic farming must be encouraged even if synthetic fertilizers are used. To get the most out of 2 crops in the same growing season, current farming practices such as intercropping should be used. To prevent the product from being lost, weeding, and pest control treatment must be done on a regular basis.

### 8.13 HARVESTING AND YIELD

The harvested bunch of tuberous roots is collected with sand stick, then heaped inside the shading. That heaped agitated usually in every 3 to 4 days for the following 8–12 days. Then tuber bunches are removed from sand and washed with water. Corpulent root usually detached out the bundle by exerting moderate force of the fingers and thumb on each root which leads to separation of the roots from the main bunch. Tuberous musli typically stored in vented racks in regulable temperatures of 25–31C and at 50–65% relative humidity and these tubers are used as a planting material for the next year (Manjunatha et al., 2004).

Average Safed musli yield is around 6–8 times of the planting material utilized. Around 80,000 plants are seeded each acre, with >70,000 plants survive up to harvest. If a plant's tuber weighs approximately 30 grams, an one acre field can provide 2,100 kg (21 quintal) fresh tubers and 400–500 kg of dry musli (Manjunatha et al., 2004). Tiwari (2006) conducted field experiment to evaluate yield and quality of *C. borivillianum* at Mandsaur (M. P.). Fresh fasciculated roots of Safed musli var. MCB-412 have been reported to have significantly greater yield characteristics and yield (3,980 kg ha<sup>-1</sup>). After application of 2 doses of NPK fertilizers, N45:P60:K60 followed by N30:P40:K40 production climbed to 3,640 kg per hectare. In another study, organically fertilizing with FYM with an extent of 10 to 20 tons per hector or vermicompost at a rate of 5 tons per hector were shown to be effective beneficial in elevating production of freshly fasciculated roots (2,036 kilogram–2,127 kilogram per hector, as compared to control 1,873 kilogram per hector). The 30 x 10 cm plant spacing also resulting in a much higher roots yield of 2,299 kg ha<sup>-1</sup>.

## 8.14 POST-HARVEST HANDLING AND STORAGE

As indicated by Manjunatha et al. processing is a part of marketing service. For small scale cultivation manual processing is carried out while large scale cultivation demands semi-automized or fully automized technology.

The musli tubers are properly cleansed in fresh water after being plucked outside the ground. The tubers are taken from the large and healthy fingers, and the little ones are set aside to utilized as planting materials for the following seasons. The larger fingers are considered for processing (Manjunatha et al., 2004). Musli tubers typically processed in the following stages:

1. **Peeling:** To save the tubers' most valuable component, the skin of cleansed and healthy tubers is painstakingly removed with special blades. A special skill is needful for this process.
2. **Drying:** The peeled fingers are wet and removal of moisture is necessary. To obtain better quality dry musli, they are dried in greenhouses with regulated sunlight. This process is carried out for 7 days to ensure complete drying. The moisture percentage of the dried tubers is diminished by around 20–25% of the moisture percentage of the wet tubers.
3. **Grading:** These of fully dried fingers in 'A,' 'B' and 'C' categories is carried out on the basis of their color and size.
4. **Packing:** Musli tubers being wrapped using hermetic polythene bags for preventing the entry of moisture.

CSIR institutes (most notably the Central Institute of Medicinal and Aromatic plants, Regional Research Laboratory, Jammu) and ICAR Institutions based on their All India Coordinated trials have standardized Agrotechnology Packages for various Indian medicinal species and *Chlorophytum borivilianum* and *C. tuberosum* have been, included in the list of such species (Natesh, 2001).

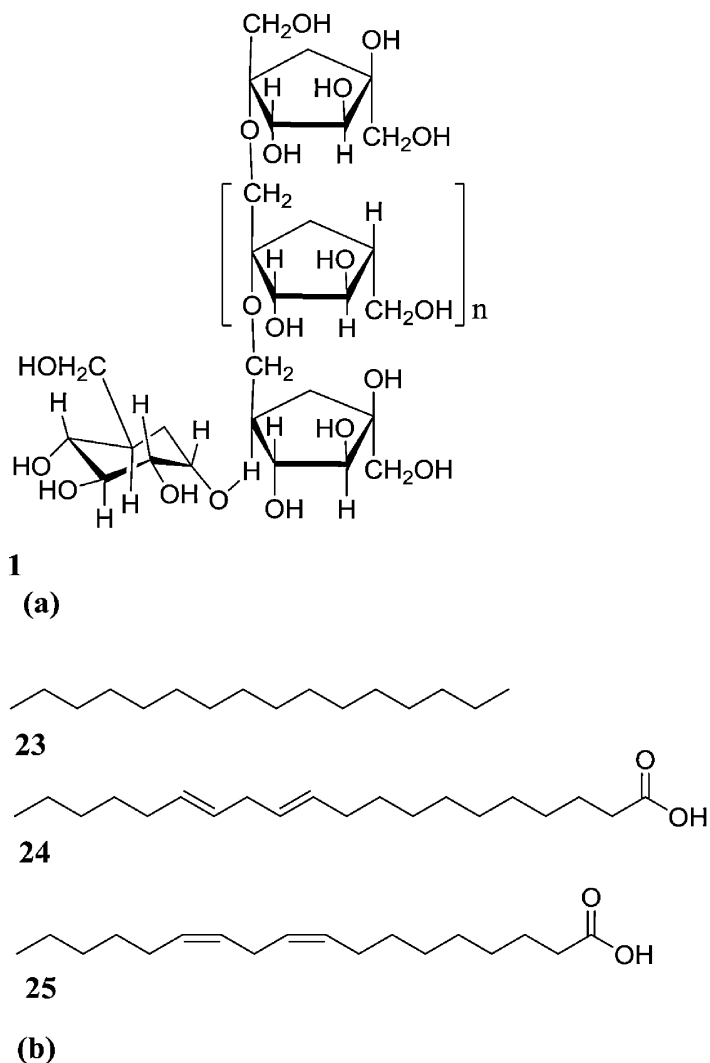
## 8.15 PROCESSING AND CHARACTERIZATION OF PHYTOCONSTITUENTS

Safed musli comprises wider range of phytoconstituents, for example, alkaloids, saponins, phenolic acids and flavonoids (Visavadiya et al., 2010). *C. borivilianum* roots contain 42% glucose, 8 to 9% proteins, 3 to 4% fiber, and 2 to 17% saponins (Wagle et al., 2000; Bordia et al., 1995). According to another researchers, the root contains roughly 30% alkaloids,

10 to 20% saponins, 40 to 45% polysaccharides (mucilage), and 5 to 7% proteins (Mayank et al., 2008; Deore et al., 2009a; Tandon et al., 1992). Moreover, musli additionally comprises of steroid, triterpenoids, vitamins, calcium, magnesium, potassium, gallo-tannins, rarer components like Cu, P, Zn, resins, and higher amount of sugars particularly glucose, fructose, galactose, sucrose, xylose, and mannose (Singh et al., 2012; Thakur et al., 2005; Kokate et al., 2004).

Despite the facts that there has been no specific scientific study on Chlorophytum species yet at the same time a few sapogenins, saponins, furostane as well as spirostane glycosides have already been procured in latest times (Kaushik, 2005). However, research on *C. borivilianum* secondary metabolites is limited. All things considered, there're a few literatures on qualitative phytochemical screenings in *C. borivilianum*. The composition of fasciculated safed musli root extracts was qualitatively investigated by research teams from the National Research Centre for Medicinal and Aromatic Plants in Boriavi, India, through contrasting identical *C. aurundinaceum* species' high performance thin layer chromatography (HPTLC) chromatograms. The majority of their peaks were comparable in both species (Phurailatpam et al., 2009). Kothari et al. (2004) were the first to reveal relative reverse phase high-pressure anion exchange (RP-HPAE) chromatography to identify inulin type 2→1 linked fructans. Later on Narasimhan et al. (2006) have effectively separated the fructo-oligosaccharide from safed musli for the first time and named it *O*-β-D-fructofuranosyl-(2→1)-(β-D-fructofuranosyl)<sub>n</sub>-(2→1)-α-D-glucopyranoside (n=5–30) (**1**) utilizing HPAE chromatography (Figure 8.1(a)). The extract and inulin type 2→1 related fructans displayed significant anti-diabetic potential in streptozotocin-induced diabetic rats. On the 21<sup>st</sup> day after the extract along with the compound (at 10 mg per kg dosing) administering, male albino rats revealed a significant drop in blood sugar levels (118.32 ± 3.56 mg/dL, 110.21 ± 4.22 mg/dL) when comparing with control (231.25 ± 3.03 mg/dL).

*C. borivilianum* is broadly utilized as a raw medication and there're various investigations have been conducted only on the plant's extracts. Their high saponin concentration is responsible for several vital biological functions (Liu et al., 2002; Estrada et al., 2000), ginseng root (*Panax ginseng*) is primarily found in underground tubers (Pullaiah, 2002; Marker et al., 1943); well known as an aphrodisiac and immunomodulator in ancient oriental therapy and throughout the world (Fukuda et al., 2000). *C. borivilianum*'s roots contain the most saponins of any Chlorophytum species found in India, and it's the most preferred species for treating sexual issues in male (Bordia



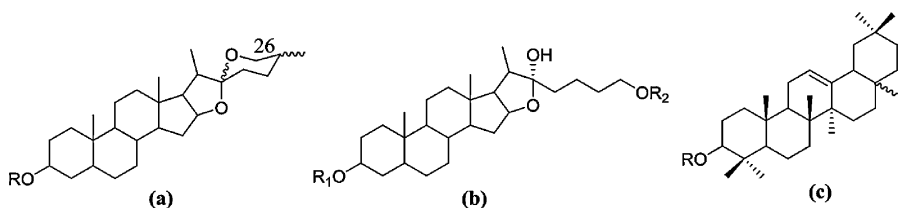
**FIGURE 8.1** Miscellaneous components procured from *C. borivilianum* (a) Fructans ( $n = 5\text{--}30$ ) (compound 1). (b) Longer chain hydrocarbon (compound 23) and fatty acids (compounds 24 and 25).

*Source:* Reprinted with permission from Khanam et al., 2013. Copyright 2013. Elsevier.

et al., 1995). In the context of quest for new saponins from musli, Acharya et al. (2008a, b, 2009) has undertaken substantial study, that is detailed in the ensuing texts.

### 8.15.1 SAPONINS

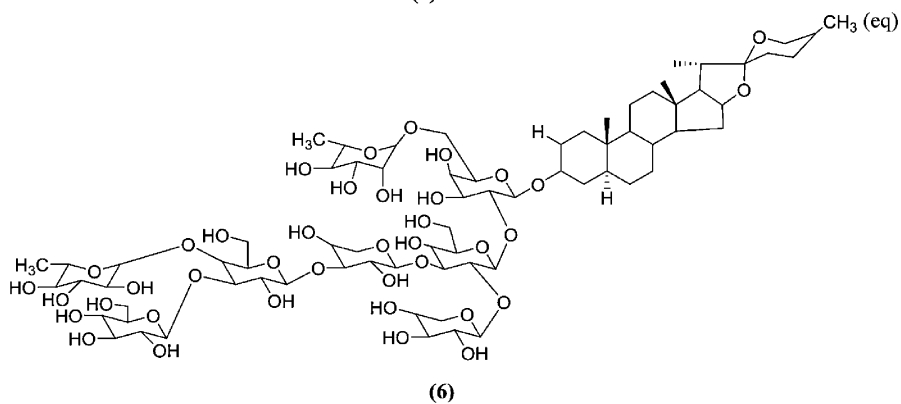
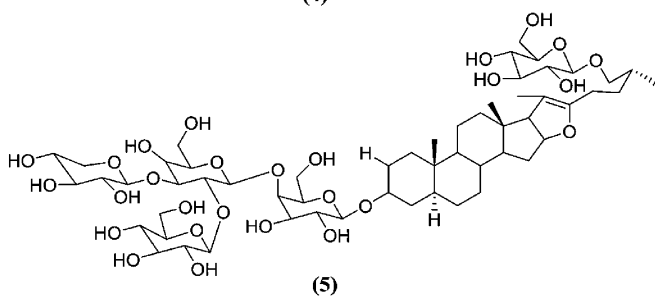
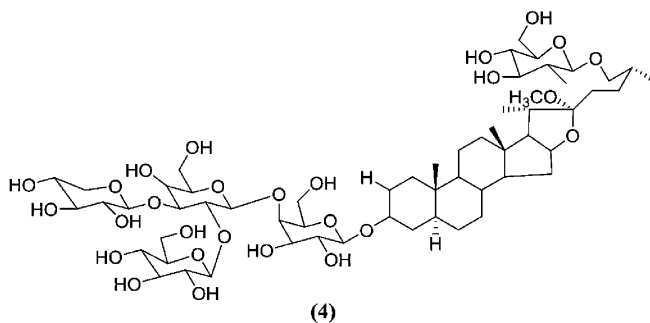
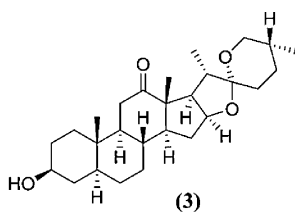
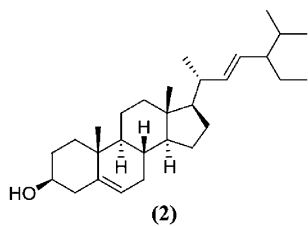
Many herbal remedies and folk treatments are said to include saponins, which are responsible for a variety of pharmacological effects (Sparg et al., 2004; Estrada et al., 2000). Saponins are distinguished from other glycosides by their surface-active characteristics (Tyler et al., 1981). So far, saponins of the steroidal furostane and spirostane kinds have been found in *C. borivilianum* (Bruneton, 1995) (Figure 8.2).



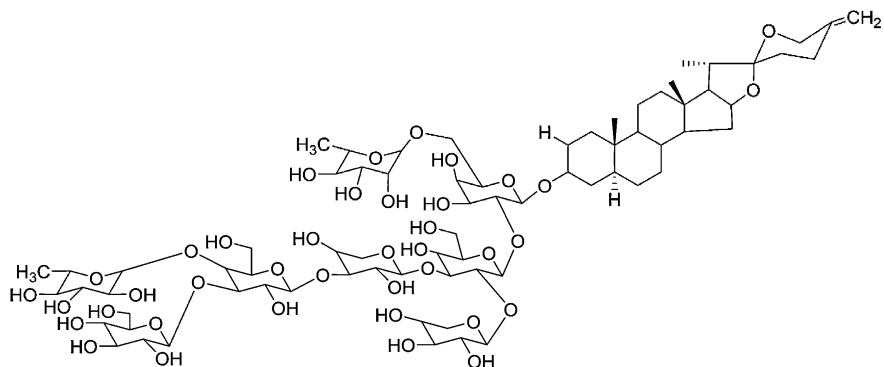
**FIGURE 8.2** Saponin's algycone skeletons. (a) spirostane (steroidal); (b) furostanes (steroidal); and (c) triterpenoid saponins [R: sugar moiety].

Source: Reprinted with permission from Khanam et al., 2013. Copyright 2013. Elsevier

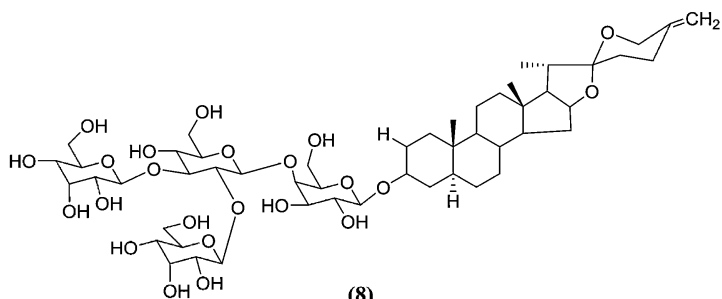
Saponins, stigmasterol (2), and hecogenin (3) (Figure 8.3) are *C. borivilianum*'s primary secondary metabolites, which have antioxidant, aphrodisiac, anticancer, and immune-boosting properties (Patel et al., 2011; Kumar et al., 2011). Stigmasterol has a structure comparable to testosterone and is principally responsible for safed musli's aphrodisiac action. Hecogenin, on the other hand, aids in the generation of anabolic hormones. *C. borivilianum*'s cultures have been shown to enhance the synthesis of medicinally relevant stigmasterol and hecogenin *in vitro* (Bathoju et al., 2012a, b). For qualitative investigation of saponins and to standardize the sapogenin and saponins of musli, scientists utilized high performance liquid chromatography and HPTLC (Joshi et al., 2000; Thakur et al., 2009a; Govindarajan et al., 2005). Sharma et al. (2012) have published an enhanced saponin detecting methodology. TLC plates were developed using a suspension of sheep erythrocytes, with saponin appearing as whiter spots against a pinkish background. Barve et al. (2010) determined the most effective conditions for extracting saponins from *C. borivilianum* tubers. According to this investigation, after 4 hours of extraction using water or methanol at 60°C having 30/60 mesh size, the saponin yield was appreciable.



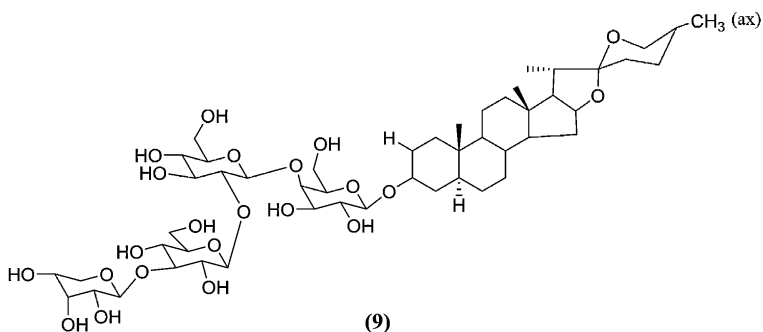
(Continued...)



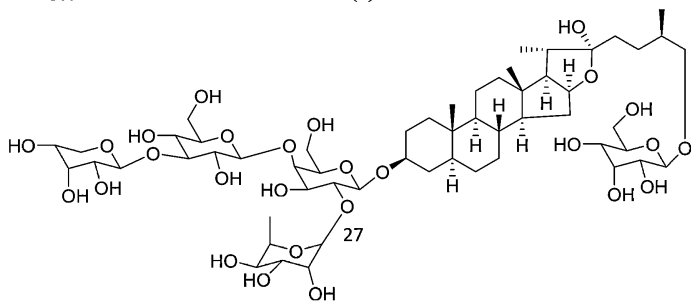
(7)



(8)



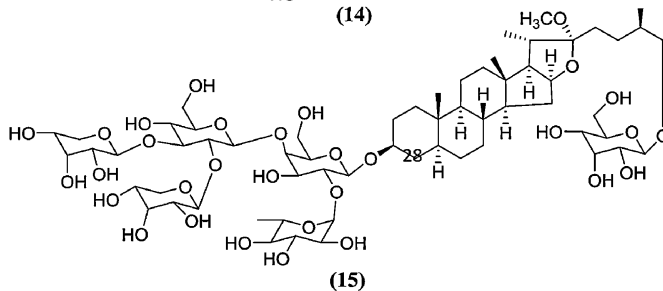
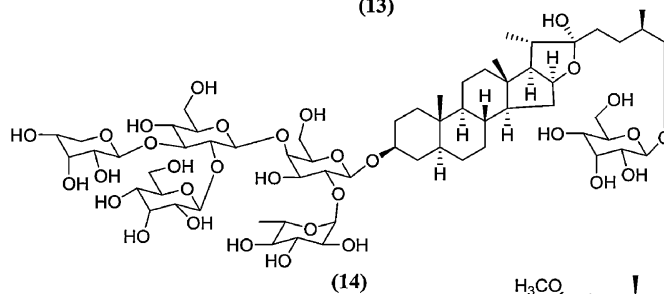
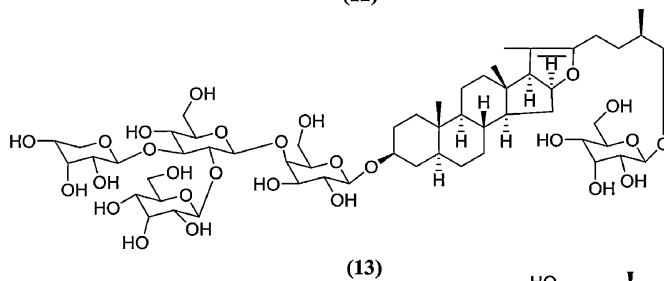
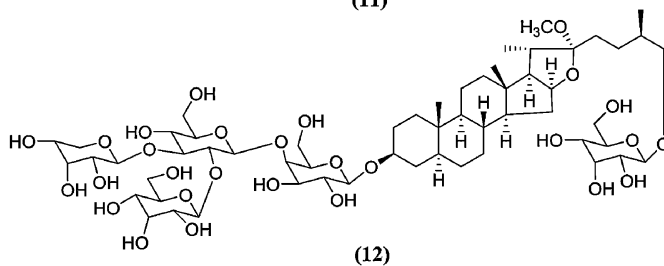
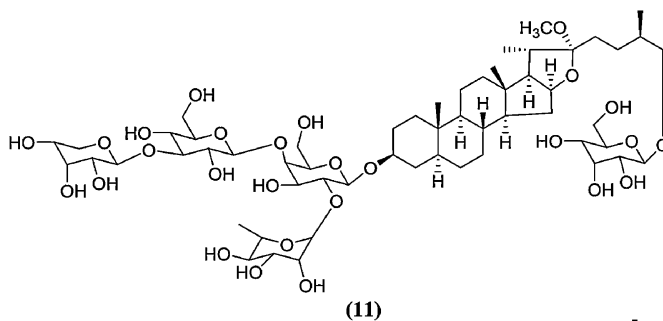
(9)



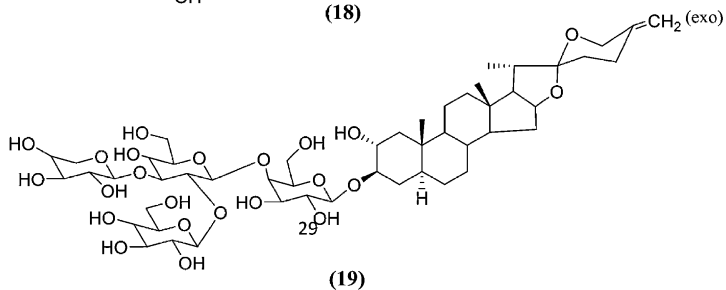
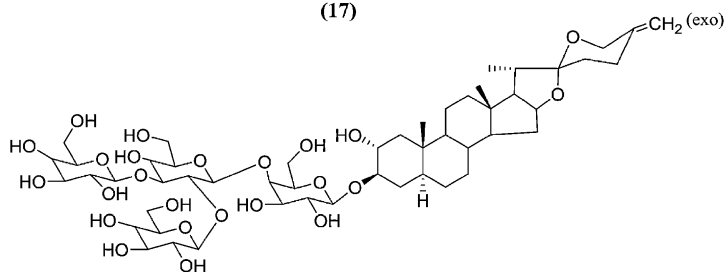
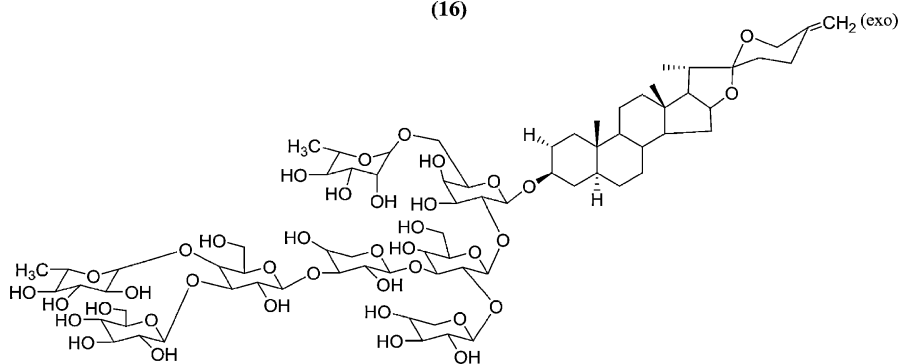
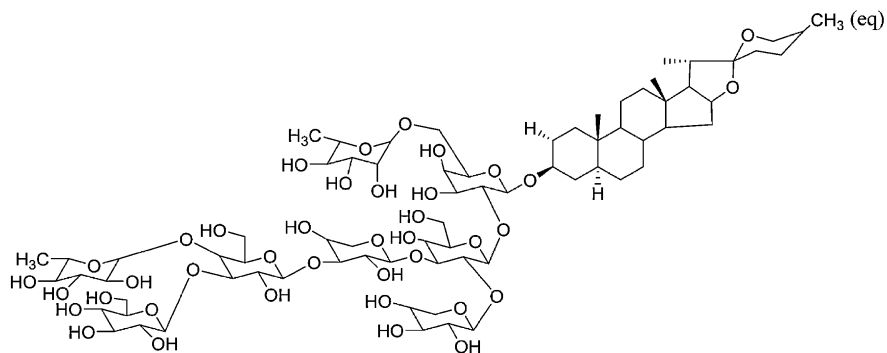
(10)

(Continued...)

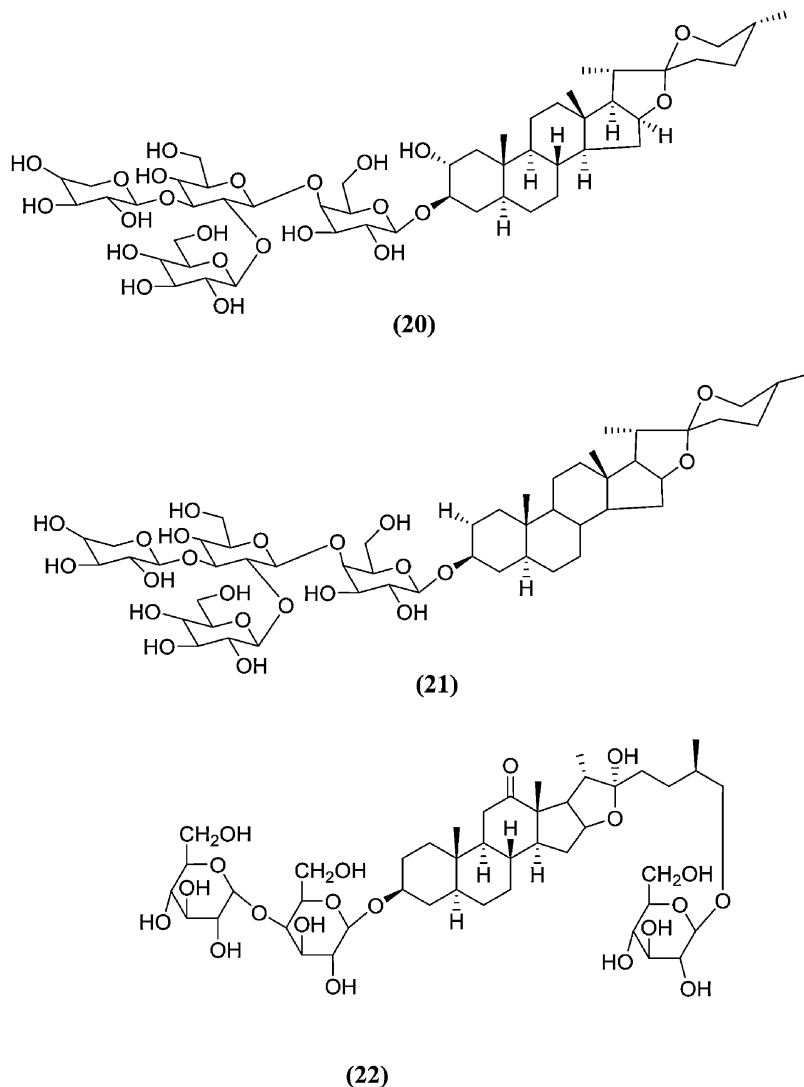




(Continued...)



(Continued...)



**FIGURE 8.3** Chemical structures of saponins procured from *C. borivilianum* (compounds 2–22).

Source: Reprinted with permission from Khanam et al., 2013. Copyright 2013. Elsevier

Only a few investigations on systematic saponin isolation have been documented to yet. Lately, Acharya et al. (2008a, b, 2009) recently resulted in the isolation of more than twenty steroidal saponins from the butanol (n-BuOH) fraction of an ethanolic roots extract (Table 8.4). Such saponins were separated and characterized utilizing various chromatographical steps

(MPLC, VLV, and FLASH) with RP-18 and silica gel columns, as well as different spectral techniques. Acharya et al. (2007) procured 4 new cytotoxic and insecticidal furostane saponins for the first time. Further research of the n-BuOH fraction of *C. borivillianum* root ethanolic extract resulted in isolating 6 newer steroidal saponins (Acharya et al., 2008a). Amongst those 6 newer steroidal saponins, 2 seemed to be furostanol (**4**, **5**) and 4 seemed to be steroidal spirostanol saponins (**6–9**). The furostanol saponins isolated seemed to be structurally analogs with almost the same sugar pattern. On human colon cancer HT-29 and HCT-116 cells, MTT (methyl thiazolyldiphenyl-tetrazolium bromide) cytotoxic assays of those components revealed modest cytotoxicity throughout the range of 9 to 85 µg per ml toward paclitaxel as control group. Such components were indeed moderately insecticidal against *Helicoverpa armigera*. In another survey conducted the same year by Acharya et al. (2008b), borivillianoside A-D (**10–13**), four novel furastanol saponins (steroidal), as well as 2 known compounds, were discovered (**14**, **15**). The sugar moiety in borivillianosides A and B has been recognized as rhamnose, galactose, as well as glucose. Whilst also borivillianosides C and D contained xylose, galactose, and glucose. The exact structures of the sugar moieties were confirmed by GC assessments and were D for xylose, galactose, glucose, and L as rhamnose. Acharya et al. (2009) recently procured 4 newer spirostane kind saponins, borivillianosides E-H (**16–19**) using ethanolic root's extracts together with two existing steroid saponins (**20**, **21**). In the MTT assay, borivillianoside H demonstrated strong toxic effects toward HT 29 (2.6 µM) and HCT 116 (0.38 µM) cell lines. Paclitaxel has been utilized as standard in the study, with IC<sub>50</sub> values of 3.6 nM for HT-29 and 1.1 nM for HCT 116 cell lines.

## 8.16 BIOLOGICAL ACTIVITIES OF *C. BORIVILIANUM*

Table 8.5 summarizes *in vitro* as well as *in vivo* pharmacologic benefits of extracts of *C. borivillianum* and components procured from it.

### 8.16.1 APHRODISIAC ACTIVITY

Thakur et al. published the first animal study on musli's aphrodisiac potential (Table 8.6) (Thakur et al., 2006). That research has been one of the first to provide scientific support for the use of musli conventionally as an aphrodisiac. The impact of ethanol extracts and saponin from roots of musli onto spermatogenesis and sexual behavior in albino rats was studied at 2 distinct doses, 100 mg as well as 200 mg per kilogram body weight (b.w.) (Thakur

**TABLE 8.4** Saponins Separated from *C. borivilianum* Roots (Khanam et al., 2013)

Compound Name	Activity	References
3 $\beta$ -hydroxy-24-ethyl 5,22-cholestadiene/Stigmasterol (2)	–	Deore et al. (2010)
5 $\alpha$ -Spirostan-3 $\beta$ -ol-12-one/Hacogenin (3)	–	Bathoju et al. (2012a, b)
(25R)-3 $\beta$ ,5 $\alpha$ ,22 $\alpha$ -22-methoxyfurostan-3,22,26-triol 3- <i>O</i> - $\beta$ -D-xylopyranosyl-(1 $\rightarrow$ 3)-[ $\beta$ -D-glucopyranosyl-(1 $\rightarrow$ 2)]- $\beta$ -Dglucopyranosyl-(1 $\rightarrow$ 4)- $\beta$ -Dgalactopyranosyl 26- <i>O</i> - $\beta$ -D-glucopyranoside (4)	Cytotoxic activity (9–85 $\mu$ g/ml), insecticidal activity (moderate)	Acharya et al. (2008a)
(25R)-3 $\beta$ ,5 $\alpha$ ,furost-en-20(22)-3,26-diol 3- <i>O</i> - $\beta$ -D-xylopyranosyl-(1 $\rightarrow$ 3)-[ $\beta$ -D-glucopyranosyl-(1 $\rightarrow$ 2)]- $\beta$ -Dglucopyranosyl-(1 $\rightarrow$ 4)- $\beta$ -D-galactopyranosyl-26- <i>O</i> - $\beta$ -D-glucopyranoside (5)	Cytotoxic activity (9–85 $\mu$ g/ml), insecticidal activity (moderate)	Acharya et al. (2008a)
(25R)-3 $\beta$ -5 $\alpha$ -spirostan-3-ol 3- <i>O</i> - $\alpha$ -L-rhamnopyranosyl (1 $\rightarrow$ 4)-[ $\beta$ -D-glucopyranosyl-(1 $\rightarrow$ 3)]- $\beta$ -D-glucopyranosyl-(1 $\rightarrow$ 3)- $\alpha$ -L-arabinopyranosyl-(1 $\rightarrow$ 3)-[ $\beta$ -D-xylopyranosyl-(1 $\rightarrow$ 2)]- $\beta$ -D-glucopyranosyl-(1 $\rightarrow$ 2)-[ $\alpha$ -L-rhamnopyranosyl-(1 $\rightarrow$ 6)]- $\beta$ -D-galactopyranoside (6)	Cytotoxic activity (9–85 $\mu$ g/ml), insecticidal activity (moderate)	Acharya et al. (2008a)
3 $\beta$ -5 $\alpha$ -spirost-ene-25(27)-3-ol 3- <i>O</i> - $\alpha$ -L-rhamnopyranosyl(1 $\rightarrow$ 4)-[ $\beta$ -D-glucopyranosyl-(1 $\rightarrow$ 3)]- $\beta$ -D-glucopyranosyl-(1 $\rightarrow$ 3)- $\alpha$ -L-arabinopyranosyl-(1 $\rightarrow$ 3)-[ $\beta$ -D-xylopyranosyl-(1 $\rightarrow$ 2)]- $\beta$ -D-glucopyranosyl-(1 $\rightarrow$ 2)-[ $\alpha$ -L-rhamnopyranosyl-(1 $\rightarrow$ 6)]- $\beta$ -D-galactopyranoside (7)	Cytotoxic activity (9–85 $\mu$ g/ml), insecticidal activity (moderate)	Acharya et al. (2008a)
3 $\beta$ -5 $\alpha$ -spirost-ene-25(27)-2,3-diol 3- <i>O</i> - $\beta$ -D-glucopyranosyl-(1 $\rightarrow$ 3)-[ $\beta$ -D-glucopyranosyl-(1 $\rightarrow$ 2)]- $\beta$ -D-glucopyranosyl-(1 $\rightarrow$ 4)- $\beta$ -D-galactopyranoside (8)	Cytotoxic activity (9–85 $\mu$ g/ml), insecticidal activity (moderate)	Acharya et al. (2008a)
(25S)-3 $\beta$ -5 $\alpha$ -spirostane-3-ol 3- <i>O</i> - $\beta$ -D-xylopyranosyl-(1 $\rightarrow$ 3)- $\beta$ -D-glucopyranosyl-(1 $\rightarrow$ 2)- $\beta$ -D-glucopyranosyl-(1 $\rightarrow$ 4)- $\beta$ -D-galactopyranoside (9)	Cytotoxic activity (9–85 $\mu$ g/ml), insecticidal activity (moderate)	Acharya et al. (2008a)
Borivilianoside A (10)	Negative cytotoxic activity against HCT 116 and HT 29 cell lines	Acharya et al. (2008b, 2009)
Borivilianoside B (11)	–	Acharya et al. (2008b)

**TABLE 8.4** (Continued)

Compound Name	Activity	References
Borivilianoside C ( <b>12</b> )	Negative cytotoxic activity against HCT 116 and HT 29 cell lines	Acharya et al. (2008b, 2009)
Borivilianoside D ( <b>13</b> )	–	Acharya et al. (2008b)
Tribuluside A ( <b>14</b> )	–	Acharya et al. (2008b)
(3 $\beta$ ,5 $\alpha$ ,22R,25R)-26-( $\beta$ -glucopyranosyloxy)-22-methoxyfurostan-3-yl O- $\beta$ -D-xylopyranosyl-(1 $\rightarrow$ 2)-O-[ $\beta$ -D-xylopyranosyl-(1 $\rightarrow$ 3)]-O- $\beta$ -D-glucopyranosyl-(1 $\rightarrow$ 4)-O-[ $\alpha$ -L-rhamnopyranosyl-(1 $\rightarrow$ 2)]- $\beta$ -D-galactopyranoside ( <b>15</b> )	–	Acharya et al. (2008b)
Borivilianoside E ( <b>16</b> )	–	Acharya et al. (2009)
Borivilianoside F ( <b>17</b> )	Negative cytotoxic activity against HCT 116 and HT 29 cell lines	
Borivilianoside G ( <b>18</b> )	Negative cytotoxic activity against HCT 116 and HT 29 cell lines	Acharya et al. (2009)
Borivilianoside H ( <b>19</b> )	Cytotoxic activity (0.38 $\mu$ M in HCT 116 cell lines and 2.6 $\mu$ M in HT 29 cell lines.	Acharya et al. (2009)
Gitogenin 3-O- $\beta$ -D-glucopyranosyl-(1 $\rightarrow$ 3)-[ $\beta$ -D-glucopyranosyl-(1 $\rightarrow$ 2)]- $\beta$ -D-glucopyranosyl-(1 $\rightarrow$ 4)- $\beta$ -D-galactopyranoside ( <b>20</b> )	–	Acharya et al. (2009)
25( <i>R</i> , <i>S</i> )-5 $\alpha$ -spirostan-3 $\beta$ -ol 3-O- $\beta$ -D-xylopyranosyl-(1 $\rightarrow$ 3)-[ $\beta$ -D-glucopyranosyl-(1 $\rightarrow$ 2)]- $\beta$ -D-glucopyranosyl-(1 $\rightarrow$ 4)- $\beta$ -D-galactopyranoside ( <b>21</b> ).	Negative cytotoxic activity against HCT 116 and HT 29 cell lines.	Acharya et al. (2009)
Chlorophytoside-I ( <b>22</b> )	–	Deore et al. (2010)

*Source:* Deore et al. (2010) procured a newer furostanol saponin, chlorophytoside-I (**22**), from methanol roots extract of safed musli. Furthermore, methanol root extracts produced stigmasterol (**2**) (Figure 8.3), a longer chain hydrocarbon, hexadecane (**23**), and 2 longer-chain fatty acids, 11,14 eicosadienoic acid (**24**) and linoleic acid (**25**) (Figure 8.1(b)).

et al., 2006). The increment in body as well as reproductive organ weight, as well as histological actions, reported a significant spermatogenic and anabolic effects in treated animals. There's a drastic reduction in mount, ejaculation, post-ejaculatory, and intromission latency, as well as an increment in mount frequency and affection to females, indicating improved sexual behavior. Thakur et al. (2007) investigated the pedunculation actions and sperm counts of istar strain male albino rats exposed to 'Vajikaran' plants like *Curculigo orchioides* Gaertn., *Asparagus racemosus* Willd., *Orchis latifolia* Linn., *Dactylorhiza hatagirea* (D. Don) Soo, and *C. borivilianum* (200 mg per kg b.w.). After 14 days of administering drugs, these 'Vajikaran' trees markedly increased *in vitro* sperm counts and pedunculatory behavior, as per their studies.

Thakur et al. (2008, 2009b, c, 2011a, b) researched various prospectus of sexual behavior and variables to assess the aphrodisiac potency of roots of *C. borivilianum* in the subsequent decade. Thakur et al. (2008) expanded on their past research on 'Vajikaran' trees and identified that those trees could prevent testicular damages caused by heat by dipping male scrotal sacs in steam baths ( $40^{\circ}\text{C} \pm 2$ , daily 15 minutes for 2 weeks). When rats were manifested to heat following by extract treatment, the intromission, mount, as well as ejaculation latency have been down regulated, whereas the frequencies for the same parameters were substantially restored while contrasted to the heat expositioned control group alone. Thakur et al. (2009c) observed comparative aphrodisiac actions of the trees (*C. orchioides* and *A. racemosus*) inclusive of *C. borivilianum* as a result of ongoing investigation on 'Vajikaran Rasayana' trees. Administering 200 mg per kg b.w. root water extracts resulted in a significant anabolic impact in treated albino male rats, as evaluated by weight gaining in the body along with reproduction system. The testosterone-alike impacts caused a major variation in animal sexual behavior. Thakur et al. (2011b) recently investigated the aphrodisiac impact of the same 'Vajikaran Rasayana' trees (*C. orchioides*, *A. racemosus*, *C. borivilianum*, and *D. hatagirea*) on various many sexual parameters at 100 mg per kg b.w. Visual observation was used to determine the sperm counts and penile erection index; spectrophotometric assay has been utilized to assess nitric oxide (NO) release and seminal fructose concentration in mouse macrophage RAW264.7 cells by respectively utilizing a reagent resorcinol and a commercially available Griess reagents kit. The *C. borivilianum* demonstrated a massively important response in all analyzed factors in both *in vivo* as well as *in vitro* investigations, i.e., specifically linked to erectile function.

Another study, Kenjale et al. (2008) found that aqueous *C. borivilianum* root extract had spermatogenic and aphrodisiac potential when compared to

the standard aphrodisiac drug, sildenafil citrate, also referred as Viagra®. This aphrodisiac analysis seemed to be truly revolutionary to include a comparative analysis with a positive control group. *C. borivilianum* at lesser dosage (125 mg per kg) increased libido, sexual vigor and sexual arousal (1, 7, 14, 21, and 28 days after treating). At a high dosage (250 mg per kg), all variables of sexual behavior improved on days 1, 7, and 14, but reached saturation after 2 weeks of treating. After 60 days of drug administering, the sperm counts risen exponentially at both dosages. As a result of those discoveries, it's determined that *C. borivilianum* could be used to treat specified types of sexual inadequacies, including oligospermia and premature ejaculation.

Thakur et al. (2009b) explored sexual dysfunctions throughout hyperglycemic albino male rats triggered by alloxan (100 mg per kg) or streptozotocin (50 mg per kg) in another study. The male diabetic rats were given *C. borivilianum* extract (200 mg per kg) and were tested for sexual behavior in the context of female rats, as well as other sexual variables. *C. borivilianum* extract treated animals showed enhanced diabetes-induced sexual dysfunctions. Howsoever, when compared to the normo-glycemic control group, the alloxan and streptozotocin treated groups had substantially lower sexual behaviors ( $P < 0.05$ ). Recently, the effectiveness of herbal compositions of medicinal herbs, which have conventionally been regarded to have aphrodisiac potency, was tested using barren male (Mahajan et al., 2012). After 40 and 90 days of treating, the herbal formulations of *Eulophia campestris* (Wall), *Mucuna pruriens* (Linn.), and *C. borivilianum*, improved significantly sperm quality and motility in oligozoospermic patients. In a recent report, methanol, and successive water extracts of 30 plant species, including *C. borivilianum*, were evaluated for their ability to inhibit Rho-kinase 2 (ROCK-II) (Goswami et al., 2012). ROCK-II inhibiting action of extracts was determined utilizing HTRFK in the EASE™ STK S2 Kit (Cisbio Bioassays), with Y-27632 serving as the standard inhibitor. The methanolic *C. borivilianum* fraction exhibited considerable inhibition (4.11%), whereas the subsequent aqueous extract found substantial percentage inhibition (40.50%). As a result, plant extracts that inhibit the ROCK-II enzyme could be used to treat of erectile dysfunctions (ED) via relaxation of corpora cavernosa. The researchers noted that the *C. borivilianum* aqueous extract's moderate action was because of the existence of steroidal saponins. *C. borivilianum*'s dual mechanisms of androgen synthesizing and ROCK-II inhibitory demonstrates its significance as a 'Vajikaran' herb (Thakur et al., 2009b; Goswami et al., 2012).

Basis of the observations of the preceding investigations, this is feasible to conclude that the study results on *C. borivilianum* provide an evidence base for its presumed conventional use as a 'Vajikaran Rasayana' tree. As a result



of the findings, the plant could even act as an aphrodisiac, and its use in Indian traditional medicinal system is reasonable. Only ethanol and aqua extracts of the root have been studied *in vivo* thus far, and there's scope to investigate numerous other extracts of the herb for aphrodisiac potency. The minimal tested dosing of crude extracts as well as fractions on animal models at 100, 125, 200, and 250 mg per kg body weight, are a major source of concern.

### **8.16.2 IMMUNOMODULATORY ACTIVITY**

Immunomodulators are synthetic or biological chemicals that have the ability for inducing, suppressing, or modulating different immune system aspects (Kumar et al., 2012), inclusive of both the innate and adaptive arms. Those trees classified as 'Rasayanas' are rejuvenators, nutraceuticals, and have high antioxidant activity. They have the inverse effects on oxidative stressors, causing the formations of various free radicals. They're primarily utilized to counter the issue of atherosclerosis, aging, rheumatoid arthritis, cancer, diabetes, Parkinson's disease, and autoimmune disease. The 'Rasayana' trees appear to have immunoadjuvant, immunostimulant, and immunosuppressive properties. The mechanism of immunomodulatory action occurs primarily through phagocytosis stimulations, then activation of macrophages (Kumar et al., 2012), then immunostimulatory effects on peritoneal macrophages, after that lymphoid cell stimulations, then cellular immune functions enhancing and non-specific cellular immune system effects, afterward antigen-specific immunoglobulin (IgG) productions, then increment in non-specific immunity factors along with NK cells, afterward reduction in chemotherapy-induced leukopenia, and lastly increment in interleukin-2 level along with circulatory total white cells (Chulet et al., 2010).

Thakur et al. (2007) investigated the immunomodulatory effects of safed musli root ethanol and sapogenin extracts (Table 8.6). The immunomodulatory action was determined by stimulating myelosuppression with azathioprine and measuring hematological and serological parameters after extract administering. When contrasted to sapogenins, the ethanol extract demonstrated greater activities. Extract therapies greatly improved survival over *Candida albicans* infections, with ethanol extracts achieving  $94 \pm 5.56\%$  survival and sapogenin extracts achieving  $88.86\% \pm 5.6$  survivability. In sapogenins and ethanol extract-treated groups, the increased sheep red blood cell (SRBC) mediated delayed-type hypersensitivity response (DTH), percent neutrophil adhesion, and *in vivo* phagocytosis with phagocytic indexes of around  $20\% (1.2 \pm 0.03)$  and  $25\% (1.36 \pm 0.51)$ , respectively. The immunomodulatory action of safed musli's aqueous extract,

non-polysaccharide, and polysaccharide fractions were tested (Thakur et al., 2011a). The comprehensive phytochemical analysis of *C. borivilianum* hot water-soluble root extracts resulted in the quantifying of approximately 60% w/w polysaccharides, primarily 31% inulin-kind fructans along with acetylated mannans (25%) (Thakur et al., 2009b). The effect of those extracts over natural killer (NK) cellular function was studied *in vitro*. Human PBMCs (peripheral blood mononuclear cells) isolates obtained out of total blood on a Ficoll-Hypaque density gradient have been evaluated for modulating of NK cell cytotoxicity against K562 cells upon absence or presence of varying quantities of every *C. borivilianum* fractions. In comparison with control, the polysaccharide fraction had a considerably higher influence ( $P < 0.01$ ) in enhancing NK cellular activities ( $98 \pm 2.5\%$  at  $5 \mu\text{g}$  per ml). Despite the fact that the aquatic extraction significantly activated NK cells ( $P < 0.05$ ), the majority of the effects emerged to be attributed by the polysaccharide fraction without one. The polysaccharide fraction ( $IC_{50} = 722.31 \text{ gm per ml}$ ) and aqueous extract ( $IC_{50} = 1219.67 \text{ gm per ml}$ ) were found to be non-toxic against sensitive mouse leukemia P388 cell lines in the study. Markedly increased HA titer readings of approximately 169.2, 174.3, and 168.6 have been obtained against control (147.6) in polysaccharide fraction and aqueous extract at 50 and 100  $\mu\text{g}$  per ml, respectively. Moreover, an *in vivo* study utilizing Wistar rats to evaluate humoral response to SRBCs and IgG-levels using enzyme linked immunosorbent assay (ELISA) revealed that aqueous *C. borivilianum* extract was beneficial in enhancing immune function. Aqueous extract administering resulted in a substantial increment ( $P < 0.01$ ) for IgG levels (1.93), trailed by polysaccharide fraction at 50 mg per kg b.w. ( $1.81 \pm 0.04$ ) and at 100 mg per kg b.w. ( $1.85 \pm 0.01$ ) (Thakur et al., 2011a).

In concluding, the accessible knowledge suggests that *C. borivilianum* could be utilized as an immunostimulant, and further research on different fractions of diverse extracts is meant to investigate the most effective immunostimulating fraction one. As of now, ethanol and aqua fractions at 50 mg, 100 mg, and 200 mg per kilogram b.w. have been studied, but more research on effective dosage is needed. Furthermore, previous research has validated the plant's conventional usage as a "Rasayana" in the Ayurvedic medicinal system.

### **8.16.3 ANTICANCER ACTIVITY**

Jamal reported on the effects of *C. borivilianum* on apoptosis and cell kinetics in human breast cancer cell lines (Jamal, 2005). Deore et al. tested the antiproliferative action of *C. borivilianum*'s methanol extract as well as

crude saponin fraction (Deore et al., 2010b). MTT and SRB assays were used in the study, accompanied by a DNA fragmentation assay. The study's finding suggests that crude *C. borivilianum* saponin fraction shows powerful anti-cancer potential exhibiting very higher percent inhibitions. Kumar et al. (2010) discovered antimutagenic, chemomodulatory, and antitumor action in *C. borivilianum* aqueous root extracts (Table 8.6). In preliminary investigations, mice were given different doses of root's fractions (100 mg, 400 mg, and 800 mg per kilogram b.w. daily) and no toxicity was noticed. The huge reduction in lipid per oxidation (LPO) levels as well as substantial increment in CAT (catalases), SOD (superoxide dismutase), and GSH (reduced glutathione) level contrasted to control was used to select a dose for anti-tumor studies. For seven days, 100  $\mu$ l of root extract (800 mg per kg b.w.) was administered orally every day at the pre-, peri-, and post-initiation stages of papillomagenesis. 7,12-dimethylbenz-(a)-anthracene (DMBA) carcinogen accompanied by croton oil (promoter) was used to induce papilloma in animals. When comparing with control (100%,  $43 \pm 0.94$ ), the extract significantly reduced cumulative number of papillomas (22,  $P < 0.001$ ) and tumor occurrence (56.7%,  $P < 0.001$ ). In an antimutagenic investigation, treated animals with *C. borivilianum*'s root fraction during the peri-, post-, and pre-initiation periods of papillomagenesis had a substantial decrease in overall chromosome deformities (46.11,  $P < 0.001$ ) as in context of chromosome and chromatid breaks, exchanges, dicentrics, centric rings, acentric fragments, pulverized cells, and polyploids when contrasted to controls ( $153.14 \pm 1.05$ ). In addition, the micronuclei analysis demonstrated a remarkable decrease in micronuclei quantity (14.91,  $P < 0.001$ ) when contrasted with control ( $25.43 \pm 0.89$ ). When the anticancer actions described in the literature are summarized, it's clear that the work done is somewhat preliminary and limited. Acharya et al. (2008a, 2009) conducted a few *in vitro* cytotoxic studies upon human colon carcinoma cells, and these studies could be expanded to include other cancer cell lines. The *in vitro* investigations are limited because they were conducted only on methanol extract and only few pure saponins separated from roots, which permit at least preliminary study toward diverse plant extracts. As a whole, rather than directly evaluating in animal models, the promising results from *in vitro* studies must be selected before conducting *in vivo* studies. As of now, only one *in vivo* experiment has been reported, with an efficient dose of 800 mg per kg b.w. and toxicological evidence suggesting the safety of the tested aqua extract at this concentration. Since there is little data on *in vivo* anticancer investigations, additional thorough studies should be conducted in the future.

#### **8.16.4 ANTIOXIDANT ACTIVITY**

The antioxidant properties of *C. borivilianum* aqueous extract (250 mg per kg for 1 week) was investigated using the lipid peroxidation assay and 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radical scavenging test. In a dose-depending basis, the musli aquatic extraction (250 mg per kilogram b.w. for 7 days) diminishes the level of DPPH free radicals as well as thio-barbituric acid reactive constituents (Kenjale et al., 2007).

The antioxidant potential of safed musli root extract was demonstrated once more utilizing chemicals/metals-mediated oxidation. While utilized in graded-dose (25–1,000 µg/ml), aqua extract possesses quite good antioxidant efficacy as indicated by powerful superoxide, hydroxyl, nitric oxide, DPPH, and ABTS [2,20-azinobis (3-ethylbenzothiazoline-6-sulfonic acid)] radicals scavenging action, as well as reducing capability (ferricyanide couple assays), metal chelating capability, and substantially suppressed the lipid peroxidation in mitochondrial fractions. Furthermore, water extract considerably lowered ( $P < 0.05$ ) copper-mediated human serum and LDL oxidation kinetics (Visavadiya et al., 2010).

When 100, 400, and 800 mg/kg body weight of safed musli root extract was contrasted to the control value, there was a considerable rise ( $p < 0.05$  to  $p < 0.001$ ) in the action of reduced catalase, glutathione, and superoxide dismutase, as well as a marked decline in the hepatic malondialdehyde level (Kumar et al., 2010).

#### **8.16.5 ANTIULCER ACTIVITY**

The alcoholic *C. borivilianum* extract has found to have ulcer-healing properties. To assess antiulcer action, a cold stress-mediated gastric ulceration model was used. The action of a single oral administration of alcohol extracts at a dosage of 200 mg per kg greatly decreases the ulcer index ( $p < 0.001$ ) when compared with the control group (Deore et al., 2009b).

#### **8.16.6 ANTISTRESS ACTIVITY**

The chronic cold restraint stress rat model was used for this action. In comparison to controls, chronic stress results in a considerable increment in plasma cholesterol, plasma glucose, triglyceride level, adrenal gland weight, and serum corticosterone level. Pre-treatment with aqua extract of safed musli at both dose levels (125 and 250 mg per kg) drastically decreased the emergence in plasma glucose levels, plasma cholesterol levels, implying

adaptogenic potency, triglyceride levels, adrenal gland hypertrophy, and serum corticosterone levels (Kenjale et al., 2007).

#### **8.16.7 ANTIDIABETIC ACTIVITY**

In streptozotocin-mediated diabetic animals, a fructo-oligosaccharide extracted from *C. borivilianum* extract was exhibited to have the greatest antidiabetic action, including blood glucose concentration of approximately 118.32 and 110.21, respectively, when contrasted with the control value of  $231.25 \pm 3.03$ , as well as modest antioxidant action (Narasimhan et al., 2006).

#### **8.16.8 ANTIMICROBIAL ACTIVITY**

Using the microbroth dilution assay, the antimicrobial potential of *C. borivilianum* was tested toward 8 bacteria and four pathogenic fungi. The extract's minimum inhibitory concentration was determined to be the minimum concentration that inhibited any visible microbial growth after treating with *p*-iodo-nitrotetrazolium violet. Aqueous *C. borivilianum* extract demonstrated antimicrobial action in the 75–1,200 gm per ml range (Dabur et al., 2007).

#### **8.16.8 LARVICIDAL ACTIVITY**

On the basis of  $LC_{50}$  and  $EC_{50}$  values, the larvicidal features of *C. borivilianum*'s saponin fractions (crude saponin, purified saponin, and methanolic) were investigated for the mosquito species *Culex quinquefasciatus*, *Aedes aegypti*, and *Anopheles stephensi*. All extracts have been reported to have larvicidal action, with the purified saponin fraction being the most efficient (Deore et al., 2009b). Another recently reported effect is the antiviral action (BHV-1 virus) of *C. borivilianum* extract, which demonstrates potential antiviral action (Goel et al., 2011). Utilizing the cup diffusion method, various extracts of *C. borivilianum* were tested for antibacterial action toward four bacteria: *E. coli*, *Staphylococcus aureus*, *Bacillus substalis* and *Pseudomonas aeruginosa*. Acetic acid extract has antibacterial activity against *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *E. coli*, and *Bacillus substalis* in the order of sensitivity (Sundaran et al., 2011).

### **8.17 PRECLINICAL AND CLINICAL TRIALS**

Many preclinical examinations have been performed on the sweet flag plant from a long period of time. The performed experiments for preclinical trials are described in Table 8.6.

**TABLE 8.5** Pharmacologic Activities of *C. borivilianum* *In Vitro* (Khanam et al., 2013)

Plant Part	Extract	Dose	Activity	Observations/Effects	In Vitro Models/Control/Standard	References
Roots	Ethanollic extract	100 µg/ml	Antioxidant activity	Scavenge DPPH (84.51%), hydroxyl radical (48.95%), ferryl bi-pyridyl complex (84.53%) along with the inhibition of lipid peroxidation (67.17%).	DPPH, ferryl bi-pyridyl complex and lipid peroxidation assay.	Govindarajan et al. (2005)
	Acetone and methanol extract	75–1,200 µg/ml	Antimicrobial activity	Strong activity with minimum inhibition concentration (MIC) was observed at 1,200 µg/ml and 600 µg/ml of acetone and methanol extract, respectively against <i>Staphylococcus aureus</i> . MIC of methanol extract reported at 600 µg/ml concentration against <i>Escherichia coli</i> , <i>Pseudomonas aeruginosa</i> .	Microbroth dilution assay.	Dabur et al. (2007)
	Aqueous extract	500–2,500 mcg/ml and 100–600 mcg/ml (dose-dependent manner) ( $P < 0.05$ )	Antioxidant activity	Low levels of DPPH free radicals (maximum 92% inhibition, $IC_{50} = 1,200$ mcg) and thio-barbituric acid reactive substances (maximum 66.91% inhibition, $IC_{50} = 300$ mcg).	DPPH and lipid peroxidation assay	Kenjale et al. (2007)
	Hydro-alcoholic, methanolic, and chloroform extract.	Not specified	Antimicrobial activity	Moderate activity against <i>S. aureus</i> , <i>Proteus vulgaris</i> , <i>E. coli</i> , <i>P. aeruginosa</i> , <i>Shigella sonni</i> , <i>Aspergillus niger</i> , <i>Candida albicans</i> .	Well diffusion method	Deore et al. (2007)
	Methanolic, hydroalcoholic, and aqueous extract	100, 250, 500, 1,000 µg/ml	Antioxidant activity	Methanolic extract showed good activity, while hydroalcoholic extract exhibited moderate and aqueous extract showed poor activity in both types of method.	DPPH and nitric oxide assay, without test sample as control, butylated hydroxyl anisole (BHA) as standard.	Deore et al. (2008)

**TABLE 8.5** (Continued)

Plant Part	Extract	Dose	Activity	Observations/Effects	In Vitro Models/ Control/Standard	References
	Methanolic extract, crude saponin extract and purified saponin fractions	Not specified	Larvicidal activity	All extracts are found to be larvicidal but purified saponin fractions were found more effective with LC <sub>50</sub> 4,000–3,850 ppm and EC <sub>50</sub> 4,872–2,290 ppm. Standard exhibited LC <sub>50</sub> 0.00547–0.00477 ppm and EC <sub>50</sub> 0.0036–0.0022 ppm.	Against mosquito species <i>Anopheles stephensi</i> , <i>Culex quinquefasciatus</i> , and <i>Aedes aegypti</i> , malathion as standard.	Deore et al. (2009b)
	Methanolic extract and crude saponin fraction	Not specified	Antiproliferative activity	Crude saponin extract of <i>C. borivilianum</i> has potential MTT and SRB assay, anticancer activity.	DNA fragmentation assay	Deore et al. (2010b)
	Aqueous and ethanolic extracts	25–1,000 µg/ml	Antioxidant activity	Aqueous extract exhibited high antioxidant activity evidenced by nitric oxide, superoxide, hydroxyl, DPPH, ABTS radical scavenging activity, reducing capacity, metal chelating ability, and suppressed lipid peroxidation in mitochondrial fractions as compared to ethanolic extract. Copper-mediated human serum and kinetics of LDL oxidation has been significantly decreased (P < 0.05) by aqueous extract.	DPPH, ABTS, FRAP assays	Vijaya et al. (2009a)
	Methanolic extract	10, 25, 50, and 100 mg/ml (dose dependent manner)	Anthelmintic activity	Causes paralysis as well as death.	Adult earthworms, <i>Pherentima posthuma</i> , 2% w/v gum acacia in distilled water as control, piperazine citrate as standard.	Panda et al. (2011b)
	Ethanolic extract	50–200 µg/disc	Antibacterial activity	Maximum antibacterial inhibition was obtained against <i>S. aureus</i> (12 nm) followed by <i>E. coli</i> , <i>P. aeruginosa</i> and <i>B. cereus</i>	Disc-diffusion method, streptomycin (50–200 µg/ disc) as positive control	Sriram et al. (2012)

TABLE 8.5 (Continued)

Plant Part	Extract	Dose	Activity	Observations/Effects	In Vitro Models/Control/Standard	References
	Aqueous, Tris-HCl, phosphate buffer, isopropanol, butanol-water, and acetone extract.	100 µl and 200 µl	Antibacterial activity	The extracts were tested against <i>S. aureus</i> , <i>E. coli</i> , Klebsiella, Proteus, and <i>P. aeruginosa</i> . Butanol-water extract showed maximum antibacterial activity against all the organisms (10–28 nm at 100 µl and 16–34 nm at 200 µl).	Agar-diffusion method, compared with positive and negative control.	Roselin et al. (2012)
	Methanol/ aqueous extract	50 µg/ml	Rho-kinase 2 inhibitory activity (used in management of erectile dysfunction).	Mean percent inhibition of ROCKII was found to be 4.11% and 40.54% for methanolic and successive aqueous extract, respectively.	ROCK-II inhibition assay by HTRF method, Y-27632 (4 ml of 375 nM) was used as the standard inhibitor.	Goswami et al. (2012)
Leaves	Petroleum ether, ethyl acetate, methanol, and water extract.	Not specified	Antioxidant activity	Not specified	DPPH and nitric oxide radical inhibition assays, ascorbic acid and quercetin as standard.	Chakraborty. (2008)
Leaves, nodes, and flowers	n-hexane, ethyl acetate and n-butanol fractions of methanolic extract	Not specified	Antimicrobial activity	Ethyl acetate extract of leaves showed strong activity against <i>S. aureus</i> , <i>S. epidermidis</i> , <i>A. niger</i> and <i>C. albicans</i> . Hexane and ethyl acetate extract of nodes exhibited activity against <i>Klebsiella pneumoniae</i> and <i>Microsporium gypseum</i> .	Disc diffusion method, DMSO as control, ampicillin (1 mg/ml) and voriconazole (1% w/v) as positive control.	Chakraborty et al. (2009)



**TABLE 8.5** (Continued)

Plant Part	Extract	Dose	Activity	Observations/Effects	In Vitro Models/ Control/Standard	References
Leaves and stem	Methanolic extract	250, 500, 1,000 mg/ml	Antimicrobial activity	Leaves and stem extract displayed concentration dependent antimicrobial properties far above ampicillin, zone of inhibition ranges from 10 to >20 mm. The extracts showed activity against <i>S. aureus</i> , <i>E. coli</i> , <i>B. cereus</i> , <i>A. niger</i> and <i>C. albicans</i> .	Disc diffusion method, DMSO as control, ampicillin (1 mg/ml) and voriconazole (1% w/v) as positive control.	
Peels of tubers	Aqueous extracts	Not specified	Antioxidant activity	Radical scavenging activity of aqueous extract was found to be dose dependent in all the assays.	DPPH, deoxyribose degradation, reducing power, ferrous ion chelation and lipid peroxidation assays	Kaur et al. (2010)
Plantlets	Water, ethanol, acetone, glacial acetic acid extract	DMSO stock concentration of 100 mg/ml	Antibacterial activity	Zone of inhibition ranges from 3–24 mm against human pathogenic bacteria, <i>S. aureus</i> , <i>Bacillus subtilis</i> , <i>E. coli</i> , and <i>P. aeruginosa</i> .	Agar cup diffusion method, DMSO as control.	Sundaram et al. (2011)
Leaves and roots	Saponin fraction from methanol extracts	1% w/v	Transdermal enhancer activity	Increased flux of the drug, permeability coefficient (Kp), cumulative amount release (Q24) and enhancement ratio (ER) against control.	Human cadaver skin, 3 ml saturated solution of pramipexole as standard.	Pawankumar et al. (2012)

**TABLE 8.6** Pre-Clinical Researches on *C. borivilianum*'s Roots (Khanam et al., 2013)

Extract	Dose	Activity	Observations/Effects	<i>In Vivo</i> Models/Control/Standard/Induction	References
Sapogenin and ethanolic extract	100 and 200 mg/kg b.w., p.o.	Androgenic activity and enhanced sexual behavior	Weight gain in the body and reproductive organs, reduction of mount, ejaculation, post ejaculatory and intromission latency. Increase in mount frequency and attraction towards female.	Male albino rats	Thakur et al. (2006)
Methanolic extract	100 and 200 mg/kg b.w., p.o.	Hypoglycemic and analgesic activity	Significant reduction of blood glucose after 2–4 hours of drug administration. Analgesic effect was observed after 45 and 30 minutes.	Normoglycemic and alloxan induced hyperglycemic rats, tail flick and tail immersion method.	Panda et al. (2007)
Powder	0.75 and 1.5 g root powder/rat/day for 4 weeks, p.o.	Hypolipidemic and antioxidant activity.	Increase in HDL cholesterol levels and decrease in plasma and hepatic lipid profiles. Increase in SOD and ascorbic acid levels.	Hyperlipemic and hypercholesteremic male albino rats, basal diet as normal control.	Vijaya et al. (2009a)
Aqueous extract	125 and 250 mg/kg b.w. for 7 days, p.o. (dose dependent manner).	Anti-stress activity	Reverted the elevated levels of plasma glucose, triglycerides, cholesterol, and serum corticosterone. Reduction in ulcer index, adrenal gland weight.	Chronic cold restrain stress model of Wistar albino rats, diazepam (1 mg/kg b.w.) as standard.	Kenjale et al. (2007)
	200 mg/kg b.w., p.o. (P < 0.05)	Pendiculatory activity and <i>in vitro</i> sperm counts.	Significant improvement in the pendiculatory activity and <i>in-vitro</i> sperm count as compared to control group after 30 minutes of incubation.	Wistar strain male albino rats	Thakur et al. (2007)
Ethanolic and sapogenin extract	200 mg/kg (ethanolic) and 100 mg/kg b.w. (sapogenin extract), p.o. (P < 0.05)	Immunomodulatory activity	Improved survival against <i>C. albicans</i> infection, increase in SRBC induced delayed-type hypersensitivity response (DTH), percent neutrophil adhesion and <i>in vivo</i> phagocytosis.	Male albino rats, carbon clearance method, administered vehicle as control, azathioprine (100 mg/kg b.w.) induced myelosuppression.	

**TABLE 8.6** (Continued)

Extract	Dose	Activity	Observations/Effects	<i>In Vivo</i> Models/Control/Standard/Induction	References
Methanolic, hydroalcoholic, and aqueous extract	500 mg/kg and 700 mg/kg b.w., p.o. (P < 0.01)	Anti-inflammatory activity	After 3 hours of treatment aqueous (700 mg/kg) and methanolic extract (500 mg/kg) exhibited maximum activity with 83.33 and 80.55% inhibition, respectively. While as, hydroalcoholic extract (500 mg/kg) showed inhibition of 50.55% against standard (91.11%).	Carragenan induced rat paw edema model, 2% v/v aqueous Tween 80 as control, diclofenac (5 mg/kg b.w.) as standard.	Deore et al. (2008)
Aqueous extract	125 and 250 mg/kg b.w., (in a dose dependent manner), p.o.	Aphrodisiac and spermatogenic activity.	Enhanced aphrodisiac action, increased libido, sperm count, sexual vigor and sexual arousal.	Male Wistar albino rats, Viagra® (sildenafil citrate, 4 mg/kg b.w.) as standard.	Kenjale et al. (2008)
	200 mg/kg b.w., p.o.	Prevent sexual dysfunction against heat induced testicular damage.	Prevented the decrease in sperm count in rats and protected the genital organs against physical stress, i.e., heat.	Male albino rats, administered vehicle as control, i.e., double distilled water (DDW).	Thakur et al. (2008)
Alcoholic extract	200 mg/kg b.w., p.o. (p < 0.001)	Anti-stress and anti-ulcer activity.	Alcoholic extract exhibited significant increase in swimming time and reduces the ulcer index compared to that of control.	Swim endurance stress, anorexic test, despair swim test and cold stress induced gastric ulceration model in albino rats.	Deore et al. (2009a)
Aqueous extract	200 mg/kg b.w., p.o. (P < 0.05), (P < 0.01)	Prevent sexual dysfunction in hyperglycemic rats.	Very low weight loss, low latency time, mount, and intromission as well as high ejaculation frequencies in <i>C. borivilianum</i> treated animals as compared to the diabetic control.	Hyperglycemic Wistar strain male albino rats induced with streptozotocin (50 mg/kg b.w.) or alloxan (100 mg/kg b.w.), polyvinylpyrrolidone solution (2%) as control.	Thakur et al. (2009b)

**TABLE 8.6** (Continued)

Extract	Dose	Activity	Observations/Effects	<i>In Vivo</i> Models/Control/Standard/Induction	References
	200 mg/kg b.w., p.o.	Aphrodisiac activity	Weight gain in the body and reproductive organs, reduction of mount, ejaculation, post ejaculatory and intromission latency. Increase in mount frequency, enhanced penile erection and reduced hesitation time.	Male albino rats.	Thakur et al. (2009c)
	250 and 500 mg/kg b.w., p.o. (P<0.01)	Anti-diabetic activity	Dose dependent reduction of blood glucose levels particularly 6 h after treatment. Reduction of the elevated level of blood glucose from 285.56 to 221.79 at 250 mg/kg b.w. and 281.62 to 206.82 g/dl at 500 mg/kg b.w. of extract.	Streptozotocin induced hyperglycemic Wistar rats of either sex, glibenclamide (3 mg/kg b.w.) as standard.	Mujeeb et al. (2009)
	800 mg/kg b.w./ day orally in double distilled water (P< 0.05–0.001)	Anti-tumor, antimutagenic, and chemo-modulatory activity at pre, peri, and post initiation stages of carcinogenesis.	Increase in activity of GSH, CAT, and SOD, decrease in the hepatic MDA level, decrease in cumulative numbers of papilloma, tumor incidence, tumor burden, tumor size and tumor weight. Increase in average latent period, decreased chromosomal aberration and micronuclei.	Albino mice, lipid peroxidation, SOD, CAT assay, chromosomal aberration assay, micronuclei assay, DMBA (100 µg/50 µl acetone per animal) followed by croton oil for papilloma induction.	Kumar et al. (2010)
Aqueous and alcoholic	300 and 100 mg/kg b.w., p.o. (P< 0.001)	Anti-arthritic activity	Aqueous extract (300 mg/kg b.w.) inhibited the rat paw edema by 43.61% and alcoholic extract (300 mg/kg b.w.) by 46.29% as compared to methotrexate (48.50%) after 21 days.	Freund's adjuvant induced arthritis in Wistar albino rats, DDW as control, methotrexate (0.75 mg/kg b.w.) as standard.	Deore et al. (2010c)

**TABLE 8.6** (Continued)

Extract	Dose	Activity	Observations/Effects	<i>In Vivo</i> Models/Control/Standard/Induction	References
Polysaccharide fraction derived from hot water extraction	50 and 100 mg/kg b.w., p.o.	Immunomodulatory activity	Extract exhibited non-toxicity against P388 cells, showed stimulation of NK cell cytotoxic activity toward K562 cells, humoral response to SRBCs and enhancement of IgG level.	Wistar strain albino rats of either sex ( <i>in vivo</i> ), cellular cytotoxicity against P388 cell lines and ELISA ( <i>in vitro</i> ), administered vehicle as control, chlorambucil, and curcumin was used as positive controls.	Kumar et al. (2012); Thakur et al. (2011a)
Methanolic extract	200 and 400 mg/kg b.w., p.o. (dose dependent manner)	Anti-ulcer activity	Exhibited free radical scavenging property, inhibition of acid secretory parameters and strengthening of gastric mucosa barrier.	Pyloric ligation and aspirin induced ulceration of albino rats.	Panda et al. (2011a)
Aqueous extracts	100 mg/kg b.w., p.o.	Aphrodisiac activity	Improved penile erection, sperm count, seminal fructose level ( <i>in vivo</i> ) and NO release in a mouse macrophage cell line (RAW264) ( <i>in vitro</i> ).	Wistar strain male albino rats	Thakur et al. (2011b)
Composite extracts of <i>Glycyrrhiza glabra</i> , <i>Withania somnifera</i> , <i>A. racemosus</i> , <i>C. borivilianum</i> and seeds of <i>Sesamum indicum</i>	5 g, administration for four weeks, p.o.	Hypolipidemic and antioxidant activity	Reduced plasma and hepatic lipid profiles. Increased fecal excretion of cholesterol, neutral sterol and bile acid. Increased hepatic HMG-CoA reductase activity, improved hepatic antioxidant status (CAT, SOD, ascorbic acid levels) and plasma antioxidant capacity with reduced hepatic lipid peroxidation.	Hypercholesterolemic rats	Vijaya et al. (2009a)

**TABLE 8.6** (Continued)

Extract	Dose	Activity	Observations/Effects	<i>In Vivo</i> Models/Control/Standard/Induction	References
Methanolic extract	200 mg/kg and 400 mg/kg b.w., p.o. (P < 0.05)	Anti-inflammatory activity	Administration of extract inhibited the edema starting from the first hour, showed a significant inhibitory effect on granuloma formation. Reduction of edema up to 35.06% and 42.8% (200 mg/kg b.w.) and 34.6% and 42.3% (400 mg/kg b.w.) after 2 and 3 h, respectively was observed. The standard drug exhibited 58.4% and 55.1% of inhibition respectively at 2 h and 3 h as compared to the control group.	Carrageenan induced rat paw edema (acute test model) and cotton pellet induced granuloma (chronic test model) in Wistar albino rats of either sex, indomethacin (10 mg/kg b.w.) as standard.	Panda et al. (2011c)
	200 and 400 mg/kg b.w., p.o. (P < 0.05)	Anti-pyretic activity	Significant dose dependent reduction in the yeast elevated rectal temperature was observed.	Fever induced Wistar strain of albino rats of either sex, paracetamol (150 mg/kg b.w.) as standard.	Panda et al. (2011d)
Aqueous extract	800 mg/kg b.w., p.o.	Hepatoprotective activity	Increased body and liver weight, increased ATPase levels and almost normal hepatoarchitecture were observed in combination group as compared to arsenic treated group.	Arsenic (NaAsO <sub>2</sub> ) intoxicated (4 mg/kg b.w.) male Swiss albino mice, reducing power assay, total ATPase assay, DDW as control.	Sharma et al. (2011)
Mixture (powder form) of <i>Mucuna pruriens</i> (Linn), <i>C. borivilianum</i> and <i>Eulophia campestris</i> (Wall)	40 days and 90 days treatment (in oligozoospermic males), o.p.	Improved semen quality and motility	Increased body weight, testis, epididymes weight, increased sperm motility, sperm density (40 days). Increased sperm density and motility in oligozoospermic patients as a result of elevation in serum testosterone levels (90 days). When compared with neem oil treated males there was significant reduction in almost all the parameters.	Neem oil treated male albino rats (infertile male).	Mahajan et al. (2012)

**TABLE 8.6** (Continued)

<b>Extract</b>	<b>Dose</b>	<b>Activity</b>	<b>Observations/Effects</b>	<b><i>In Vivo</i> Models/Control/ Standard/Induction</b>	<b>References</b>
Dietary supplement containing <i>C. borivilianum</i> and velvet bean	Subjects has consumed 1–3 capsule per day (each capsule 750 mg), for 28 days	Improves sleep quality	Improved sleep quality as evidenced by PSQI questionnaire ( $P < 0.05$ ). No adverse outcomes reported as indicated by heart beats, blood pressure and blood borne parameter.	Sleep quality of Men (n=9) and women (n=9) were assessed by Pittsburg sleep quality index (PSQI)	McCarthy et al. (2012)
Aqueous extract	800 mg/kg b.w./day for 30 days	Antioxidant and modulatory activity	Arsenic treatment of animals has increased LPO, cholesterol, acidic, and alkaline phosphatase level, significantly, and decreased sperm count, sperm motility, GSH, and serum testosterone level. Reverse trend was observed in combined treatment.	Sodium arsenite treated (4 mg/kg b.w.) Swiss albino mice (toxicity induced by arsenic), radical scavenging activity measured by DPPH assay.	Sharma et al. (2012)

## 8.18 COMMERCIAL/PHARMACEUTICAL PRODUCTS AVAILABLE

There are many herbal drug formulations obtainable in the market, manufactured by numerous companies, which are portrayed in Table 8.7 (Thakur et al., 2009a).

**TABLE 8.7** List of Some Commercial Products Containing *C. borivilianum* in India

Product Name	Manufacturer	Manufacturer Address
Natural Safed Musli tablets	Prakruti Bio-farms	Borivali, Mumbai
Safed Musli Powder, Eterna		
Safed Musli, Granule		
Musli Safed Capsules	Dehlvi Natural	New Delhi
Tribulus Power	Planet Ayurveda	Chandigarh
Safed Musli Power	Vadamalai Enterprises	India
Herbal Hills Safed Musli Powder	Royal Herbal Land Pvt. Ltd.	Mumbai, Maharashtra
Safed Musli	Nutriherbs	New Delhi
Musli Power-Xtra	World Viewer Dot Com Private Limited	Kerala
Safed Musli Capsule	Healthkart	Gurugram
Dabur Shilajit Gold	Dabur India	New Delhi
Swet Mushli Churna	Patanjali Ayurved	Haridwar
Safed Musli Capsules	Shudhanta Herbal	Noida, Uttar Pradesh

## 8.19 TECHNOLOGY TRANSFER/PATENTS

Two patents have been issued for the musli plant. The specifics are shown within Table 8.8.

### KEYWORDS

- **Asparagaceae**
- ***Chlorophytum borivilianum***
- **kharif crop**
- **larvicidal activity**
- **Liliaceae**
- **monocot**
- **pest and disease management**
- **phytoconstituents**
- **Safed Musli**



**TABLE 8.8** Patents Reported Over the Plant

<b>Work Done</b>	<b>Special Features</b>	<b>Status</b>	<b>Inventor Name</b>	<b>Date of Patent</b>	<b>References</b>
Nutraceutical contents and application techniques of <i>C. borivilianum</i> extracts	This patent unveils the functional ingredients of musli's extract and juice as well as technique of usage of the same as adaptogen, in strengthening or maximizing lascivious function, reduces stress, increases nitric oxide levels, antioxidant activity, sex hormone levels in male, restricting aging, and treat or prevent sexual dysfunctions.	Patented	Jayakumar Bhavanasi; Gopinathan Sinnathurai; Swati Kamlesh Kshirsagar	21/02/2008	Bhavanasi et al. (2008)
Safed Musli herbal composition in ready to drink form and process for preparation thereof	Ready-to-drink herbal safed musli formations containing musli extraction with some pharmaceutical grade additives such as sweeteners, flavors, preservatives, pH adjusting agents, viscosity adjusting agents, and distilled water, alternatively in conjunction with aloe vera syrup.	Patented	Laddha Kirti Shivchandraji; Bhavanasi Jaya Kumar; Barve Kalyani Himanshu	05/02/2010	Shivchandraji et al. (2010)

## REFERENCES

- Acharya, D., Mitaine-Offer, A. C., Kaushik, N., Miyamoto, T., & Lacaille-Dubois, M. A., (2007). Furostanol glycosides from the roots of *Chlorophytum borivilianum*. *Planta Medica*, 73, 430.
- Acharya, D., Mitaine-Offer, A. C., Kaushik, N., Miyamoto, T., Paululat, T., & Lacaille-Dubois, M. A., (2008b). Furostane-type steroidal saponins from the roots of chlorophytum. *Helvetica Chimica Acta*, 91, 2262–2269.
- Acharya, D., Mitaine-Offer, A. C., Kaushik, N., Miyamoto, T., Paululat, T., Mirjolet, J. F., Duchamp, O., & Lacaille-Dubois, M. A., (2009). Cytotoxic spirostane-type saponins from the roots of *Chlorophytum borivilianum*. *J. Nat. Prod.*, 72, 177–181.
- Acharya, D., Mitaine-Offer, A. C., Kaushik, N., Miyamoto, T., Paululat, T., & Lacaille-Dubois, M. A., (2008a). Steroidal saponins from the roots of *Chlorophytum borivilianum*. *Planta Medica*, 74, PB23.
- Banerjee, S., Banerjee, S., Jha, G. K., & Bose, S., (2021). *Barleria Prionitis L.: An Illustrative Traditional, Phytochemical, and Pharmacological Review*, 11(3), 258–274.
- Barve, K. H., Laddha, K. S., & Jayakumar, B., (2010). Extraction of saponins from Safed Musli. *Pharmacog. J.*, 2, 561–564.
- Bathoju, G., & Giri, A., (2012a). Production of medicinally important secondary metabolites (stigmasterol and hecogenin) from root cultures of *Chlorophytum borivilianum* (Safed Musli). *Recent Res. Sci. Tech.*, 4, 45–48.
- Bathoju, G., & Giri, A., (2012b). Production of stigmasterol and hecogenin from *in vitro* cultures of *Chlorophytum borivilianum*. *J. Pharmacog.*, 3(2), 101–103.
- Bentham, G., & Hooker, J. D., (1880). *Genera Plantarum* (Vol. III). 2<sup>nd</sup> Indian reprint 1988, Delhi periodical experts' book agency, India.
- Bhandary, M. J., Chandrashekhar, K. R., & Kaveriappa, K. M., (1995). Medical ethnobotany of the siddis of Uttara Kannada district, Karnataka, India. *J. Ethnopharmacol.*, 47, 149–156.
- Bhavanasi, J., Kshirsagar, S. K., & Sinnathurai, G., (2008). World intellectual property organization (PCT). *Nutraceutical compositions and methods of use of Safed Musli extracts*. WO2008020451A3.
- Bordia, P. C., & Jat, R. D., (1990). *Role of Stem Disc in Vegetative Propagation of Safed Musli (Chlorophytum spp.)*. The paper presented in the “National symposium on advances in plant sciences, current status and emerging challenges” held at M.L. Sukhadia University, Udaipur, India.
- Bordia, P. C., Joshi, A., & Simlot, M. M., (1995). Safed Musli. In: Chadha, K. L., & Gupta, R., (eds.), *Advances in Horticulture: Medicinal and Aromatic Plant* (pp. 429–451). Malhotra publishing house, New Delhi, India.
- Bruneton, J., (1995). *Pharmacognosy, Phytochemistry, Medicinal Plants*. Lavoisier Publishing, Paris.
- Chadha, Y. R., Gupta, R., & Nagarajan, S., (1980). Scientific appraisal of some commercially important plants of India. *Indian Drugs Pharma Industries*, 15, 7, 8.
- Chakraborty, G. S., & Aeri, V., (2009). Phytochemical and antimicrobial studies of *Chlorophytum borivilianum*. *Int. J. Pharm. Sci. Drug Res.*, 1, 110–112.
- Chakraborty, G. S., (2008). Antioxidant activity of the successive extracts of *Chlorophytum borivilianum* leaves. *Asian J. Chem.*, 20, 5782–5784.

- Chandra, R., Kumar, D., & Aishwath, O. P., (2007). Growth, yield, and nutrients uptake as influenced by different planting methods in Safed Musli (*Chlorophytum borivilianum*). *Indian J. Agric. Sci.*, 77, 558–560.
- Chauhan, H. S., Singh, A., Singh, H. P., Singh, A. K., Chattopadhyay, P., & Rajkumari, P. A., (2005). Influence of FYM and NPK fertilizers on growth and yield of Safed Musli (*Chlorophytum borivilianum*). *J. Med. Aromat. Plant Sci.*, 27, 280–282.
- Chetty, K. M., & Rao, K. N., (1989). Ethnobotany of Sarakallu and adjacent areas of Chittoor district. *Vegetos.*, 2, 5z, 52.
- Chouhan, G. G., & Joshi, A., (2002). *Response of Safed musli (Chlorophytum borivilinum)* (Vol. 1, pp. 505, 506). Extended summaries 2<sup>nd</sup> International Agronomy Congress, New Delhi.
- Chouhan, G. S., & Joshi, A., (2000). *Performance of Safed Musli (Chlorophytum Borivilianum) Under Various Cropping Systems Based on Kharif and Rabi Intercrops*. National symposium on agronomy: Challenges and strategies for the new millennium, GAU Campus, Junagadh.
- Chulet, R., & Pradhan, P., (2010). A review on rasayana. *Pharmacog. Rev.*, 3, 229–234.
- Dabur, R., Gupta, A., Mandal, T. K., Singh, D. D., Bajpai, V., Gurav, A. M., & Lavekar, G. S., (2007). Antimicrobial activity of some Indian medicinal plants. *Afr. J. Tradit. Complement. Altern. Med.*, 4(3), 313–318.
- Dalal, K. C., (1987). *C. borivilianum. Annual Report: Medicinal and Aromatic Plant Project*. GAU, Anand.
- Deore, S. L., & Khadabadi, S. S., (2008). Antiinflammatory and antioxidant activity of *Chlorophytum borivilianum* root extracts. *Asian J. Chem.*, 20, 983–986.
- Deore, S. L., & Khadabadi, S. S., (2009a). Screening of antistress properties of *Chlorophytum borivilianum*. *Pharmacologyonline*, 1, 320–328.
- Deore, S. L., & Khadabadi, S. S., (2009b). Larvicidal activity of the saponin fractions of *Chlorophytum borivilianum* santapau and Fernandes. *J. Entomol. Nematol.*, 1(5), 64–66.
- Deore, S. L., & Khadabadi, S. S., (2010a). Isolation and characterization of phytoconstituents from *Chlorophytum borivilianum*. *Pharmacog. Res.*, 2, 343–349.
- Deore, S. L., & Khadabadi, S. S., (2010b). Antiproliferative activity of saponin fractions of *Chlorophytum borivilianum*. *Pharmacog. J.*, 2, 29–33.
- Deore, S. L., & Khadabadi, S. S., (2010c). Effect of *Chlorophytum borivilianum* on adjuvant induced arthritis in rats. *Annals Biol. Res.*, 1, 36–40.
- Deshwal, R. K., & Trivedi, P. C., (2011). Effect of kinetin on enhancement of tuberous root production of *Chlorophytum borivilianum*. *Int. J. Innov. Biol. Chem. Sci.*, 1, 28–31.
- Elizabeth, K. G., (2001). Safed musli, a promising medicinal plant. *Ind. J. Arecanut, Spices, and Med. Plants.*, 5, 65–69.
- Estrada, A., Katselis, G. S., Laarveld, B., & Barl, B., (2000). Isolation and evaluation of immunological adjuvant activities of saponins from *Polygala senega* L. *Comp. Immunol. Microbiol. Infect. Dis.*, 23, 27–43.
- Fukuda, N., Tanaka, H., & Shoyama, Y., (2000). Isolation of the pharmacologically active saponin ginsenoside Rb1 from ginseng by immunoaffinity column chromatography. *J. Nat. Prod.*, 63, 283–285.
- Goel, A., Dash, S., Gupta, D., Pillai, A., & Yadav, S., (2011). Antiviral activity of few selected indigenous plants against bovine herpes virus-1. *J. Immunol. Immunopathol.*, 13(1), 30–37.
- Goswami, S. K., Pandre, M. K., Jamwal, R., Dethé, S., Agarwal, A., & Inamdar, M. N., (2012). Screening for Rho-kinase inhibitory potential of Indian medicinal plants used in management of erectile dysfunction. *J. Ethnopharmacol.*, 144, 483–489.

- Govaerts, R., (1999). *World Checklist of Seed Plants* (pp. 1–1532). 3(1, 2a and 2b). Continental Publishing, Deurne.
- Govindarajan, R., Sreevidya, N., Vijayakumar, M., Thakur, M., Dixit, V. K., Mehrotra, S., & Pushpangadan, P., (2005). *In vitro* antioxidant activity of ethanolic extract of *Chlorophytum borivilianum*. *Nat. Prod. Sci.*, 11, 165–169.
- Haines, H. H., (1961). *Botany of Bihar and Orissa* (Vol 3). Botanical Survey of India, Calcutta, India.
- Haque, R., Saha, S., & Bera, T., (2011). A peer reviewed of general literature on *Chlorophytum borivilianum* commercial medicinal plant. *International. J. Drug Dev. Res.*, 3, 140–155.
- Hooker, J. D., (1894). *The Flora of British India* (6<sup>th</sup> edn.). Dehra Dun, India.
- Hooper, A., (2002). *Kamasutra: Classic Love Making Techniques Reinterpreted for today's Lovers*; D.K. Publishing, Hongkong.
- Ingle, V. G., Wankhade, S. G., Jadhao, B. J., & Men, M. U., (2004). Effect of manure and fertilizer levels of yield of Safed Musli. *Agric. Sci. Digest.*, 24, 311, 312.
- Jamal, M. A., (2005). *Effects of Safed Musli on Cell Kinetics and Apoptosis in Human Breast Cancer Cell Lines*: International conference on promotion and development of botanicals with international co-ordination exploring quality, safety, efficacy, and regulation, School of natural product study, Jadavpur university, Kolkata, India.
- Jat, R. D., (1993). *Study on Variability and Micropropagation in Safed Musli (Chlorophytum Borivilianum)*. M.Sc. Thesis, Rajasthan College of Agriculture, Udaipur, India.
- Joshi, A., Ganesh, R., Sharma, A., & Audichya, P., (2000). Sapogenin content determination in *Chlorophytum borivilianum*. *Bionature.*, 20, 47–49.
- Kaur, R., Arora, S., & Thukral, A. K., (2009). Enhancing seed germination of *Chlorophytum borivilianum* Sant. and Fernand. with PGRs, steroidal hormones and Zinc. *Res. J. Seed Sci.*, 2, 32–39.
- Kaur, R., Thukral, A. K., & Arora, S., (2010). Attenuation of free radicals by an aqueous extract of peels of Safed Musli tubers (*Chlorophytum borivilianum* Santet Fernand). *J. Chinese Clin. Med.*, 5, 7–11.
- Kaushik, N., (2005). Saponins of chlorophytum species. *Phytochem Rev.*, 4, 191–196.
- Kenjale, R. D., Shah, R. K., & Sathaye, S. S., (2007). Anti-stress and anti-oxidant effects of roots of *Chlorophytum borivilianum* (Santa Pau & Fernandes). *Indian J. Exp. Biol.*, 45(11), 974–979.
- Kenjale, R., Shah, R., & Sathaye, S., (2008). Effects of *Chlorophytum borivilianum* on sexual behavior and sperm count in male rats. *Phytoth. Res.*, 22, 796–801.
- Khanam, Z., Singh, O., Singh, R., & Bhat, I. U. H., (2013). Safed Musli (*Chlorophytum borivilianum*): A review of its botany, ethnopharmacology, and phytochemistry. *J. Ethnopharmacol.*, 150(2), 421–441.
- Kirtikar, K. R., & Basu, B. D., (1956). In: Basu, L. M., (ed.), *Indian Medicinal Plants* (2<sup>nd</sup> edn.). Publishers, Allahabad.
- Kirtikar, K. R., & Basu, B. D., (1975). Liliaceae: Chlorophytum. In: Kirtikar, K. R., & Basu, D., (eds.), *Indian Medicinal Plants* (pp. 2508–2509). L.M. Basu, Publishers, Allahabad.
- Kokate, C. K., Purohit, A. P., & Gokhale, S. B., (2004). *Pharmacognosy* (29<sup>th</sup> edn.). Nirali Prakashan, Pune, India.
- Kothari, S. K., & Singh, K., (2001). Evaluation of Safed Musli (*Chlorophytum borivilianum* Santapau and Fernandes) germplasm. *J. Spices Aromat. Crops.*, 10, 147–149.
- Kothari, S. K., & Singh, K., (2003). Production technique for the cultivation of Safed Musli (*Chlorophytum borivilianum*). *J. Hortic. Sci. Biotech.*, 78(2), 261–264.

- Kothari, S. K., & Singh, K., (2004). Safed Musli (*Chlorophytum borivilianum*) revisited. *J. Med. Aromat. Plant Sci.*, 26, 60–63.
- Kumar, D., Arya, V., Kaur, R., Bhat, Z. A., Gupta, V. K., & Kumar, V., (2012). A review of immunomodulators in the Indian traditional health care system. *J. Microbiol. Immunol. Inf.*, 45, 165–184.
- Kumar, K. A., Chitra, V., Leela, K. V., & Soujanya, J., (2011). Evaluation of immunomodulatory effect of hydroalcoholic root extract of *Chlorophytum arundinaeaceum* Baker in mice. *Int. J. Pharm. Pharm. Sci.*, 3, 355–359.
- Kumar, M., Meena, P., Verma, S., Kumar, M., & Kumar, A., (2010). Anti-tumor, antimutagenic, and chemomodulatory potential of *Chlorophytum borivilianum*. *Asian Pac. J. Cancer Prev.*, 11(2), 327–334.
- Liu, J., & Henkel, T., (2002). Traditional Chinese medicine (TCM): Are polyphenols and saponins the key ingredients triggering biological activities? *Curr. Med. Chem.*, 9, 1483–1485.
- Mahajan, G. K., Mahajan, A. Y., & Mahajan, R. T., (2012). Efficacy of aphrodisiac plants towards improvement in semen quality and motility in infertile males. *J. Complement. Integr. Med.*, 9(1), 1–12.
- Mandal, G. D., & Nandi, A. K., (2012). Morphological and anatomical circumscription for the identification of two source plants of aphrodisiac medicine-*Chlorophytum borivilianum* Santapau and Fernandes and *Chlorophytum tuberosum* (Roxb.) Baker. *Int. J. Med. Aromat. Plants.*, 2, 406–410.
- Manjunatha, G., Tyagi, S. K., & Srinivasan, K., (2008). *Safed Musli: A White Gold*. In: Cultivation practices of Safed Musli. Agrobios, Chopasani Road, Jodhpur, India.
- Manjunatha, G., Tyagi, S., & Srinivasan, K., (2004). *Safed Musli: A White Gold*. Agrobios, India.
- Marker, R. E., Wagner, R. B., Ulchafer, P. R., Wittbecker, E. L., Goldsmith, D. P. J., & Ruoff, C. H., (1943). Sterols CLVII saponins LXIX. Isolation and structure of new steroidal saponinins. New sources for known saponinins. *J. Am. Chem. Soc.*, 65, 1199–1209.
- Mayank, T., & Dixit, V. K., (2008). A review on some important medicinal plants *Chlorophytum* spp. *Plant Rev.*, 2, 168–172.
- McCarthy, C. G., Alleman, R. J., Bell, Z. W., & Bloomer, R. J., (2012). A dietary supplement containing *Chlorophytum borivilianum* and velvet bean improves sleep quality in men and women. *Integr. Med. Insights.*, 7, 7–14.
- Meena, A. K., & Rao, M. M., (2010). Folk herbal medicines used by Meena community in Rajasthan. *Asian J. Trad. Med.*, 5, 19–31.
- Mishra, S. N., (2005). *Bhaisajya Ratnavali* (1<sup>st</sup> edn.). Chaukambha Surbharti Prakashan, Varanasi, India.
- Mujeeb, M., Khan, S. A., Ali, M., Mall, A., & Ahmad, A., (2009). Antidiabetic activity of the aqueous extract of *Chlorophytum borivilianum* L. in streptozotocin induced- hyperglycemic rats- A preliminary study. *J. Pharm. Res.*, 2, 5–53.
- Mukherji, K. G., & Bhasin, J., (1986). *Plant Diseases of India. A Source Book*. Tata McGraw Hill Publishing Co. Ltd, New Delhi.
- Nair, V. N., (1974). Cytological studies in *Chlorophytum bruchae*. *Curr. Sci.*, 43, 161, 162.
- Narasimhan, S., Govindarajan, R., Madhavan, V., Thakur, M., Dixit, V. K., Mehrotra, S., & Madhusudan, K. P., (2006). Action of (2→1) Fructo-oligo polysaccharide fraction of *Chlorophytum borivilianum* against streptozotocin-induced oxidative stress. *Planta Med.*, 72(15), 1421–1424.

- Natesh, S., (2001). The changing scenario of herbal drugs: Role of botanists. In: Rangaswamy, N. S., (ed.), *Phytomorphology* (pp. 75–96). Golden Jubilee Issue.
- Nayar, M. P., & Sastry, A. R. K., (1988). *Chlorophytum borivilianum*. In: Nayar, M. P., & Sastry, A. R. K., (eds.), *Red Data Book of Indian Plants* (Vol. 2, p. 1423). Botanical Survey of India, Calcutta.
- Negi, K. S., Tiwari, J. K., Gaur, R. D., & Pant, K. C., (1993). Notes on ethnobotany of five districts of Garhwal Himalaya, Uttar Pradesh, India. *Ethnobot.*, 5, 73–81.
- Oudhia, P., (1996). *Parthenium: A Curse for the Bio-diversity of Chattisgarh Plains*. National Reen. R.D. govt. P.G. College, Mandla, India.
- Oudhia, P., (2000c). Record of orange banded blister beetle *Zonabris pustulata* Thunb (*Coleoptera: Meloidae*) on Safed Moodli (*Chlorophytum borivilianum* L.). *Insect Environ.*, 6, 138–139.
- Oudhia, P., (2001). *My Experiences with Wonder Crop Safed Musli*. In: Souvenir. International Seminar on Medicinal Plants and Quality Standardization, VHERDS, Chennai.
- Oudhia, P., (2001a). *My Experiences with Wonder Crop Safed Musli* (pp. 9, 10). In Sovenier. International seminar on medicinal plants and quality standardization, VHERDS, Chennai, India.
- Panda, S. K., Das, D., & Tripathy, N. K., (2011a). Studies on anti-ulcer activity of root tubers of *Chlorophytum borivilianum* Santapau and Fernandes. *Int. J. Pharm. Sci. Rev. Res.*, 9, 65–68.
- Panda, S. K., Das, D., & Tripathy, N. K., (2011b). Evaluation of anthelmintic activity of *Chlorophytum borivilianum* Santapau and Fernandes. *Int. J. Res. Pharm. Biomed. Sci.*, 2, 676–679.
- Panda, S. K., Das, D., & Tripathy, N. K., (2011c). Anti-inflammatory potential of *Chlorophytum borivilianum* Sant. and Fern. root tubers. *J. Global Trends Pharm. Sci.*, 2, 242–251.
- Panda, S. K., Das, D., & Tripathy, N. K., (2011d) A study on antipyretic activity of *Chlorophytum borivilianum* Sant. and Fern. root tubers. *Int. J. Pharm. Res. Dev.*, 3, 153–156.
- Panda, S. K., Si, S. C., & Bhatnagar, S. P., (2007). Studies on hypoglycaemic and analgesic activities of *Chlorophytum borivilianum* Sant and Ferz. *J. Nat. Remedies*, 7, 31–36.
- Paques, M., & Boxus, P., (1987). A model to learn 'vitrification,' the root stock apple M.26. Present results. *Acta Horticulturae.*, 212, 193–219.
- Patel, D. K., Kumar, R., Prasad, S. K., & Hemalatha, S., (2011). Pharmacologically screened aphrodisiac plant—A review of current scientific literature. *Asian Pac. J. Trop. Biomed.*, 1, S131–S138.
- Patil, D. A., (2000). *Flora of Dhule and Nandurbar Districts*. Bishen Singh Mahendra Pal Singh Publishers, Dehra Dun, India.
- Paturde, J. T., Wankhade, S. G., Khode, P. P., Chatol, P. U., Deo, D. D., & Bhuyar, S. A., (2002). Effect of organic manures and plant population on yield of Safed Musli (*Chlorophytum borivilianum*). *Agric. Sci. Digest.*, 22, 51, 52.
- Paturde, J. T., Wankhade, S. G., Dipali, D., & Khode, P. P., (2000). Safed Musli an important medicinal plant. *Indian Farming.*, 49, 8, 9.
- Pawankumar, G., & Shiradkar, M., (2012). Evaluation of synergistic effect of *Chlorophytum borivilianum* extract on transdermal delivery of pramipexole with its mechanism of action. *Advances Appl. Sci. Res.*, 3, 261–267.
- Phurailatpam, A. K., Geetha, K. A., Gajbhiye, N. A., Saravanan, R., & Maiti, S., (2009). Comparative study of *Chlorophytum borivilianum* Sant. and Fernand. and *C. arundinaceum*

- baker - Two 'safed musli' species used as vital tonics in Indian system of medicine. *Phytomorphology: An International Journal of Plant Morphology*, 59, 77–81.
- Pullaiah, T., (2002). *Medicinal Plants of India*. Regency Publications, New Delhi.
- Puri, H. S., (2003). *Rasayana—Ayurvedic Herbs for Longevity and Rejuvenation*, Taylor, and Francis Group Publishers: London.
- Purohit, S. D., Dave, A., & Kukda, G., (1994). Micropropagation of Safed Musli (*Chlorophytum borivilianum*), a rare Indian medicinal herb. *Plant Cell, Tissue, and Organ Culture.*, 39, 93–96.
- Purohit, S. S., & Prajapati, N. D., (2003). *Agro's Color Atlas of Medicinal Plants*. Agrobios Publications, Jodhpur.
- Pushpangadan, P., (2005). *In vitro* antioxidant activity of ethanolic extract of *Chlorophytum borivilianum*. *Nat. Prod. Sci.*, 11, 165–169.
- Raghavendra, V. B., Lokesh, S., Kumar, T. V., & Shetty, H. S., (2005). Compatibility of phyton with common fungicide and their role on the yield of Safed Musli. *World J. Agric. Sci.*, 1, 62–64.
- Rai, P. K., & Lalramnghinglova, H., (2011). Ethnomedicinal plants of India with special reference to an Indo-Burma hot spot region: An overview. *Ethanobot. Res. Appl.*, 9, 379–420.
- Roselin, P., & Raj, M. S., (2012). *In vitro* testing of the antibacterial activity of root extracts of *Chlorophytum borivilianum* against organisms causing postnatal infections. *Res. Rev: J. Herbal Sci.*, 1, 24–31.
- Santapau, H., & Fernandes, R. R., (1955). A new species of *Chlorophytum* from Salsette Island. *J. Bombay Nat. Hist. Soc.*, 3, 898–900.
- Sattar, A., Alam, M., Khaliq, A., Shukla, R. S., & Khanuja, S. P. S., (2006). First report of leaf blight of *Chlorophytum borivilianum* caused by *Colletotrichum capsici* in northern India. *Plant Pathol.*, 55, 301, 302.
- Satyabrata, M., & Geetha, K. A., (2005). Characterization, genetic improvement, and cultivation of *Chlorophytum borivilianum*-an important medicinal plant of India. *Plant Genet Resour.*, 3, 264–272.
- Sebastian, M. K., & Bhandari, M. M., (1988). Medicinal plant Flore of Udaipur district, Rajasthan. *Bull. Med. Ethanobot. Res.*, 5, 133, 134.
- Sharma, G., & Kumar, M., (2012). Antioxidant and modulatory role of *Chlorophytum borivilianum* against arsenic induced testicular impairment. *J. Env. Sci. (China)*, 24, 2159–2165.
- Sharma, S. K., & Kumar, M., (2011). Hepatoprotective effect of *Chlorophytum borivilianum* root extract against arsenic intoxication. *Pharmacologyonline.*, 3, 1021–1032.
- Sharma, S. K., Chuneekar, K. C., & Paudal, K., (1999). *Plants of Sharangdhar Samhita*. RAV Publications, New Delhi.
- Sheriff, A., & Chennaveeraiah, M. S., (1972). Karyomorphology of four diploid species of *Chlorophytum*. *Nucleus*, 15, 39–45.
- Shivchandraji, L. K., Kumar, B. J., & Himanshu, B. K., (2010). World intellectual property organization (PCT). *Safed Musli Herbal Composition in Ready to Drink Form and Process for Preparation Thereof*. 238212.
- Shrivastava, D. K., Mishra, P. K., Gangrade, S. K., & Verma, S., (2001). Studies on propagation methods and dormancy in Safed Musli (*Chlorophytum spp.*). *J. Med. Aromat. Plant Sci.*, 22, 275–276.

- Singh, A., & Chauhan, H. S., (2003). Safed Musli (*Chlorophytum borivilianum*): Distribution, biodiversity, and cultivation. *J. Med. Aromat. Plant Sci.*, 25, 712–719.
- Singh, A., Khanuja, S. P. S., & Singh, S., (2003). Agronomic practices for the production of Safed Musli (*Chlorophytum borivilianum* Santapau and Fernandes). *Nat. Prod. Radiance.*, 2, 308–313.
- Singh, A., Khanuja, S. P. S., Singh, S., Singh, U. B., Gupta, S. K., & Singh, M., (2001b). *Prospects of Safed Musli (Chlorophytum borivilianum) Cultivation in Sub-tropical North India: Initial Observations and Future Research Needs*. National research seminar on herbal conservation, marketing, and utilization with special emphasis on Chhattisgarh, the herbal State, Sristhi Herbal Academy and Research Institute (SHARI), Raipur, India.
- Singh, A., Singh, S., Patra, D. D., Singh, M., Arya, S. J. K., & Khanuja, S. P. S., (2004b). Cultivation and processing techniques of Safed Musli (*Chlorophytum borivilianum*). *J. Med. Aromat. Plant Sci.*, 26, 70–76.
- Singh, D., (1974). *Udwijj Aushadhravya, Unani Dravyagunadarsh in Hindi*, India.
- Singh, D., Pokhriyal, B., Joshi, Y. M., & Kadam, V., (2012). Phytopharmacological aspects of *Chlorophytum borivilianum* (Safed Musli): A review. *Int. J. Res. Pharm. Chem.*, 2, 853–898.
- Singh, H. B., Singh, A., Tripathi, A., Tiwari, S. K., & Johri, J. K., (2001a). Collar rot of *Chlorophytum borivilianum* caused by *Corticium rolfsii*: A new disease. *Bulletin OEPP/EPPO Bulletin.*, 31, 112–113.
- Singh, M., Pandey, R., & Singh, U. B., (2004a). Development of cultivation practices of Safed Musli (*Chlorophytum borivilianum*) for sub tropical north India. *J. Trop. Med. Plants*, 44–49.
- Singh, M., Singh, A., Singh, S., Tripathi, R. S., & Patra, D. D., (2011). Production potential and economics of Safed Musli (*Chlorophytum borivilianum*) under intercropping system. *Arch. Agron. Soil Sci.*, 57, 669–678.
- Singh, R., Singh, S., Dosi, S., Kabra, M., & Gupta, R., (2013). Safed Musli (*Chlorophytum borivilianum*) a unique gift of ayurveda as Divya Aushadhi. *Asian J. Pharm. Res. Dev.*, 1, 117–124.
- Singhania, A., (2003). Biovedic cultivation of Safed Musli (*Chlorophytum borivilianum*). *Agrobios Newsletter*, 3, 22, 23.
- Somanath., (2008). *Response of Safed Musli (Chlorophytum Borivilianum) to Npk, Fym, and Mulching in Northeast Transitional Zone of Karnataka*. Thesis, Department of agronomy, College of Agriculture, Dharwad University of Agricultural Sciences, Dharwad.
- Sparg, S. G., Light, M. E., & Van, S. J., (2004). Biological activities and distribution of plant saponins. *J. Ethnopharmacol.*, 94, 219–243.
- Sriram, S., Meenaa, V., & Kavitha, S. J., (2012). Evaluation of antibacterial activity of *Chlorophytum borivilianum* against selected pathogens. *J. Res. Antimicrob.*, 1, 28–31.
- Sundaram, S., Dwivedi, P., & Purwar, S., (2011). Antibacterial activities of crude extracts of *Chlorophytum borivilianum* to bacterial pathogens. *Res. J. Med. Plants*, 5, 343–347.
- Sundaran, S., Dwivedi, P., & Purwar, S., (2011). Antibacterial activity of crude extract of *Chlorophytum borivilianum* to Bacterial pathogens. *Res. J. Med. Plant.*, 1–5.
- Tandon, M., & Shukla, Y. N., (1995). Phytoconstituents of *Asparagus adscendens*, *Chlorophytum arundinaceum* and *Curculigo orichoides*: A review. *CROMAP*, 12, 202–204.
- Tandon, M., Shukla, Y. N., & Thakur, R. S., (1992). 4 hydroxy, 8-11 oxidoheneicosanol and other constituents from *Chlorophytum arundinaceum* roots. *Phytochem.*, 31, 2525–2526.



- Tekade, A., Raut, B. T., Koche, M., & Gouli, R., (2009). Efficiency of different chemicals and bioagents against fungal pathogens causing diseases in Musli. *Pestol.*, 33, 16–19.
- Thakur, G. S., Bag, M., Sanodiya, B. S., Debnath, M., Zacharia, A., Bhadauriya, P., Prasad, G. B., & Bisen, P. S., (2009a). *Chlorophytum borivilianum*: A white gold for biopharmaceuticals and nutraceuticals. *Curr. Pharm. Biotechnol.*, 10(7), 650–666.
- Thakur, M., & Dixit, V. K., (2005). Fructan. The polymer with unexplored potential. *Indian Pharmacist*, 4, 7–12.
- Thakur, M., & Dixit, V. K., (2006). Effect of *Chlorophytum borivilianum* on androgenic & sexual behavior of male rats. *Indian Drugs.*, 43, 300–306.
- Thakur, M., & Dixit, V. K., (2007). Effect of some vajikaran herbs on pendiculation activities and *in vitro* sperm count in male. *Sexuality and Disability*, 25, 203–207.
- Thakur, M., Bhargava, S., Praznik, W., Loeppert, R., & Dixit, V. K., (2009b). Effect of *Chlorophytum borivilianum* Santapau and Fernandes on sexual dysfunction in hyperglycemic male rats. *Chinese J. Integr. Med.*, 15, 448–453.
- Thakur, M., Chauhan, N. S., Bhargava, S., & Dixit, V. K., (2009c). A comparative study on aphrodisiac activity of some ayurvedic herbs in male albino rats. *Arch. Sex. Behav.*, 38, 1009–1015.
- Thakur, M., Connellan, P., Deseo, M. A., Morris, C., & Dixit, V. K., (2011a). Immunomodulatory polysaccharide from *Chlorophytum borivilianum* roots. *Evidence-based Complement. Alter. Med.*, 598521.
- Thakur, M., Loeppert, R., Praznik, W., & Dixit, V. K., (2008). Effect of some Ayurvedic Vajikaran Rasayana herbs on heat induced testicular damage in male albino rats. *J. Complement. Integr. Med.*, 5, 5.
- Thakur, M., Thompson, D., Connellan, P., Deseo, M. A., Morris, C., & Dixit, V. K., (2011b). Improvement of penile erection, sperm count and seminal fructose levels *in vivo* and nitric oxide release *in vitro* by ayurvedic herbs. *Andrologia.*, 43, 273–277.
- Tiwari, P. N., (2006a). Effect of organic manures and plant spacing on yield and quality of Safed Musli (*Chlorophytum borivilianum*). *Crop Res.*, 32(3), 551–553.
- Toth, K., Haapala, T., & Hohtola, A., (1994). Alleviation of browning in oak explants by chemical pretreatments. *Biologia Plantarum.*, 36, 511–517.
- Trivedi, K. P., & Yadav, B. R., (1989). *Seed Germination Studies in Chlorophytum Tuberosum (Safed Musli)*. All India Coordinated Project on Medicinal and Aromatic Plants, Project Report, Indore Centre.
- Triveni, A., (1977). *Rasendrasarasangrah: Vajikaranadhikar*. Nutan Press, Rajkot, India.
- Tyagi, S., & Sharma, V., (2011). Ecophysiological studies for boosting commercial production of tuberous roots of *Chlorophytum borivilianum* Sant and Fernan. *J. Sci. Ind. Res.*, 70, 60–63.
- Tyler, V. E., Brady, L. R., & Robbers, J. E., (1981). *Pharmacognosy* (8<sup>th</sup> edn.) Lea and Febiger, Philadelphia.
- Vartak, V. D., (1981). In: Jain, S. K., (ed.), *Observations of Wild Edible Plants from Hilly Regions of Maharashtra and Goa: Resume and Future Prospects* (pp. 261–271). Glimpses of Indian Ethnonotany, Oxford & IBH Publishing Co., New Delhi, India.
- Verma, R., Misra, V., & Bisen, P. S., (2020). Nutritional and medicinal values of *Chlorophytum borivilianum*: Mini review of current status and future possibilities. *Curr. Nutri. Food Sci.*, 16, 1–8.

- Vijaya, K. N., & Chavan, P. D., (2009a). Influence of water deficit and waterlogging on the mineral status of a medicinal plant *Chlorophytum borivilianum*. *Acta Botanica Hungarica*, 51, 105–113.
- Visavadiya, N. P., Soni, B., Dalwadi, N., & Madamwar, D., (2010). *Chlorophytum borivilianum* as potential terminator of free radicals in various *in vitro* oxidation systems. *Drug Chem. Toxicol.*, 33(2), 173–182.
- Wagle, A., Kelkar, G. D., & Heble, M. R., (2000). In *Biotechnology: Secondary Metabolites* (pp. 219–220). Oxford and IBH Publishing Co. Pvt. Ltd., New Delhi.
- Wankhade, S. G., Ganorkar, S. R., & Hadole, S. S., (2004). Effect of FYM and nitrogen on yield, quality, and uptake of nutrients by Safed Musli (*Chlorophytum borivilianum*). *Dr. Punjabrao Deshmukh Krishi Vidyapeeth Research Journal.*, 28, 105–107.
- Yaseen, M., Singh, M., Singh, U. B., Singh, S., & Ram, M., (2013). Optimum planting time, method, plant density, size of planting material, and photo synthetically active radiation for Safed Musli (*Chlorophytum borivilianum*). *Industrial Crops and Products*, 43, 61–64.

## CHAPTER 9

---

# Bishop's Weed or Ajwain (*Trachyspermum ammi* Linn.): A Traditional Medicinal Plant with Pharmacological Importance, Ethno- Botanical Uses, and Nutritional Benefits for Quality Life Improvement

SOMENATH DAS

*Department of Botany, Burdwan Raj College, Burdwan, West Bengal, India*

---

### ABSTRACT

*Trachyspermum ammi* Linn., a common aromatic medicinal and spice plant belonging to the family Apiaceae and has been widely distributed across the globe. The leaves and fruits of the plants are utilized in folk medicinal practices as well as preventive measure against painful menstruation, gastrointestinal problems, and chronic arthritis. Mature fruits and seeds of the plant are common source for different phytochemicals such as essential oil, tannins, glycosides, dietary fibers, saponins, and alkaloids. Essential oil containing major bioactive ingredients *viz.* p-cymene,  $\beta$ -phellandrene, thymol, and  $\gamma$ -terpinene possess antioxidant, antihelminthic, antispasmodic, and antiseptic properties. The essential oil and the fruit extract have been used as potent anti-cancerous agent against HepG2 cells. Bioactive components of *T. ammi* essential oil have anti-proliferative activity against hepatic carcinoma by phosphorylation and dephosphorylation of JNK/MAPK pathway. Moreover, the essential oil actively modulated the different cellular enzymes such as cytochrome oxidase, lactate dehydrogenase and pancreatic lipase

with maximum degradation of aflatoxin G<sub>1</sub>. Seeds have remarkable role in controlling blood pressure by modulation of Ca<sup>2+</sup> ions channels. Based on the above background, the present article highlights the detailed survey of novel indigenous medicinal plant, *T. ammi* with emphasis on pharmaceutical significance, phyto-chemical profiling, nutritional benefits, and ethno-medicinal properties.

## 9.1 INTRODUCTION

*Trachyspermum ammi*, commonly called Bishop's weed or Ajwain is a small herb with pungent odor and widely grown in India, Pakistan, Iraq, Iran, Afghanistan, Asia, and Central Europe (Anwar et al., 2016). The plant is quiet similar to the parsley (*Petroselinum crispum*), another common medicinal plant belongs to family Apiaceae. Cultivation of ajwain is commonly occurred in Uttar Pradesh, Madhya Pradesh, Bihar, West Bengal, Tamil Nadu, and Karnataka (Takeda et al., 2008). The whole plant body is medicinally important to cure a number of health disorders viz. asthma, fever, bronchitis, malaria, arthritis, and cardiovascular problems. The leaves are commonly used in salads while the seeds have been consumed worldwide as spice ingredient with a lot of functional medicinal properties (Chahal et al., 2017). The seeds have been administered against dyspepsia and cholera (Dubey & Kashyap, 2015). The aqueous extract of seeds and leaves are used against fungitoxic effects, bacterial inhibition and act as potent anti-inflammatory agent (Boskabady et al., 2014). Extracts as well as essential oil of *T. ammi* seeds have significant inhibitory action on cellular aflatoxin biosynthesis by modulation in metabolic process suggesting the chemo-preventive efficacy against cancer and metastatic cell proliferation (Velazhahan et al., 2010; Kedia et al., 2015; Siddiqui et al., 2019). In India and China the traditional practitioners utilized the seeds for Ayurvedic and Unani medicines as a functional remedial measure of gastric disturbances (Dwivedi et al., 2012). Seeds of ajwain are used as galactogogue and possible regulator in biosynthesis of cellular ATP (Moein et al., 2015; Paul et al., 2011). The seeds and leaves contain a number of fatty acids and essential oil bioactive ingredients necessary for functioning as carminative, diuretic, aphrodisiac, and laxative properties (Kaur & Arora, 2010). Phytochemical analysis of mature ajwain seeds exhibited carbohydrates (24%), proteins (17%), fats (21.1%), minerals (7.95) and moisture content (7.4%). Fruits of *T. ammi* are rich source of vitamin, phosphorus, zinc, cobalt, cadmium, aluminum, nicotinic acid and iodine. Major essential oil components of *T.*

*ammi* are thymol, myrcene, carvacrol, and  $\gamma$ -terpinene (Abdel-Hameed et al., 2014). The essential oil components mainly provide the antioxidant, hypotensive, antiseptic, and anti-tussive properties (Akbar, 2020). The leaf juice of the plant is antihelmintic, febrifuge, and active agent for preventing stomach troubles (Aggarwal et al., 2011). Saleem et al. (2017) demonstrated the efficacy of *T. ammi* fruits in catabolism of lipoproteins, inhibition of lysosomal hydrolytic enzymes and cellular HMG-CoA reductase enzymes. Therefore, this article is aimed to highlight the phytochemical constituents, pharmacological importance, ethnobotanical uses and commercial utilization of *T. ammi* medicinal plant with possible mechanism of action.

## 9.2 BOTANICAL DESCRIPTION

*T. ammi* is an annual, branched, and grassy herb reaching up to 65 cm in height. Stem is glabrous or somewhat pubescent with pinnately arranged leaves. The leaves are mostly decomposed and feather like much branched striations. The inflorescences are compound umbel up to 16 flowers. The flowers are bisexual, actinomorphic, pentamerous, and alternipetalous with superior ovary. Fruits are cremocarp consisting of two mericarps attached with stylopodium. Fruits are grayish brown with 5 ridges and 6 vittae in each mericarp (Rajeshwari et al., 2011).

## 9.3 PHYTOCHEMICAL CONSTITUENTS

The primary constituents of seed and fruits of *T. ammi* are fat (18.2%), proteins (15.4%), carbohydrate (38.6%), fiber (11.9%), tannin, glycosides, moistures, saponin, and flavonoids (Javed et al., 2012). Mineral content such as manganese, iron, cobalt, calcium, copper, phosphorus, and vitamins *viz.* thiamine, nicotinic acid and riboflavin are of common occurrence in seeds of ajwain (Chauhan et al., 2012). The spicy aroma of the fruits, seeds as well as in leaves are mainly contributed by the volatile fragments specially the essential oil. Approximately, 5% of essential oil has been accumulated in the seed compartments (cremocarps and mericarps). Around 3–5% of volatile essential oil and 25–30% of fatty oils contributes the major volatile fragments of ajwain seeds and fruits (Raghavan, 2007). GC-MS analysis of volatile fragments exhibited thymol as the major bioactive ingredient of ajwain essential oil. In addition,  $\alpha$ -pinene,  $\beta$ -pinene,  $\gamma$ -pinene, p-cymene, styrene,  $\beta$ -phellandrene, carvacrol, delta 3-carene and terpene-4-ol were reported as non-thymol constituents of essential oil (Shukla & Dikshit,

2011). In a study on leaf essential oil, apiole, limonene, and carvone were recognized as major components. Abdel-Hameed et al. (2015) demonstrated the bicyclic monoterpene (52.45 mg/g), phenolic monoterpene (282.41 mg/g) and monoterpene alkyl benzene (203.74 mg/g) as major aliphatic, aromatic hydrocarbons and sesquiterpenes in ajwain seed essential oil. Variation in distribution of volatile components in ajwain seeds have been reported by several researchers which possibly depend on the geographical variation, climatic factors, pollinating insects, chemotypic variation and limonene as well as terpene synthase genes involve for biosynthesis of terpenoids and sesquiterpenoids. Ishikawa et al. (2001) reported the aqueous phase of aromatic glucosides in methanolic extract of ajwain seeds. Petroselinic acid has been reported as major component of fixed oil in ajwain basically from Indian cultivation (Dwivedi et al., 2012). Extraction of dried ajwain seeds in dichloromethane exhibited cadinol, caryophyllene, limonene, eudesmol, elemene, and humuline as major component (Lockwood et al., 2002). Sayed-Ahmad et al. (2017) demonstrated that the occurrence frequency of bioactive components in essential oil depends on the sowing season, site of secondary metabolite synthesis, growth stages and plant parts used for extraction of essential oil. It has been reported that in the month of October yield of seed essential oil is much higher reaching up to 3.3% and the precursor component p-cymene and  $\gamma$ -terpene is easily converted in to thymol. Maximum yield of essential oil in October may also depend on the higher temperature and long time blossoms with excessive up-regulation of terpene biosynthesis pathway. Moreover, the development of mericarps and cremocarps is a major determinant of the yield of essential oil because the volatile components are compartmentalized in the fragments of the fruit.

In addition to essential oil, several esters *viz.* petroselinic, oleic, and palmitic acids have been as major chemical constituents of ajwain seeds and fruits (Chahal et al., 2017). Seeds and fruits also contain several water soluble glycosides, glucosides, and glucopyranosides with diversifying stereoisomers. Ishikawa et al. (2001) demonstrated the p-menth-3-ene-1 $\beta$ ,2 $\beta$ ,5 $\beta$  triol as major monoterpene of seed extract. Aromatic glucosidic compound 3,4-dihydroxyphenyl propanol-3-O- $\beta$ -D glucopyranoside has been found associated with cellular nucleoside.

#### 9.4 PHARMACOLOGICAL SIGNIFICANCE

The whole plant of *T. ammi* has pharmacological importance against a number of health disorders and act as a major ingredient of poly-herbal formulation.

The fruits are traditionally used for remedial of diarrhea, abdominal pain, bronchitis, asthma, and atonic dyspepsia (Bairwa et al., 2012). The fruits and seeds have been utilized as antimicrobial, antihypertensive, hypolipidemic, antifungal, antihelminthic, antitussive, and antioxidants in both Ayurvedic and modern medical system. Basically, the phenolic, terpenoids, and glycoside molecules in the seed and fruit extract contribute the gastroprotective, antihypertensive, and abortifacient activities (Meena et al., 2018). The hydrophobic essential oil molecules also act as carrier for drugs and easily transmit by crossing the lipid bilayer. Thymol and carvacrol has significant activity for digestion by modulating the lactic dehydrogenase, cytochrome oxidase and acetyl choline esterase (Velazhahan et al., 2012). In this context, we have described several pharmacological effects of seeds and fruits of *T. ammi* in the section below.

#### **9.4.1 CARDIOVASCULAR EFFECTS**

The seeds and leaves of *T. ammi* contain phytosterol which after absorption in the cellular system improve the serum cholesterol and help to reduce the cardiovascular problems. Steroidal analysis exhibited maximum amount of stigmasterol and  $\beta$ -sitosterol in seeds with significant diminution properties. Moreover, the seeds have remarkable role in controlling the blood pressure by modulation of  $\text{Ca}^{2+}$  ions channels (Aftab & Usmanhane, 1995). Kumar et al. (2010) demonstrated the positive result of seed extract on ionotropic movement and chronotropic effect on frog heart. Bioactive ingredients of ajwain seeds have exhibited the lipid-lowering activity (decrease in total cholesterol, LDL-cholesterol, and increase in HDL) which is mainly due to the lipoprotein catabolism and inhibitory action against HMG CoA reductase (Javed et al., 2006, 2009). Ramakrishna Rao et al. (2003) reported dose dependent increment in pancreatic amylase and lipase by seed extract as a potential regulator for lowering the blood pressure in rat. Haque et al. (2014) conducted an experiment on bioactive component especially the thymol of *T. ammi* seed and suggested the oral administration of thymol maintain the antioxidant level and decrease the serum lipid peroxidation in rat.

#### **9.4.2 GASTRO-INTESTINAL EFFECTS**

The seeds of *T. ammi* potentially increase the gastric acid secretion and significant effect on reduction of ulcer index in animal model (Eftekhari et al., 2019). The fruit extract have declining effect on stomach pain due to

promising antioxidant efficacy. Gilani et al. (2005) described the improvement in  $\text{CCl}_4$  and paracetamol induced liver injury by *T. ammi* seed extract with reduced secretion of liver enzymes (ALT, ASP, and ALP). Hejazian and coworkers (2009) demonstrated the relaxant effect of ajwain seed on smooth muscle contraction of ileum by modulation in cellular acetylcholine level. Improvement in hepatic tissue recovery and membrane stabilization has been studied by utilization of polyherbal formulation containing major portion of *T. ammi* seed extract (Lateef et al., 2006). Fruits of *T. ammi* enhanced the mucus secretion containing NSAIDs (non-steroidal anti-inflammatory drugs) viz. indomethacin by gastric mucosa and prevent the diffusion of  $\text{H}^+$  ions and physical damage caused by ulcerogens (Hejazian et al., 2007). In a study conducted by Jeet et al. (2012) demonstrated different doses viz. 125, 250, 500 mg/kg of *T. ammi* extract for significant protection of peptic ulcer in rat by increasing the cellular aspartate transferase (AST) and alanine transferase (ALT). Carvacrol, the major bioactive ingredient of *T. ammi* essential oil has anti-proliferative activity against hepatic carcinoma by phosphorylation and dephosphorylation of JNK/MAPK pathway (Yin et al., 2012).

### **9.4.3 EFFECT ON NEURAL SYSTEM**

The fruits and seeds of *T. ammi* have been traditionally used against joint, rheumatic pain and headache. Extract of *T. ammi* effectively reduced the cellular reduced glutathione (GSH) and antioxidants of enzymatic origin viz. superoxide dismutase and catalase which bring significant improvement in rheumatoid arthritis in rat (Umar et al., 2012). Bioactive components of *T. ammi* have significant effect for progression of osteoarthritis in rabbit model with significant modulation in SGOT enzymes and alkaline phosphatase (Khan et al., 2016). Ghannadi et al. (2012) suggested the suppression in morphine withdrawal in mice model by oral administration of *T. ammi* extract which modulates the GABA receptor in neurotransmission and suppressed of nitric oxide pathway by altering cellular glutamate molecules. Rezvani et al. (2011) demonstrated the anticonvulsant, sedative, and antiepileptic property of ajwain in kindling models by dose dependent increment in GABA mediated neurotransmission in brain with effective reduction in neural activity.

### **9.4.4 ANTIBACTERIAL ACTIVITY**

Thymol represents an active ingredient of Iranian *T. ammi* and displayed broad spectrum bacterial toxicity (Vitali et al., 2016). Recent finding suggested the



participation of thymol as third and fourth generation antibiotic formulation against multidrug resistant *Bacillus subtilis*, and *Escherichia coli* (Khanuja et al., 2003). In case of dysbiosis, microbial flora of intestine viz. *Bifidobacterium* spp., *Lactobacilli*, and coliform bacteria has been decreased, which can be overcome by oral administration of *T. ammi* seed extract (Myers et al., 2009). Hassanshahian and coworkers (2014) observed antibacterial efficacy of *T. ammi* essential oil against *E. coli*, *S. aureus* and *Klebsiella pneumonia* isolated from a patient suffered from urinary infection. *T. ammi* essential oil effectively inhibit the food contaminating bacteria viz. *Pseudomonas aeruginosa* KCTC2004, *Enterobacter aerogenes* KCTC2190, *Salmonella typhimurium* KCTC2515, *Staphylococcus aureus* ATCC 6538 by significant regulatory effects on membrane permeability and ATP transportation (Paul et al., 2011). Antibacterial activity of *T. ammi* essential oil against water borne pathogens such as *E. coli*, *Salmonella* spp., and *Vibrio cholerae* has been demonstrated by Shukla & Dikshit (2011). Recent report of Grădinaru et al. (2018) suggested the inhibitory efficacy of *T. ammi* essential oil against three important respiratory bacteria viz. *Streptococcus pneumonia*, *Pseudomonas aeruginosa* and *Staphylococcus aureus* by micro-dilution method.

#### 9.4.5 ANTIFUNGAL ACTIVITY

Ethanollic extract of seeds of ajwain displayed considerable antifungal effectiveness against a range of pathogenic fungi and especially suppressed the spore germination of *Aspergillus ochraceus* and ochratoxin production (Murthy et al., 2009). Gandomi et al. (2014) described the fungitoxic potentiality of *T. ammi* essential oil isolated from dried seeds against *Penicillium citrinum*, *Aspergillus parasiticus*, *A. niger* and *P. chrysogenum* by disk diffusion assay. Shokri et al. (2016) demonstrated the efficacy of ajwain seeds as antifungal drug against the infection of pathogenic fungi such as *Trichophyton* spp., *Candida* spp. and *Chrysosporium* spp. Kedia and coworkers (2015) showed the inhibition of growth of *A. flavus* and aflatoxin secretion in food commodities by *T. ammi* essential oil with considerable reduction in ergosterol biosynthesis and enhanced leakage of cellular cations ( $\text{Ca}^{2+}$ ,  $\text{K}^+$ , and  $\text{Mg}^{2+}$ ). Sharifzadeh et al. (2015) reported the role of *T. ammi* essential oil for the treatment of oropharyngeal candidiasis and suggested its prominent efficacy as effective medical measure. Ajwain seed extracts significantly inhibited the conidial germination and hyphal proliferation of *Fusarium solani*, an important pathogen for wilt disease (Nateqi et al., 2018). Hajare

and coworkers (2005) observed the aflatoxin inhibitory efficacy of *T. ammi* seed with relative reduction of  $AFG_1 > AFG_2 > AFB_1 > AFB_2$ . Considerable reduction in aflatoxin concentration also depends on the  $\gamma$ -irradiation and alteration in temperature which inactivate the toxin biosynthesis.

#### **9.4.6 ANTI-DIARRHEAL ACTIVITY**

Diarrhea is a bacterial disease characterized by abdominal pain, wet stool and enhanced bowel movement. Balaji et al. (2012) described the anti-diarrheal potency of ajwain seeds with minimum 0.1 g/kg dose in experimental rat. They reported the increased re-absorption of fluids mixed with this seed extract helped in normal function of  $Na^+$  and  $K^+$  ATPase in body. Volatile essential oil 2–4 drops mixed with food ingredients simply inhibited the diarrheal symptom in human body. Hassanshahian and coworkers (2014) observed potential effectiveness of ajwain essential oil against major bacteria viz. *Staphylococcus aureus*, *Klebsiella pneumonia* and *E. coli* causing diarrheal symptoms in human body. Fazeli-Nasab & Fooladvand (2016) demonstrated the crude extract of *T. ammi* seeds for increasing in body's resistance against diarrheal pathogens and profusely used by traditional practitioners in Ayurvedic and Unani system of alternative medicines.

#### **9.4.7 ANTI-INFLAMMATORY ACTIVITY**

Inflammation is normal response of body for protective mechanism against any injury by secretion of kinin, serotonin, histamine, and prostaglandins. Thangam & Dhananjayam (2003) described the ability of ajwain seed extract (in water as well as in alcohol) for inhibition of inflammation with 41.11 and 38.32% at 100 mg/kg. Kazemi (2014) reported the reduced secretion of NO ( $80 \pm 0.50\%$ ) with major anti-inflammatory responses in addition with *T. ammi* essential oil at a dose of 45  $\mu\text{g/mL}$ . Umar et al. (2012) demonstrated efficacy of *T. ammi* and thymol against collagen mediated arthritis and reduced the inflammation in rat model. Rajput and coworkers (2013) observed considerable reduction in inflammation in strychnine induced epilepsy with seizure model by *T. ammi* extract. Aggarwal et al. (2011) reported the anti-inflammatory activity of *T. ammi* essential oil and suggest the importance of the major bioactive components for practical application through “bed to benchside” and “reverse pharmacology” approach in medical biology.

### 9.4.8 ANALGESIC EFFECT

Hejazian (2006, 2009) described the analgesic effect of *T. ammi* essential oil and fruit extract in mice model against chronic pain involving histamine and cholinergic mediated mode of action. Dashti-Rahmatabadi et al. (2007) conducted an analgesiometric test on thymol isolated from ajwain seed and found that significant pain relieving potentiality within 45 min of essential oil mixed drug injection. Table 9.1 represents the pharmacological and ethno-botanical use of different plant parts, extracts, and essential oil against different human disorders with effective mechanisms.

**TABLE 9.1** Pharmacological and Ethno-Botanical Use of Different Plant Parts of *Trachyspermum ammi* with Respect to Their Effective Mechanism of Action

Pharmacological/ Ethnobotanical Use of <i>Trachyspermum ammi</i>	Plant Parts	Effective Mode of Action	References
Cardiovascular effects	Seeds and leaves	Effect by lowering the lipid profile.	Saleem et al. (2017)
	Seed extract	Effect on ionotropic movement and chronotropic results.	Kumar et al. (2010)
	Seed bioactive components	Lipoprotein catabolism and inhibitory action against HMG CoA reductase.	Javed et al. (2006; 2009)
	Leaves/seeds	Lowering the blood pressure by modulation in pancreatic amylase and lipase.	Ramakrishna Rao et al. (2003)
	Seed essential oil and components.	Maintaining antioxidant level and decrease the serum lipid peroxidation.	Haque et al. (2014)
	Seed aqueous extract	Maintaining the mRNA level of iNOS enzyme.	Korani & Jamshidi (2020)
Gastro-intestinal effects	Leaves and seeds	Inhibition of intestinal contraction.	Platel & Srinivasan (2001); Hejazian et al. (2007)
	Leaves	Inhibitory effect on ulcer development	Komeili et al. (2012)
	Seeds	Hepatoprotective mechanism of action	Gilani et al. (2005)
	Fruits	Increment in secretion of gastric juices	Alqasoumi (2011)

**TABLE 9.1** (Continued)

<b>Pharmacological/ Ethnobotanical Use of <i>Trachyspermum ammi</i></b>	<b>Plant Parts</b>	<b>Effective Mode of Action</b>	<b>References</b>
	Seeds and fruits	Hepatic tissue recovery by membrane stabilization.	Lateef et al. (2006)
	Fruits	Increasing secretion of aspartate transferase (AST) and alanine transferase (ALT) for inhibition of peptic ulcers.	Jeet et al. (2012)
	Seeds and leaves	Phosphorylation and dephosphorylation of JNK/MAPK pathway for antiproliferative action.	Yin et al. (2012)
Neural system	Leaves	Effect on cellular catalase and superoxide dismutase.	Umar et al. (2012)
	–	Modulation in SGOT enzymes and alkaline phosphatase against osteoarthritis.	Khan et al. (2016)
–	–	Reduction in numbness, allodynia, and feet burning intensity.	Petramfar et al. (2016)
	–	Action on GABA mediated neurotransmission in brain.	Rezvani et al. (2011)
	–	Effect on PMS/NADH system and NO modulation.	Bajpai & Agrawal (2015)
	–	Effect on brain acetylcholine esterase, malondialdehyde, and glutathione.	Soni & Parle (2017)
	Seeds	Proliferate favorable development of nervous system.	Pai et al. (2018)
Bacteriostatic and bactericidal potency.	Solvent extract of whole plant.	Effect on drug resistant capacity of pathogenic microbes.	Khan et al. (2010)
	–	Urine associated troubles.	Mehdi et al. (2014)
	Essential oil	Effect on plasma membrane.	Paul et al. (2011)
	–	Effect on colony growth.	Kaur & Arora (2009)

**TABLE 9.1** (Continued)

<b>Pharmacological/ Ethnobotanical Use of <i>Trachyspermum ammi</i></b>	<b>Plant Parts</b>	<b>Effective Mode of Action</b>	<b>References</b>
Fungitoxic and fungicidal potency	Essential oil	Antioxidant mediated inhibition of bacterial growth.	Gandomi et al. (2014)
	–	Action against multidrug mechanism.	Tariq et al. (2014)
	–	pH gradient mediated bacterial inhibition.	Mehdizadeh et al. (2016)
	Polysaccharides	Oxidation and decomposition mediated bacterial inhibition.	Basu et al. (2017)
	Essential oil	Effect on spore germination.	Gemeda et al. (2014)
	Essential oil	Inhibition of mycelia development as fumigant.	Kim et al. (2016)
	Essential oil	Effect on cell growth.	Shokri et al. (2016)
Anti-inflammatory activity	Ethanollic extract of leaves.	Inhibition of mycelia growth and conidial germination.	Nateqi et al. (2018)
	Seed extract	Antioxidant based fungal inhibition.	Goswami & Chatterjee (2014)
	Essential oil	Reduction in NO synthesis.	Kazemi (2014)
	Essential oil	Modulation in collagen biosynthesis.	Umar et al. (2012)
	Aqueous and alcoholic extract of seed	Secretion of histamine and prostaglandin.	Thangam & Dhananjayam (2003)
	Methanolic extract	Inhibition of epilepsy.	Rajput et al. (2013)
	Seed extract	Inhibition of inflammation based on antioxidant activity.	Kaur & Arora (2010)
Analgesic effect	Whole plant extract	Novel delivery mechanism for anti-inflammatory activity.	Tomar & Malik (2015)
	Aqueous extract of leaves and seeds	Pain relieving property based on thymol.	Dashti-Rahmatabadi et al. (2007)
	Extract as topical cream	Reduce feet burning and worst pain by essential oil.	Petramfar et al. (2016)
	Seed	By reducing chronic pain	Hejazian (2006, 2009)

## 9.5 ETHNO-MEDICINAL USES AND COMMERCIAL IMPORTANCE

Powder of dried seeds and leaves are used as galactogue, carminative, and diuretic agent by marwar community of Jodhpur, India. Moreover, thymol, the bioactive component of *T. ammi* essential oil has prominent gastro-protective activities (Goyal, 2017). Bronchodilatory and anticholinergic effects of *T. ammi* essential oil have been determined by Boskabady et al. (1998). It effectively regulates the  $\text{Ca}^{2+}$  and  $\text{K}^{+}$  dependent aminotransferase and alkaline transferase for significant hepatoprotective action. Ghildiyal et al. (2008) demonstrated the *T. ammi* seed and leaves for the treatment of eczema, ringworm, etching, hypersensitivity, leprosy, and leucoderma. Leaves of *T. ammi* are commonly used for different Ayurvedic formulation and helpful for treatment of tonsillitis, worm infection, cough, urticaria, and digestive disorders (Asima & Satyesh, 1995). Roots of *T. ammi* have been used to cure abdominal pains, piles, and stomach troubles (Krishnamoorthy et al., 1999). Ajwain leaf juice critically acts as antihelmintic agent while the powder of roots are diuretic and carminative in nature (Lateef et al., 2006). The dried seeds fried with oil have been used as galactogue. The decoction of seeds in addition to germ free water has been used against poor appetite and to cure vomiting (Shah & Rahim, 2017). Patnaik (1993) reported the utilization of *T. ammi* as special herbal formulation for the treatment of healing in Mudpur village. Recently, in a clinical trial it has been confirmed that, the herbal extract of the plant is a prime regulator of ophthalmic disorders and used as eye drop (Biswas et al., 2001, 2003).

Besides ethno-medicinal features, the plant is also utilized in food and agricultural industries for commercial purposes. The extract of the whole plant exhibited specific inhibitory activity against infiltration of inflammatory cells (Mahboubi & Kazempour, 2011). The crushed seeds have been used for protection of different food commodities against stored insect pests viz. *Tribolium confusum* and *Sitophilus granarius* (Ziaee & Moharramipour, 2013). Indian and Chinese traditional herbal practitioners suggested the consumption of dried seeds for significant elevation in gastric acid and digestive enzymes with increased secretion of bile salts (Vasudevan et al., 2000; Platel & Srinivasan, 2001). *Callosobruchus maculatus* is a cosmopolitan pest for infestation in postharvest cowpea and chickpea, the ajwain essential oil exhibited significant fumigant toxicity against larvae, egg as well as the adult insect suggesting its commercial implementation as smart food preservative in place of adverse effects of chemical preservatives. Therefore, the seeds and leaves of *T. ammi* have been traditionally used as grain protectant in India, China, Greece, Iran, and Egypt (Sahaf & Moharramipour, 2008).

## 9.6 NUTRITIONAL BENEFITS

The seeds of *T. ammi* exhibits considerably higher nutritional value as compared to the other plant parts. Proximate analysis of the seeds displayed high energy content (314.55%) and rich amount of fiber, ash, protein (4.3–20.23%) and carbohydrate (~47%) (Figure 9.1). Occurrence frequency of fatty acids was in the range of 4.8–21.1% (Council of Scientific and Industrial Research, India, 1985). Higher nutritional benefits recommend its potential use as dietary supplements and active potentiality against different health disorders (Javed et al., 2012). Recent investigation of Kolbadinejad & Rezaeipour (2020) suggested the importance of *T. ammi* essential oil as growth promoter and provide innate immunity due to the supplementation of L-threonine and antioxidants with other dietary meals.

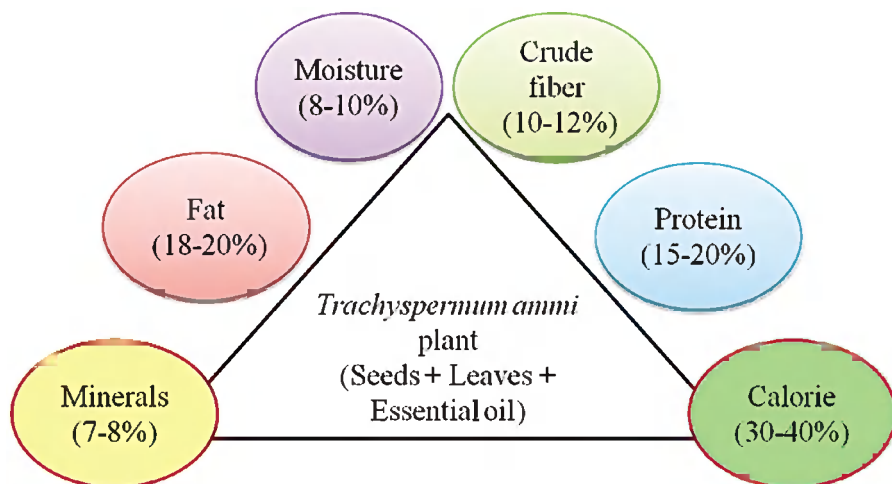


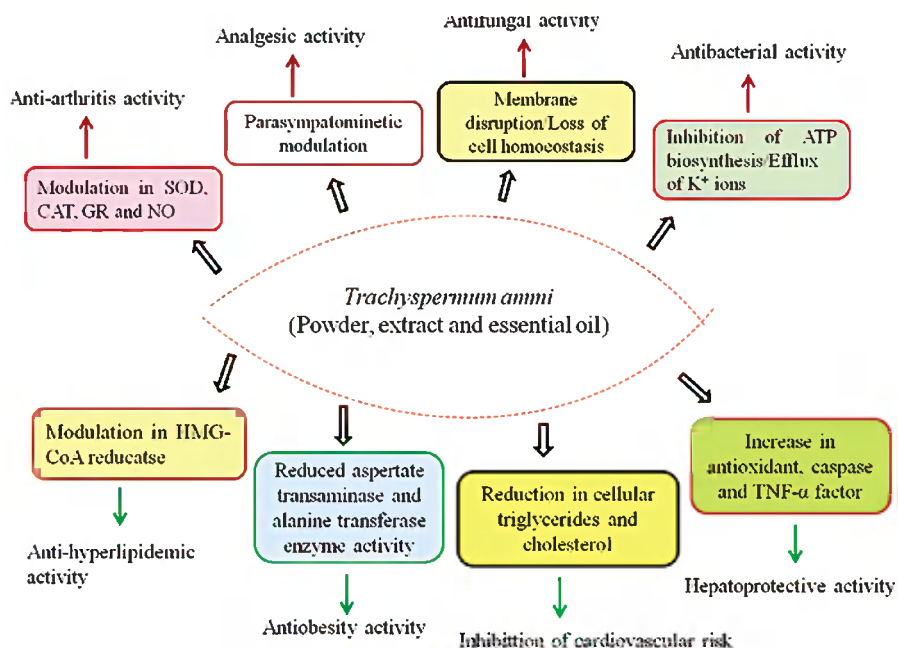
FIGURE 9.1 Nutritional components of *Trachyspermum ammi*.

## 9.7 MECHANISM OF ACTION

Several workers have demonstrated the pharmacological and ethno-medicinal importance of *T. ammi* seeds, leaves, and essential oil, however, the possible mechanism of action have not been described and elucidated. Here, we have highlighted several possible mechanism of antifungal, antibacterial, anti-inflammatory, antidiarrheal, hypolipidemic, anti-arthritis, analgesic, antihelminthic, and mycotoxin inhibitory properties.

Alavinezhad & Boskabady (2014) described the anti-arthritis activity of ajwain seed oil and the major bioactive ingredients *viz.* thymol, carvacrol,  $\alpha$ -pinene and  $\gamma$ -terpinene due to modulation in cellular oxidative defense enzymes such as superoxide dismutase (SOD), catalase (CAT) and secondary biomolecules *viz.* nitric oxide (NO) and reduced glutathione (GSH). Komeili and coworkers (2012) demonstrated the therapeutic potential of aqueous seed extract of *T. ammi* against peptic ulcer which has been associated with significant balance of liver enzyme Aspartate transferase and alanine transferase. Kazemi (2015) observed the fungitoxic potentiality of *T. ammi* essential oil due to disruption of plasma membrane and loss of cellular homeostasis. Kedia et al. (2015) demonstrated the aflatoxin B<sub>1</sub> inhibitory mechanism of *T. ammi* essential oil depend on the alteration in carbohydrate catabolism and inhibition in spore germination as well as excessive lysosome formation. Alteration in membrane permeability, inhibition in cellular ATP biosynthesis and extracellular efflux of potassium and other cell constituents determined the plasma membrane as potential antibacterial target site of action of *T. ammi* essential oil (Paul et al., 2011). Enhancement in antibiotic potency and broken down of resistance genes have been characterized as inhibitory mechanism of *T. ammi* essential oil against *Staphylococcus aureus* (Vazirian et al., 2019). Anti-hyperlipidemic activity of *T. ammi* powder involves the enhanced catabolism of cellular lipoproteins and inhibition of hydrolytic enzymes as well as modulatory action of HMG-CoA reductase (Javed et al., 2009). Anti-obesity activity of thymol significantly correlated with decreased food intake by improvement in HDL, LDL cholesterol and reduced activity of aspartate transaminase and alanine transferase enzyme (Haque et al., 2014). Cardiovascular risk factors and atrial fibrillation have been inhibited by application of *T. ammi* extract with alleviation of palpitation and reduction in cellular triglycerides and cholesterol (Zarshenas et al., 2016). Hepatoprotective nature of thymol (extracted and purified from *T. ammi* essential oil) has been contributed by significant increment in liver caspase-3 activity, TNF- $\alpha$  factor and modulatory activity on total antioxidant capacity (Geyikoglu et al., 2019). The anti-diarrheal, laxative, and anti-helminthic property of *T. ammi* extract and essential oil also depend on the alteration of membrane fluidity and dynamicity with significant disorganization in porin proteins (Khan et al., 2020). Figure 9.2 presents the possible pharmacological and ethno-botanical mechanism of action of *T. ammi*.





**FIGURE 9.2** Possible pharmacological and ethno-medicinal mechanism of action of *Trachyspermum ammi*.

## 9.8 PATENTING *TRACHYSPERMUM AMMI*: AN INITIATIVE FOR MODERN PHARMACOLOGICAL APPROACH

On the basis of pharmacological importance, ethno-medicinal value and nutritional benefits, a number of herbal formulations containing the *T. ammi* plant parts, essential oil and its bioactive component have been patented by various institutes and pharmacological companies. However, the governing authorities have filed the patent of herbal formulation based on their pharmacodynamic properties, mechanism of action and required doses by *in vivo* experimental evidences. Pruthi et al. (1999) claimed an herbal composition including thymol as active constituents of *T. ammi* for treatment of chronic viral infections including the adverse effect of Human Immunodeficiency Virus (HIV) and filed an US patent (US5980903). Sadik Tuzun et al. (2000) have filed a patent (U.S. patent WO2000021364) on thymol (extracted from *T. ammi* essential oil) for its efficient utilization as natural preservative protecting against fungi, bacteria, nematode, and insect pests. Khanuja et al. (2003) have invented a patent (U.S. patent 6514541) on thymol, isolated, and characterized from *T. ammi* essential oil for developing tablet/syrup against

the treatment of bacterial infections. Kane (2004) prepared AMAVAT-20 oil from herbal mixture of different medicinal plants including *T. ammi* and filed a patent (U.S. patent 2004/0156920) for its utilization against chronic stomachache and loose bowels. Bhadra et al. (2004) prepared an herbal composition by mixing *T. ammi*, *Murraya paniculata*, *Hibiscus abelmoschus*, *Euphorbia hirta* and *Syzygium aromaticum* extract for treatment against asthma assigned by CSIR-India and filed a patent with application number US 6,746,694 B1. Silver nanoparticle containing an extract of *T. ammi* has been patented (U.S. Patent 11/547,886) by Paknikar (2007) for wide scale antimicrobial activity at very low effective concentrations without any cytotoxic effects. Kobayashi et al. (2010) filed a patent (U.S. Patent No. 7,754,774) on thymol, an active ingredient of *T. ammi* essential oil in addition with eugenol, citronellol,  $\beta$ -pinene, terpenyl acetate and citronellal for their effective utilization to prepare antiseptic disinfectants in food, medicines and cosmetics with improved antibacterial activities. Khan & Rosina (2012) extracted a novel compound 5,8-A-D-I-1-Propyl-1-Octahydronaphthalen-1-(2H), one from *T. ammi* seeds and granted a patent (US patent 20120178971) for inhibitory effects against dental carries caused by *Streptococcus mutans*. Herbal mixture of different medicinal plants including liquid extract of *T. ammi* as an important tumor treating composition has been patented (U.S. patent 8722109) by Al-Shemmeri (2014). Gokaraju et al. (2018) developed an synergistic mixture comprising of *T. ammi*, *Curcuma longa*, *Coleus aromaticus*, *Sphaeranthus indicus*, *Cinnamomum tamala*, *Citrullus lanatus*, *Ocimum sanctum* and *Garcinia mangostana* and filed a patent (U.S. patent 9907825B2) for their utilization as dietary supplement with improvement in mental alertness, energy level, muscle strength and physical performance of the body. Table 9.2 presents some patents on composition of *T. ammi* herbal formulation with wide application number and therapeutic as well as practical applications.

## 9.9 CONCLUSION AND FUTURE PERSPECTIVE

Current generation is paying considerable attention for utilization of plant based herbal drugs or formulations inspite of excessive chemical drugs and modern allopathic system of medicines. Strong pharmacological properties such as anti-arthritis, anti-obesity, analgesic, antibacterial, antifungal, anti-diarrheal, anti-hyperlipidemic, and protection against gastrointestinal disorders, cardiovascular problems and effect on neural system suggest the

**TABLE 9.2** Some Patents on Composition of *T. ammi* Herbal Formulation with Wide Application Number and Practical Applications

Patent Number	Composition of <i>T. ammi</i> Herbal Formulation	Application	References
U.S. patent (US5980903)	Thymol as bioactive ingredient of <i>T. ammi</i> essential oil.	Treating against chronic viral infections including the adverse effect of Human Immunodeficiency Virus (HIV).	Pruthi et al. (1999)
U.S. patent WO2000021364	Thymol (extracted from <i>T. ammi</i> essential oil)	Utilization as natural preservative protecting against fungi, bacteria, nematode, and insect pests.	Sadik Tuzun et al. (2000)
U.S. patent 6514541	Thymol (extracted from <i>T. ammi</i> essential oil)	Treatment against bacterial infections.	Khanuja et al. (2003)
U.S. patent 2004/0156920	Powder of <i>T. ammi</i> leaves	AMAVAT-20 polyherbal preparation against chronic stomachache and loose bowels.	Kane (2004)
US patent 6,746,694 B1	Extract of <i>T. ammi</i>	Treatment against asthma.	Bhadra et al. (2004)
U.S. Patent 11/547,886	Extracts of <i>T. ammi</i>	Wide scale antimicrobial activity after incorporating into silver nanoparticle.	Paknikar (2007)
U.S. Patent 7,754,774.	Thymol (extracted from <i>T. ammi</i> essential oil)	Antiseptic disinfectants in food, medicines, and cosmetics with improved antibacterial activities.	Kobayashi et al. (2010)
U.S. patent 20120178971	Novel compound 5,8-A-D-I-1-Propyl-1-Octahydronaphthalen-1-(2H), one from <i>T. ammi</i> seeds	Inhibitory effects against dental carries caused by <i>Sterptococcus mutans</i> .	Khan & Rosina (2012)
U.S. patent 8722109	Extract of <i>T. ammi</i>	Anti-tumor herbal composition.	Al-Shemmeri (2014)
U.S. patent 9907825B2	Extract of <i>T. ammi</i>	Improving mental alertness, energy level, muscle strength and physical performance of body.	Gokaraju et al. (2018)

potential application of *T. ammi* fruits, seeds as well as leaves (extracts, essential oil, powders, and formulations) for beneficial health purposes. Moreover, the nutritional benefits and possible mechanism of action against different health disorders strengthen the modern application of *T. ammi* plant parts in reverse pharmacology.

## KEYWORDS

- **anticancer**
- **antioxidant**
- **ethno-medicinal properties**
- **pharmaceutical**
- **phytochemicals**
- ***Trachyspermum ammi***

## REFERENCES

- Abdel-Hameed, E. S. S., Bazaid, S. A., Al Zahrani, O., El-Halmouch, Y., El-Sayed, M. M., & El-Wakil, E., (2014). Chemical composition of volatile components, antimicrobial, and anticancer activity of n-hexane extract and essential oil from *Trachyspermum ammi* L. seeds. *Oriental Journal of Chemistry*, 30(4), 1653–1662.
- Aftab, K., & Usmanghani, K., (1995). Blood pressure lowering action of active principle from *Trachyspermum ammi* (L.) Sprague. *Phytomedicine*, 2(1), 35–40.
- Aggarwal, B., Prasad, S., Reuter, S., Kannappan, R., Yadav, V. R., Park, B., Hye, K. J., et al., (2011). Identification of novel anti-inflammatory agents from Ayurvedic medicine for prevention of chronic diseases: “Reverse pharmacology” and “bedside to bench” approach. *Current Drug Targets*, 12(11), 1595–1653.
- Akbar, S., (2020). *Trachyspermum ammi* (L.) Sprague (*Apiaceae/Umbelliferae*). In: *Handbook of 200 Medicinal Plants* (pp. 1825–1834). Springer, Cham.
- Alavinezhad, A., & Boskabady, M. H., (2014). Anti-inflammatory, antioxidant, and immunological effects of *Carum copticum* L. and some of its constituents. *Phytotherapy Research*, 28(12), 1739–1748.
- Alqasoumi, S., (2011). Gastric antisecretory and antiulcer effects of ajowan *Carum copticum* in rats. *Afr. J. Pharm. Pharmacol.*, 5(5), 572–576.
- Al-Shemmeri, A. W. F., (2014). *U.S. Patent No. 8,722,109*. Washington, DC: U.S. Patent and Trademark Office.
- Anwar, S., Ahmed, N., Habibatni, S., & Abusamra, Y., (2016). Ajwain (*Trachyspermum ammi* L.) oils. In: *Essential Oils in Food Preservation, Flavor, and Safety* (pp. 181–192). Academic Press.

- Asima, C., & Satyesh, C. P., (1995). *The Treatise on Indian Medicinal Plants* (Vol. 4). Publication and Information Directorate, New Delhi, India.
- Bairwa, R., Sodha, R. S., & Rajawat, B. S., (2012). *Trachyspermum ammi*. *Pharmacognosy Reviews*, 6(11), 56.
- Bajpai, V. K., & Agrawal, P., (2015). Studies on phytochemicals, antioxidant, free radical scavenging and lipid peroxidation inhibitory effects of *Trachyspermum ammi* seeds. *Indian J. Pharm. Educ. Res*, 49, 58–65.
- Balaji, G., Chalamaiah, M., Ramesh, B., & Reddy, Y. A., (2012). Antidiarrhoeal activity of ethanol and aqueous extracts of *Carum copticum* seeds in experimental rats. *Asian Pacific Journal of Tropical Biomedicine*, 2(2), S1151–S1155.
- Basu, S., Ghosh, M., Bhunia, R. K., Ganguly, J., & Banik, B. K., (2017). Polysaccharides from *Dolichos biflorus* Linn and *Trachyspermum ammi* Linn seeds: Isolation, characterization, and remarkable antimicrobial activity. *Chemistry Central Journal*, 11(1), 1–10.
- Bhadra, R., Pal, B. C., Das, K., & Bhattacharaya, S., (2004). *U.S. Patent No. 6,746,694*. Washington, DC: U.S. Patent and Trademark Office.
- Biswas, N. R., Gupta, S. K., Das, G. K., Kumar, N., Mongre, P. K., Haldar, D., & Beri, S., (2001). Evaluation of ophthacare® eye drops—A herbal formulation in the management of various ophthalmic disorders. *Phytotherapy Research*, 15(7), 618–620.
- Biswas, N. R., Nainiwal, S. K., Das, G. K., Langan, U., Dadeya, S. C., Mongre, P. K., Ravi, A.K. & Baidya, P., (2003). Comparative randomized controlled clinical trial of a herbal eye drop with artificial tear and placebo in computer vision syndrome. *Journal of the Indian Medical Association*, 101(3), 208, 209.
- Boskabady, M. H., Alitaneh, S., & Alavinezhad, A., (2014). *Carum copticum* L.: A herbal medicine with various pharmacological effects. *BioMed Research International*, 2014. <https://doi.org/10.1155/2014/569087>.
- Boskabady, M. H., Rakhshandah, H., & Moetamed, S. V., (1998). Bronchodilatory and an ticholinergic effects of *Carum copticum* on isolated guinea Pig tracheal chains. *Medical Journal of the Islamic Republic of Iran (MJIRI)*, 11(4), 329–334.
- Chahal, K. K., Dhaiwal, K., Kumar, A., Kataria, D., & Singla, N., (2017). Chemical composition of *Trachyspermum ammi* L. and its biological properties: A review. *Journal of Pharmacognosy and Phytochemistry*, 6(3), 131–140.
- Chauhan, B., Kumar, G., & Ali, M., (2012). A review on phytochemical constituents and activities of *Trachyspermum ammi* (L.) Sprague fruits. *Am. J. Pharmtech. Res.*, 2(4), 329–340.
- Council of Scientific & Industrial Research (India). Publications & Information Directorate, (1985). *The Wealth of India: A Dictionary of Indian Raw Materials & Industrial Products* (Vol. 1). Publications & Information Directorate, Council of Scientific & Industrial Research.
- Dashti-Rahmatabadi, M. H., Hejazian, S. H., Morshedi, A., & Rafati, A., (2007). The analgesic effect of *Carum copticum* extract and morphine on phasic pain in mice. *Journal of Ethnopharmacology*, 109(2), 226–228.
- Dubey, S., & Kashyap, P., (2015). *Trachyspermum ammi*: A review on its multidimensional uses in Indian folklore medicines. *Research Journal of Medicinal Plant*, 9(8), 368–374.
- Dwivedi, S. N., Mishra, R. P., & Alava, S., (2012). Phytochemistry, pharmacological studies and traditional benefits of *Trachyspermum ammi* (Linn.) Sprague. *International Journal of Pharmacy & Life Sciences*, 3(5), 1705–1709.

- Eftekhari, M., Hoseinsalari, A., Mansourian, M., Farjadmand, F., Ardekani, M. R. S., Sharifzadeh, M., Hassanzadeh, G., et al., (2019). *Trachyspermum ammi* (L.) Sprague, superb essential oil and its major components on peptic ulcers: *In vivo* combined *in silico* studies. *DARU Journal of Pharmaceutical Sciences*, 27(1), 317–327.
- Fazeli-nasab, B., & Fooladvand, Z., (2016). A review on Iranian *Carum copticum* (L.): Composition and biological activities. *European Journal of Medicinal Plants*, 1–8.
- Gandomi, H., Abbaszadeh, S., JebelliJavan, A., & Sharifzadeh, A., (2014). Chemical constituents, antimicrobial, and antioxidative effects of *Trachyspermum ammi* essential oil. *Journal of Food Processing and Preservation*, 38(4), 1690–1695.
- Gemeda, N., Woldeamanuel, Y., Asrat, D., & Debella, A., (2014). Effect of *Cymbopogon martinii*, *Foeniculum vulgare*, and *Trachyspermum ammi* essential oils on the growth and mycotoxins production by aspergillus species. *International Journal of Food Science*, 2014. <https://doi.org/10.1155/2014/874135>.
- Geyikoglu, F., Yilmaz, E. G., Serkan, E. H., Koc, K., Cerig, S., Simsek, O. N., & Aysin, F., (2019). Hepatoprotective role of thymol in drug-induced gastric ulcer model. *Annals of Hepatology*, 17(6), 980–991.
- Ghannadi, A., Hajhashemi, V., & Abrishami, R., (2012). Effects of the Persian *Carum copticum* fruit extracts on morphine withdrawal syndrome in mice. *Research in Pharmaceutical Sciences*, 7(3), 127–131.
- Ghildiyal, J. C., Sadana, G., Uniyal, K. M., Bebni, D., & Bebni, P., (2008). Ethno-medicinal uses of plants to cure skin disease in Garhwal Himalaya. *Journal of Mountain Research*, 3, 55–62.
- Gilani, A. H., Jabeen, Q., Ghayur, M. N., Janbaz, K. H., & Akhtar, M. S., (2005). Studies on the antihypertensive, antispasmodic, bronchodilator, and hepatoprotective activities of the *Carum copticum* seed extract. *Journal of Ethnopharmacology*, 98(1, 2), 127–135.
- Gokaraju, G. R., Gokaraju, R. R., Gokaraju, V. K. R. R., Bhupathiraju, K., Golakoti, T., Sengupta, K., & Alluri, V. K. R., (2018). *U.S. Patent No. 9,907,825*. Washington, DC: U.S. Patent and Trademark Office.
- Goswami, N., & Chatterjee, S., (2014). Assessment of free radical scavenging potential and oxidative DNA damage preventive activity of *Trachyspermum ammi* L.(carom) and *Foeniculum vulgare* Mill. (fennel) seed extracts. *BioMed Research International*, 2014. <https://doi.org/10.1155/2014/582767>.
- Goyal, M., (2017). Use of ethnomedicinal plants for prophylaxis and management of postpartum complications among the Marwari community of Jodhpur District of Rajasthan. *Food Quality and Safety*, 1(3), 203–210.
- Grădinaru, A. C., Trifan, A., Şpac, A., Brebu, M., Miron, A., & Aprotosoaic, A. C., (2018). Antibacterial activity of traditional spices against lower respiratory tract pathogens: Combinatorial effects of *Trachyspermum ammi* essential oil with conventional antibiotics. *Letters in Applied Microbiology*, 67(5), 449–457.
- Hajare, S. S., Hajare, S. N., & Sharma, A., (2005). Aflatoxin inactivation using aqueous extract of ajowan (*Trachyspermum ammi*) seeds. *Journal Of Food Science*, 70(1), C29–C34.
- Haque, M. R., Ansari, S. H., Najmi, A. K., & Ahmad, M. A., (2014). Monoterpene phenolic compound thymol prevents high fat diet induced obesity in murine model. *Toxicology Mechanisms and Methods*, 24(2), 116–123.
- Hassanshahian, M., Bayat, Z., Saeidi, S., & Shiri, Y., (2014). Antimicrobial activity of *Trachyspermum ammi* essential oil against human bacterial. *International Journal of Advanced Biological and Biomedical Research*, 2, 18–24.

- Hejazian, S. H., (2006). Analgesic effect of essential oil (EO) from *Carum copticum* in mice. *World Journal of Medical Science*, 1(2), 95–99.
- Hejazian, S. H., Bafghi, A. F., & Mahdavi, S. M., (2009). The analgesic effects of aqueous part of *Carum copticum* (L.) CB Clarke extract on chronic pain and comparison with oil part of extract in mice. *Iranian Journal of Medicinal and Aromatic Plants*, 25(1), 104–112.
- Hejazian, S. H., Dashti-R, M. H., Mahdavi, S. M., & Qureshi, M. A., (2009). The effect of *Carum Copticum* extract on acetylcholine induced contraction in isolated rat's ileum. *Journal of Acupuncture and Meridian Studies*, 2(1), 75–78.
- Hejazian, S. H., Morowatisharifabad, M., & Mahdavi, S. M., (2007). Relaxant effect of *Carum copticum* on intestinal motility in ileum of rat. *World Journal of Zoology*, 2(2), 15–18.
- Ishikawa, T., Sega, Y., & Kitajima, J., (2001). Water-soluble constituents of ajowan. *Chemical and Pharmaceutical Bulletin*, 49(7), 840–844.
- Javed, I., Iqbal, Z., Rahman, Z. U., Khan, F. H., Muhammad, F., Aslam, B., & Ali, L., (2006). Comparative anti-hyperlipidaemic efficacy of *Trachyspermum ammi* extracts in albino rabbits. *Pakistan Veterinary Journal*, 26(1), 23–29.
- Javed, I., Zia-Ur-Rahman, N., Khan, M. Z., Muhammad, F., Aslam, B., Iqbal, Z., Sultan, J. I., & Ahmad, I., (2009). Antihyperlipidaemic efficacy of *Trachyspermum ammi* in albino rabbits. *Acta Veterinaria Brno*, 78(2), 229–236.
- Javed, S., Shahid, A. A., Haider, M. S., Umeera, A., Ahmad, R., & Mushtaq, S., (2012). Nutritional, phytochemical potential and pharmacological evaluation of *Nigella sativa* (Kalonji) and *Trachyspermum ammi* (Ajwain). *Journal of Medicinal Plants Research*, 6(5), 768–775.
- Jeet, K., Devi, N., Narender, T., Sunil, T., Lalit, S., & Raneev, T., (2012). *Trachyspermum ammi* (Ajwain): A comprehensive review. *International Research Journal of Pharmacy*, 3(5), 133–138.
- Kane, S., (2004). *U.S. Patent Application No. 10/338,405*.
- Kaur, G. J., & Arora, D. S., (2009). Antibacterial and phytochemical screening of *Anethum graveolens*, *Foeniculum vulgare* and *Trachyspermum ammi*. *BMC complementary and Alternative Medicine*, 9(1), 30–40.
- Kaur, G. J., & Arora, D. S., (2010). Bioactive potential of *Anethum graveolens*, *Foeniculum vulgare* and *Trachyspermum ammi* belonging to the family umbelliferae-current status. *Journal of Medicinal Plants Research*, 4(2), 87–94.
- Kazemi, M., (2014). Chemical composition, antimicrobial, antioxidant, and anti-inflammatory activity of *Carum copticum* L. essential oil. *Journal of Essential Oil Bearing Plants*, 17(5), 1040–1045.
- Kazemi, M., (2015). Effect of *Carum copticum* essential oil on growth and aflatoxin formation by *Aspergillus* strains. *Natural Product Research*, 29(11), 1065–1068.
- Kedia, A., Prakash, B., Mishra, P. K., Dwivedy, A. K., & Dubey, N. K., (2015). *Trachyspermum ammi* L. essential oil as plant-based preservative in food system. *Industrial Crops and Products*, 69, 104–109.
- Khan, A. U., & Rosina, K., (2012). *U.S. Patent Application No. 13/343,883*.
- Khan, N., Jamila, N., Ejaz, R., Nishan, U., & Kim, K. S., (2020). Volatile oil, phytochemical, and biological activities evaluation of *Trachyspermum ammi* seeds by chromatographic and spectroscopic methods. *Analytical Letters*, 53(6), 984–1001.
- Khan, R., Zakir, M., Afaq, S. H., Latif, A., & Khan, A. U., (2010). Activity of solvent extracts of *Prosopis spicigera*, *Zingiber officinale* and *Trachyspermum ammi* against multidrug

- resistant bacterial and fungal strains. *The Journal of Infection in Developing Countries*, 4(05), 292–300.
- Khan, T. A., Shakir, L., Zaidi, A. A., & Ali, A., (2016). Efficacy and safety assessment of *Curcuma longa* (L.) and *Trachyspermum ammi* (L.) in experimentally induced osteoarthritis rabbit Model. *Bulletin of Environment, Pharmacology, and Life Science*, 5, 54–64.
- Khanuja, S. P. S., Chaturvedi, P., Singh, A. K., Shasany, A. K., Agarwal, V. K., Gupta, V. K., Gupta, S. C., et al., (2007). *U.S. Patent No. 7,291,349*. Washington, DC: U.S. Patent and Trademark Office.
- Khanuja, S. P. S., Srivastava, S., Shasney, A. K., Darokar, M. P., Kumar, T. R. S., Agarwal, K. K., & Saikia, D., (2003). *U.S. Patent No. 6,514,541*. Washington, DC: U.S. Patent and Trademark Office.
- Kim, E., Oh, C. S., Koh, S. H., Kim, H. S., Kang, K. S., Park, P. S., Jang, M. J., et al., (2016). Antifungal activities after vaporization of ajowan (*Trachyspermum ammi*) and allspice (*Pimenta dioica*) essential oils and blends of their constituents against three *Aspergillus* species. *Journal of Essential Oil Research*, 28(3), 252–259.
- Kobayashi, A., Okamoto, H., & Okada, F., (2010). *U.S. Patent No. 7,754,774*. Washington, DC: U.S. Patent and Trademark Office.
- Kolbadinejad, A., & Rezaei-pour, V., (2020). Efficacy of ajwain (*Trachyspermum ammi* L.) seed at graded levels of dietary threonine on growth performance, serum metabolites, intestinal morphology and microbial population in broiler chickens. *Journal of Animal Physiology and Animal Nutrition*, 1–10.
- Komeili, G., Sargazi, M., Soluki, S., & Maleki, S. A. D., (2012). The therapeutic effect of *Carum copticum* seed aqueous extract on peptic ulcers induced by ibuprofen in rat. *Zahedan Journal of Research in Medical Science*, 14(5), 21–24.
- Korani, M., & Jamshidi, M., (2020). The effect of aqueous extract of *Trachyspermum ammi* seeds and ibuprofen on inflammatory gene expression in the cartilage tissue of rats with collagen-induced arthritis. *Journal of Inflammation Research*, 13, 133–139.
- Krishnamoorthy, V., & Madalageri, M. B., (1999). Bishop weeds (*Trachyspermum ammi*): An essential crop for north Karnataka. *Journal of Medicinal and Aromatic Plant Sciences*, 21(4), 996–998.
- Kumar, P. P., Prabhakara, M. C., Satyavathi, K., & Kumar, S. A., (2010). Evaluation of cardiac activity of some traditionally used backyard Indian medicinal plants. *Research Journal of Pharmaceutical, Biological, and Chemical Sciences*, 1(4), 641–654.
- Lateef, M., Iqbal, Z., Akhtar, M. S., Jabbar, A., Khan, M. N., & Gilani, A. H., (2006). Preliminary screening of *Trachyspermum ammi* (L.) seed for anthelmintic activity in sheep. *Tropical Animal Health and Production*, 38(6), 491–496.
- Lateef, M., Iqbal, Z., Rauf, U., & Jabbar, A., (2006). Anthelmintic activity of *Carum copticum* seeds against gastro-intestinal nematodes of sheep. *Journal of Animal and Plant Science*, 16(1, 2), 34–37.
- Lockwood, G. B., Asghari, G., & Hakimi, B., (2002). Production of essential oil constituents by cultured cells of *Carum copticum* L. *Flavor and Fragrance Journal*, 17(6), 456–458.
- Mahboubi, M., & Kazempour, N., (2011). Chemical composition and antimicrobial activity of *Satureja hortensis* and *Trachyspermum copticum* essential oil. *Iranian Journal of Microbiology*, 3(4), 194.
- Meena, S. S., Lal, G., & Meena, R. D., (2018). Multidimensional therapeutic uses of ajwain (*Trachyspermum ammi* L.). *International Journal Seed Spices*, 8(2), 1–5.



- Mehdizadeh, T., Hashemzadeh, M. S., Nazarizadeh, A., Neyriz-Naghadehi, M., Tat, M., Ghalavand, M., & Dorostkar, R., (2016). Chemical composition and antibacterial properties of *Ocimum basilicum*, *Salvia officinalis* and *Trachyspermum ammi* essential oils alone and in combination with nisin. *Research Journal of Pharmacognosy*, 3(4), 51–58.
- Moein, M. R., Zomorodian, K., Pakshir, K., Yavari, F., Motamedi, M., & Zarshenas, M. M., (2015). *Trachyspermum ammi* (L.) Sprague: Chemical composition of essential oil and antimicrobial activities of respective fractions. *Journal of Evidence-Based Complementary & Alternative Medicine*, 20(1), 50–56.
- Murthy, P. S., Borse, B. B., Khanum, H., & Srinivas, P., (2009). Inhibitory effects of Ajowan (*Trachyspermum ammi*) ethanolic extract on *A. ochraceus* growth and ochratoxin production. *Turkish Journal of Biology*, 33(3), 211–217.
- Myers, S. R., Hawrelak, J., & Cattley, T., (2009). Essential oils in the treatment of intestinal dysbiosis: A preliminary *in vitro* study. *Alternative Medicine Review*, 14(4), 380–384.
- Nateqi, M., & Mirghazanfari, S. M., (2018). Determination of total phenolic content, antioxidant activity and antifungal effects of *Thymus vulgaris*, *Trachyspermum ammi* and *Trigonella foenum graecum* extracts on growth of *Fusarium solani*. *Cellular and Molecular Biology (Noisy le Grand)*, 64(14), 39–46.
- Pai, M. O., Pai, V. S., & Gupta, A. K., (2018). Effect of green tea leaves (*Camellia sinensis*) And carom seeds (*Trachyspermum ammi*) extracts on male mice exposed to diazinon. *Asian Journal of Pharmaceutical and Clinical Research*, 11(2), 138–142.
- Paknikar, K., (2007). *U.S. Patent Application No. 11/547,886*.
- Patnaik, N., (1993). *The Garden of Life: An Introduction to the Healing Plants of India*. New York.
- Paul, S., Dubey, R. C., Maheswari, D. K., & Kang, S. C., (2011). *Trachyspermum ammi* (L.) fruit essential oil influencing on membrane permeability and surface characteristics in inhibiting food-borne pathogens. *Food Control*, 22(5), 725–731.
- Petramfar, P., Moein, M., Samani, S. M., Tabatabaei, S. H., & Zarshenas, M. M., (2016). *Trachyspermum ammi* 10% topical cream versus placebo on neuropathic pain, a randomized, double-blind, placebo-controlled trial. *Neurological Sciences*, 37(9), 1449–1455.
- Platel, K., & Srinivasan, K., (2001). Studies on the influence of dietary spices on food transit time in experimental rats. *Nutrition Research*, 21(9), 1309–1314.
- Pruthi, S. C., Pruthy, P., & Pruthy, J. R., (1999). *U.S. Patent No. 5,980,903*. Washington, DC: U.S. Patent and Trademark Office.
- Raghavan, S., (2007). *Handbook of Spices, Seasonings, and Flavorings*. 6000 Broken Sound Parkway NW.
- Rajeshwari, C. U., Kumar, A. V., & Andallu, B., (2011). Therapeutic potential of Ajwain (*Trachyspermum ammi* L.) seeds. In: *Nuts and Seeds in Health and Disease Prevention* (pp. 153–159). Academic Press.
- Rajput, M. A., Khan, R. A., & Feroz, Z., (2013). Evaluation of antiepileptic activity of the methanol extract of *Trachyspermum ammi* (L.). *Archives of Biological Sciences*, 65(3), 815–819.
- Ramakrishna, R. R., Platel, K., & Srinivasan, K., (2003). *In vitro* influence of spices and spice-active principles on digestive enzymes of rat pancreas and small intestine. *Food/ Nahrung*, 47(6), 408–412.
- Rezvani, M. E., Roohbakhsh, A., Mosaddegh, M. H., Esmailidehaj, M., Khaloobagheri, F., & Esmaceli, H., (2011). Anticonvulsant and depressant effects of aqueous extracts of *Carum copticum* seeds in male rats. *Epilepsy & Behavior*, 22(2), 220–225.

- Sahaf, B. Z., & Moharrampour, S., (2008). Fumigant toxicity of *Carum copticum* and *Vitex pseudo-negundo* essential oils against eggs, larvae, and adults of *Callosobruchus maculatus*. *Journal of Pest Science*, 81(4), 213–220.
- Saleem, U., Saba, R. B. A., & Saleem, M., (2017). Pharmacological screening of *Trachyspermum ammi* for antihyperlipidemic activity in Triton X-100 induced hyperlipidemia rat model. *Pharmacognosy Research*, 9(Suppl 1), S34.
- Sayed-Ahmad, B., Talou, T., Saad, Z., Hijazi, A., & Merah, O., (2017). The *Apiaceae*: Ethnomedicinal family as source for industrial uses. *Industrial Crops and Products*, 109, 661–671.
- Shah, A., & Rahim, S., (2017). Ethnomedicinal uses of plants for the treatment of malaria in Soon Valley, Khushab, Pakistan. *Journal of Ethnopharmacology*, 200, 84–106.
- Sharifzadeh, A., Khosravi, A. R., Shokri, H., & Sharafi, G., (2015). Antifungal effect of *Trachyspermum ammi* against susceptible and fluconazole-resistant strains of *Candida albicans*. *Journal de Mycologie Medicale*, 25(2), 143–150.
- Shokri, H., Sharifzadeh, A., & Khosravi, A., (2016). Antifungal activity of the *Trachyspermum ammi* essential oil on some of the most common fungal pathogens in animals. *Iranian Journal of Veterinary Medicine*, 10(3), 173–180.
- Shukla, A. C., & Dikshit, A., (2011). Role of phylogenetic analysis for anti-bacterial activity of essential oil of *Trachyspermum ammi* L. against water borne pathogens. *Advances in Environmental Biology*, 5(6), 1271–1278.
- Siddiqui, M. J., Aslam, A., & Khan, T., (2019). Comparison and evaluation of different seed extracts of *Trachyspermum ammi* for immunomodulatory effect on cell-mediated immunity through delayed-type hypersensitivity assay skin thickness method. *Journal of Pharmacy & Bio Allied Sciences*, 11(1), 43.
- Soni, K., & Parle, M., (2017). *Trachyspermum ammi* seeds supplementation helps reverse scopolamine, alprazolam, and electroshock induced amnesia. *Neurochemical Research*, 42(5), 1333–1344.
- Takeda, J., De silva, S., Muthuraman, P., Rahman, S. M., & Kawet, L., (2008). Spices in Sri Lanka, India, and Bangladesh with special reference to the usages and consumptions. *Bulletin of University of Agricultural Sciences and Veterinary Medicines (Cluj-Napoca Agriculture)*, 93, 1–25.
- Tariq, M., Gore, M., & Aruna, K., (2014). Antibacterial and synergistic activity of ethanolic ajwain (*Trachyspermum ammi*) extract on ESBL and MBL producing uropathogens. *International Journal of Pharmacy and Pharmaceutical Sciences*, 6(6), 278–284.
- Thangam, C., & Dhananjayan, R., (2003). Anti-inflammatory potential of the seeds of *Carum copticum* Linn. *Indian Journal of Pharmacology*, 35(6), 388–391.
- Tomar, P., & Malik, C. P., (2015). Novel drug delivery system from essential oil of *Trachyspermum ammi*. *LS: International Journal of Life Sciences*, 4(1), 1–9.
- Tuzun, S., Univ, A., & Yegen, O., (2000). *A Natural and Safe Alternative to Fungicides, Bacteriocides, Nematicides, and Insecticides for Plant Protection and Against Household Pests*. US Patent WO2000021364 A2, PCT/US1999/023399.
- Umar, S., Asif, M., Sajad, M., Ansari, M. M., Hussain, U., Ahmad, W., Siddiqui, S. A., et al., (2012). Anti-inflammatory and antioxidant activity of *Trachyspermum ammi* seeds in collagen induced arthritis in rats. *International Journal of Drug Development and Research*, 4(1), 210–219.
- Vasudevan, K., Vembar, S., Veeraraghavan, K., & Haranath, P. S., (2000). Influence of intragastric perfusion of aqueous spice extracts on acid secretion in anesthetized albino

- rats. *Indian Journal of Gastroenterology: Official Journal of the Indian Society of Gastroenterology*, 19(2), 53–56.
- Vazirian, M., Hamidian, K., Noorollah, M., & Manayi, A., (2019). Enhancement of antibiotic activity and reversal of resistance in clinically isolated methicillin-resistant *Staphylococcus aureus* by *Trachyspermum ammi* essential oil. *Research Journal of Pharmacognosy*, 6(1), 1–10.
- Velazhahan, R., Vijayanandraj, S., Vijayasamundeeswari, A., Paranidharan, V., Samiyappan, R., Iwamoto, T., & Muthukrishnan, S., (2010). Detoxification of aflatoxins by seed extracts of the medicinal plant, *Trachyspermum ammi* (L.) Sprague ex turrill—structural analysis and biological toxicity of degradation product of aflatoxin G1. *Food Control*, 21(5), 719–725.
- Vitali, L. A., Beghelli, D., Nya, P. C. B., Bistoni, O., Cappellacci, L., Damiano, S., Lupidi, G., et al., (2016). Diverse biological effects of the essential oil from Iranian *Trachyspermum ammi*. *Arabian Journal of Chemistry*, 9(6), 775–786.
- Yin, Q. H., Yan, F. X., Zu, X. Y., Wu, Y. H., Wu, X. P., Liao, M. C., Deng, S. W., et al., (2012). Anti-proliferative and pro-apoptotic effect of carvacrol on human hepatocellular carcinoma cell line HepG-2. *Cytotechnology*, 64(1), 43–51.
- Zarshenas, M. M., Jamshidi, S., & Zargaran, A., (2016). Cardiovascular aspects of geriatric medicines in traditional Persian medicine; a review of phytochemistry and pharmacology. *Phytomedicine*, 23(11), 1182–1189.
- Ziaee, M., & Moharramipour, S., (2013). Effectiveness of medicinal plant powders on *Sitophilus granarius* and *Tribolium confusum*. *Journal of Crop Protection*, 2(1), 43–50.



# Taylor & Francis

Taylor & Francis Group

<http://taylorandfrancis.com>

## CHAPTER 10

---

# *Tinospora cordifolia* (Willd.) Miers: A Review on Medicinal Aromatic Plant with Industrial and Therapeutical Utilization

SONIA SINGH,<sup>1</sup> NITIN AGRAWAL,<sup>2</sup> and YOGESH MURTI<sup>1</sup>

<sup>1</sup>*Institute of Pharmaceutical Research, GLA University, Mathura, Uttar Pradesh, India*

<sup>2</sup>*Faculty of Pharmacy, Raja Balwant Singh Engineering Technical Campus, Bichpuri, Agra, Uttar Pradesh, India*

---

### ABSTRACT

*Tinospora cordifolia* (Willd.) Miers, most commonly included in Ayurvedic medicine. It has as a vernacular name of “Amrita” and “Guduchi” (Family: Menispermaceae). It has been used in the management of several diseases such as urinary problem, fever, dysentery, leprosy, diabetes, and skin disorders. Though, there are several therapeutic indications are available, where clinical research is required to examine the efficacy and quality of the plant. The plant contains various primary and secondary metabolites has been isolated and characterized as Tinosporine, Magnoflorine, Berberine, Choline, Jatrorrhizine, and many more chemical components. The current literature provides detailed valuable information regarding the occurrence and distribution, organoleptic, microscopical, phytochemistry, pharmacological, and clinical trial profile of the crude drug, *Tinospora cordifolia* (Willd.) Miers. In addition to this the commercial, as well as medicinal and therapeutical utilization of the *Tinospora cordifolia* (Willd.) Miers plant, has also been discussed in detail.

## 10.1 INTRODUCTION

The herbal plant, *Tinospora cordifolia* (Willd.) Miers, “guduchi” considered as a herbaceous vine belongs to Menispermaceae family. It has many beneficiary effects in treating several ailments. Even it is a well-known herb in Ayurveda system of medicine (Preeti, 2011). Specifically, it is employed as an analgesic, antipyretic, antispasmodic, cardiogenic, expectorant, anti-inflammatory, and anti-asthmatic agent. It is used in many infective conditions such as typhoid, malaria, filariasis, and leprosy; well-known plant given in intermittent fevers. It has many more other therapeutic applications including anthelmintic properties, used in skin diseases, urinary disorders, gout, rheumatoid arthritis and eye diseases (Kokate, Purohit, & Gokhale, 2010). According to Savrikar et al. it is found that the ayurvedic preparation containing *Tinospora cordifolia* (Willd.) Miers has shown a promising effect in hypothermia and gastric ulceration (Savrikar, Dole, Ravishankar, & Shukla, 2010).

These pharmacological and therapeutical properties of the plant are due to the presence of several major secondary metabolites like steroids, glycosides, phenolic components, aliphatic compounds, diterpenoid lactones, sesquiterpenoid, essential oils, polysaccharides, and fatty acids; however present in different parts of the plant including stem, leaves, aerial whole plant and root (Meena, Singh, Panda, Mishra, & Rao, 2010; Sharma et al., 2012; Goel et al., 2004; Sinha, Mishra, Singh, & Khanuja, 2004; Upreti & Chauhan, 2018; Salkar, Chotalia, & Salvi, 2017; Khan, Dul Haque, & Chowdhury, 2016). It is a dried, matured stem part of *T. cordifolia* (Willd.) Miers (Menispermaceae). It is an annual climber and found abundantly in India. It has been collected in the month of May during summer season (Saha & Ghosh, 2012).

## 10.2 VERNACULAR NAMES

**Sanskrit:** Amrtavalli, Amrta; **Hindi:** Giloe, Gurcha; **Bengali:** Gulancha; **Assamese:** Siddhilata, Amarlata; **Gujrati:** Galac, Garo; **Kashmiri:** Amrita, Gilo; **Kannada:** Amrutaballi; **Malayalam:** Chittamrutu; **Oriya:** Guluchi; **Marathi:** Gulvel; **Punjabi:** Gilo; **Telugu:** Thippateega; **Tamil:** Seendal, Seendil kodi; **Urdu:** Gilo

## 10.3 GEOGRAPHICAL SOURCE

It grows very well as a climber on shrubs and small trees. It is indigenous to India as widely expanded in lower valleys of Garhwal and also reported to found in different places of Almora, and Kumaon region. Generally, it

mainly grows over hedges; and thereby it has been called “plant of dry forest” (Kokate, Purohit, & Gokhale, 2010).

#### **10.4 MORPHOLOGICAL CHARACTERS**

This is a climbing shrub with many branches of coiled nature. The stem is a fleshy, filiform with climbing nature. The bark is of white or sometimes gray in color (Kirtikar & Basu, 1933; Upadhyay, Kumar, Kumar, & Mishra, 2010). The powdered stem is of dark brown color with bitter taste and characteristic odor. Usually, it is used in fever, dyspepsia, and even in urinary tract infections. “Guduchi-satva” is the starch found present in the stem of the plant which contains significant nutritive values and digestive properties. The leaves are simple, alternate with long-petiole of around 15 cm. The lamina region is about 10–20 cm wide with ovate (Tiwari, Nayak, Prusty, & Sahu, 2018; Arul, Miyazaki, & Dhananjayan, 2005). The flowers of the plant are unisexual, axillary position, with leaflet branches. They are greenish-yellow in color, the flowers are generally found present in cluster and some of them usually in the solitary form. Fruits are single-seeded, mainly get matured in winter. It bears flowers in summer. The seeds are in curve shaped (Spandana, Liakhat, Nirmala, Santhi, & Babu, 2013) and the entire morphological features have been depicted in Figure 10.1.

#### **10.5 MICROSCOPICAL CHARACTERS**

The histology of stem shows the cork, the outermost layer is differentiated into thick-walled, brownish colored compressed cells represented as an outer zone whereas the inner region consisted of thin-walled tangentially arranged cells which are colorless. Groups of lenticels are present within the cork region, followed by few rows of the secondary cortex. The sclereids are composed of 3–12 cells present in the secondary cortex region. The tangentially elongated collenchymatous cells are found present in the outer region of cortex. The cortical cells are polygonal-shaped, filled with starch grains that are simple, ovoid-elliptical in shape. The pericyclic fibers are lignified attached with the lumen and have a pointed ends, with fibers. The vascular bundle is composed of lignified strips of xylem, followed by a non-lignified layer of phloem. The phloem has consisted of companion cells, phloem parenchyma and sieve tube along with calcium oxalate crystals. The cambium is composed of tangentially elongated cells present in the vascular bundles as in the layer form. The xylem has consisted of parenchyma, tracheids, fibers, sclereids, and vessels.

The pith is consisted of parenchymatous thin walled cells with starch grains (The Ayurvedic Pharmacopoeia of India, 2003) (Figure 10.2).

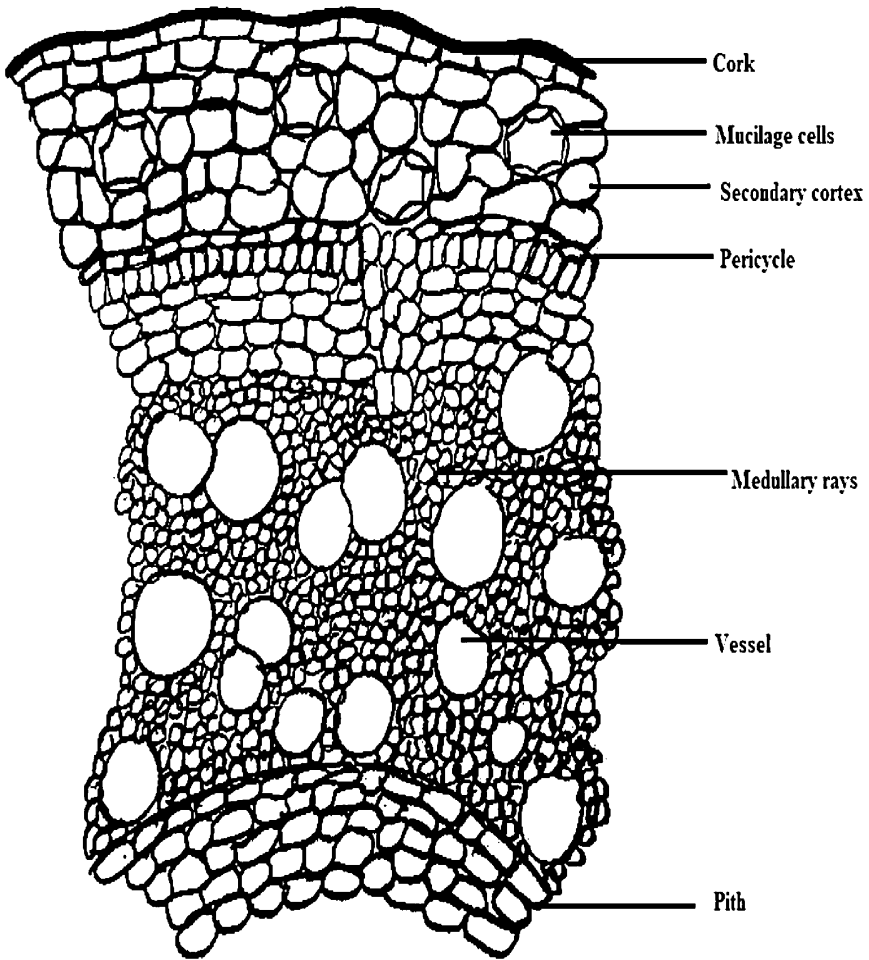


**FIGURE 10.1** *Tinospora cordifolia* (Willd.) Miers.

## 10.6 ETHNOMEDICINAL USES

Herbal juice is used in the treatment of irregular fever. A decoction is incorporated with honey that can be taken in the morning to cure jaundice. Even the decoction preparation can also be given in vomiting. Juice of the plant is mixed with Pippali powder to be used in curing fever. Leaves of *Tinospora*





**FIGURE 10.2** Microscopy of *Tinospora cordifolia* (Willd.) Miers stem.

*cordifolia* (Willd.) Miers are used to cure fever. Additionally, the continuous use of Guduchi juice mixed with oil to destroy filarial. Fresh juice of the herb admixed with turmeric powder to cure hepatitis. Juices of Guduchi, Amalaki, and Haridra, together act as synergistically in many urinary problems. The starch of Guduchi is used to reduce the burning sensation, in curing elevated body temperature and to enhance the appetite of the individual (described in Table 10.1) (Singh & Maheshwari, 1983; Shah, 1984; Bhatt & Sabnis, 1987; Joshi & Kaur, 2016).

**TABLE 10.1** Ethnomedicinal Uses of *T. cordifolia*

Preparation	Composition	Ethnomedicinal Uses	References
Decoction	<i>Tinospora cordifolia</i> (Willd.) Miers, <i>Terminalia chebula</i> , <i>Berberis aristata</i> , <i>Zingiber officinale</i>	Liver abscess	Sohni & Bhatt (1996)
	<i>Tinospora cordifolia</i> (Willd.) Miers, <i>Terminalia bellerica</i> , <i>Phyllanthus niruri</i> , <i>Phyllanthus emblica</i> <i>Terminalia chebula</i>	Hepatoprotective	Tasaduq et al. (2003)
	<i>Tinospora cordifolia</i> (Willd.) Miers	Diabetic ulcers in foot	Purandare & Supe (2007)
	<i>Tinospora cordifolia</i> (Willd.) Miers	Allergic rhinitis	Badar et al. (2005)
	<i>Tinospora cordifolia</i> (Willd.) Miers	Tuberculosis, breast cancer, obstructive jaundice and sepsis.	Panchabhai, Kulkarni, & Rege (2008)
	<i>Terminalia chebula</i> , <i>Boerhavia diffusa</i> , <i>Zingiber officinale</i> , <i>Berberis aristata</i>	Against <i>Entamoeba histolytica</i>	Sohni, Kaimal, & Bhatt (1995)
	<i>Withania somnifera</i> , <i>Zingiber officinale</i> , <i>Tribulus terrestris</i>	Arthritis	Chopra et al. (2012)
<b>Paste</b>	<i>Tinospora cordifolia</i> (Willd.) Miers <b>stems and Solanum surattense roots</b>	<b>Fever</b>	Joshi & Kaur (2016)
<b>Decoction</b>	<i>Tinospora cordifolia</i> (Willd.) Miers root and stem bark.	<b>Dysentery and diarrhea</b>	
<b>Paste or juice</b>	<i>Tinospora cordifolia</i> (Willd.) Miers leaves and <i>Brassica campestris</i> seed powder	Burning sensation	
<b>Juice</b>	<i>Tinospora cordifolia</i> (Willd.) Miers stem with honey	<b>Asthma</b>	

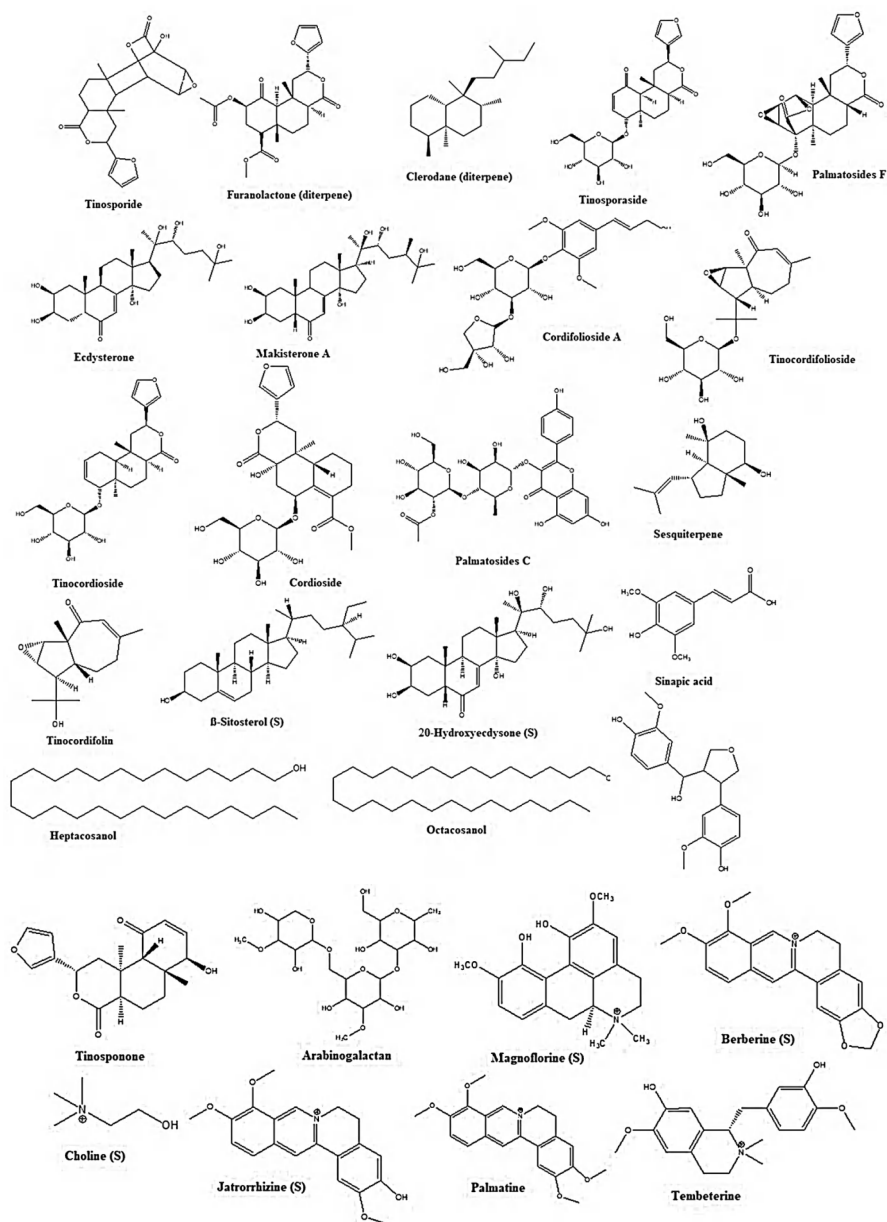
## 10.7 PHYTOCHEMISTRY

The secondary metabolites present in *Tinospora cordifolia* (Willd.) Miers are alkaloids, glycosides, polyphenolic components, steroids, polysaccharides, and aliphatic components. The leaves are found rich in calcium, phosphorus, and protein (11.2%). *Tinospora cordifolia* (Willd.) Miers stems contain furanolactone clerodane diterpene such as amritoside A, B, C, and D (Sohni & Bhatt, 1996; Tasaduq et al., 2003; Purandare & Supe, 2007; Badar et al., 2005; Panchabhai, Kulkarni, & Rege, 2008; Sohn, Kaimal, & Bhatt, 1995;

Chopra et al., 2012; Chi, She, Han, Wang, Liu, & Liu, 2016; Chaudhary, Siddiqui, & Khatoon, 2014; Maurya et al., 2004; Abhijeet & Mokat, 2018; Sumran & Aggarwal, 2019). Essential secondary metabolites are mentioned in Table 10.2 and their structure drawn in Figure 10.3.

**TABLE 10.2** Essential Secondary Metabolites Present in *T. cordifolia*

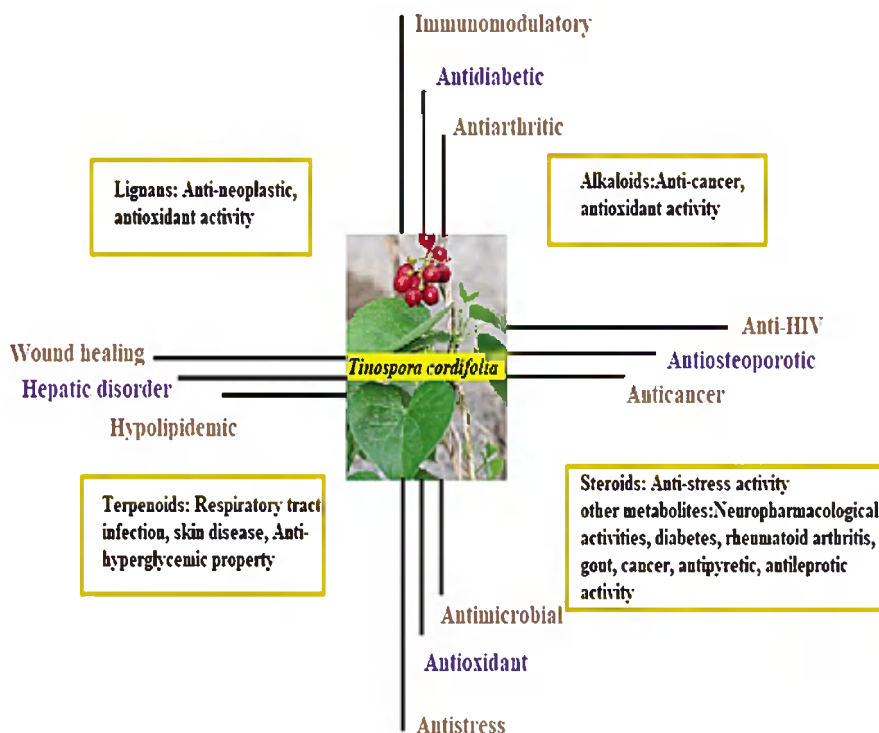
Category of Chemical Components	Secondary Metabolites	References
Terpenoid	Furanolactone clerodane diterpene, tinosporide, furanoid diterpene, tinosporaside, furanolactone diterpene, cordifolioside A-C, ecdysterone makisterone, cordifolioside D, cordioside, palmatosides C, sesquiterpene tinocordifolin, sesquiterpene glucoside tinocordifolioside, tinosponone, tinosponone tetracetate, tinocordioside, tinoscorsidic C, borapetoside B and F, tinoscripsol A, cordioside, cordioside tetracetate, tinosporaside, 8-hydroxy columbin, cordifolide A, B, and C, tinosporaclerodanoid, amritoside A, B, C, and D, tinosporaclerodanol, tinosporafurandioliol, palmatosides F, tinocordioside, cordifolioside E	Sohni & Bhatt (1996); Khuda, Khaleque, & Ray (1964); Hanuman, Bhatt, & Sabata (1986); Bhatt, Hanuman, & Sabata (1988); Hanuman, Bhatt, & Sabata (1988); Bhatt & Sabata (1989); Khan, Gray, & Waterman (1989); Gangan, Arjun, Sipahimalani, & Banerji (1994); Maurya & Handa (1998); Gangan, Arjun, Sipahimalani, & Banerji (1995); Wazir, Maurya, & Kapil (1995); Gagan, Pradhan, Sipahimalani, Banerji, & Palmatosides (1996)
Alkaloid	Tinosporine, berberine, magnoflorine, choline, 1,2-substituted pyrrolidine, jatrorrhizine, tembeterine, palmatine	Sohni & Bhatt (1996); Choudhary, Siddiqui, Azmat, & Khatoon (2013); Bisset & Nwaiwu (1983); Mahajan, Jolly, & Kundnani (1985); Sharma, Khosa, Chansauria, & Ray (1995); Pathak, Agarwal, Jain, Sharma, & Howarth (1995)
Lignan	3-( $\alpha$ ,4-dihydroxy-3-methoxybenzyl)-4-(4-hydroxy-3-methoxybenzyl)	Sohni & Bhatt (1996); Hanuman, Mishra, & Sabata (1986)
Steroid	20 $\alpha$ -hydroxy ecdysone, $\beta$ -sitosterol, giloinsterol, polypodine B 20,22-acetonide	Sohni & Bhatt (1996); Kidwai, Salooja, Sharma, & Siddiqui (1949); Khaleque, Maith, Huq, & Abul (1970); Dixit & Khosa (1971); Pathak, Jain, & Sharma (1995)
Flavonoid	(-)-Epicatechin	Sohni & Bhatt (1996)
Miscellaneous components	Tinosporan acetate, giloin, tinosporal acetate, heptacosanol, tinosporidine, octacosanol, tinosponone, sinapic acid	Khuda, Khaleque, Basar, Rouf, Khan, & Roy (1966); Khaleque, Maith, & Huq (1971); Maurya, Wazir, Tyagi, & Kapil (1995); Pradhan, Gangan, Sipahimalani, & Banerji (1997); Chintalwar et al. (1999)



**FIGURE 10.3** Structures of phytoconstituents present in *T. cordifolia* (Willd.) Miers.

## 10.8 PHARMACOLOGICAL ACTIVITY

*T. cordifolia* (Willd.) Miers extracts are commonly used in several herbal formulations as anti-spasmodic, anti-periodic, anti-microbial, anti-inflammatory, anti-osteoporotic, anti-allergic, anti-diabetic, and anti-arthritic properties as discussed in Tables 10.3 and 10.4 and Figure 10.4.



**FIGURE 10.4** Pharmacological activities of *Tinospora cordifolia* (Willd.) Miers.

## 10.9 SUBSTITUENTS AND ADULTERANTS

The plant, *Tinospora cordifolia* (Willd.) Miers is quite substituted or adulterated with some other species of *Tinospora*, including *Tinospora sinensis* and *Tinospora crispa*. Additionally, the histochemical characteristics present in *Tinospora sinensis* may resemble that of *Tinospora cordifolia* (Willd.) Miers, however few of the characteristics features would differ among them. Some of the distinguishing features are discussed as below: In *Tinospora cordifolia*

**TABLE 10.3** Pharmacological Activity of *T. cordifolia* (Willd.) Miers

Plant Part	Extract	Biological Activity	Experimental Model	Animal Model	References
Whole plant	Alcoholic	Cardioprotective	Calcium chloride induced arrhythmia.	Rats	Sharma et al. (2011)
Roots of <i>T. cordifolia</i> Miers and <i>Centella asiatica</i>	Ethanol	Antiulcer	Stress-induced ulceration	–	Sharma, Khosa, Chansauria, & Sahai (1995)
–	Aqueous	Anti-ulcer	Gastric ulcer induced by ethanol, aspirin, and pylorus ligation induced ulcer model.	Albino rats	Chandan, Deb, & Bhargavi (2013)
Stem bark	Ethanol/aqueous	Antidiarrheal	Castor oil and magnesium sulfate-induced diarrhea	Rats	Kaur, Singh, & Kumar (2014)
Capsules named as “guduchi” (Himalaya Drug Co., India)	–	Analgesic	Writhing method and hot plate method.	Albino rats	Goel, Pathak, Nim, Singh, Dixit, & Chaurasia (2014)
Stem	Water-soluble		Eddy’s plate, tail-flick test and acetic acid-induced writhing.	Albino rats	Sumanlata, Suman, Sharma, Jindal, & Khan (2019)
–	Aqueous		Tail flick model	Albino rats	Mandal, Das, Mandal, & Biswas (2020)
Stem	Aqueous/hydro alcoholic	Aphrodisiac	Observing the mounting frequency, mount latency, intromission frequency, intromission latency, genital grooming and anogenital sniffing.	–	Wani, Achur, & Nema (2011)
Himalaya Drug Company, India.	–	Immunomodulatory	Effect on macrophage activation.	Macrophage J774A.1 cell line	More & Pai (2011)
–	Ethyl acetate, water fractions and hot water	–	Phagocytic function studies, chemiluminescence assay.	–	Sharma, Bala, Kumar, Singh, Munshi, & Bhalerao (2012)

**TABLE 10.3** (Continued)

Plant Part	Extract	Biological Activity	Experimental Model	Animal Model	References
Stem	Aqueous/ methanol	–	Broth dilution and agar well diffusion assays.	<i>Salmonella typhimurium</i> infected mice	Alsuhaibani & Khan (2017)
Stem	–	Antidyslipidemic	Alloxan induced diabetic	Rats	Kumar (2015)
Whole plant	Alcoholic	Neuroprotective	Lesion induced by 6-hydroxy dopamine in rats.	Rats	Kosaraju, Chinni, Roy, Kannan, Antony, & Kumar (2014)
–	Aqueous		MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) induced nigrostriatal dopaminergic neurodegeneration.	Parkinsonian mice	Singh, Birla, Rai, Zahra, & Singh (2018)
–	–	<b>Analgesic, anti-inflammatory, and antipyretic.</b>	Antipyretic: brewer's yeast-induced pyrexia method; Analgesic: writhing test, tail-flick, and hot plate test; Anti-inflammatory: carrageenan-induced inflammation model	Rats	Patgiri et al. (2014)
–	Aqueous	<b>Anti-inflammatory and antipyretic</b>	Anti-inflammatory: carrageenan and histamine-induced rat paw edema; antipyretic: brewer's yeast induced pyrexia model.	Albino rats	Hussain, Akash, Ain, Rehman, & Ibrahim (2015)
–	Epoxy clerodane diterpene	Gastroprotective	Indomethacin induced gastric ulcers.	Rats	Sumanlata, Suman, Sharma, & Khan (2019)
Plant	Alcoholic	Antioxidant	Liver cancer induced by N-nitrosodiethylamine.	Albino rats	Antonisamy et al. (2014)

**TABLE 10.3** (Continued)

Plant Part	Extract	Biological Activity	Experimental Model	Animal Model	References
Stem	Alcoholic	Radioprotective and cytoprotective	$\gamma$ -radiation in rats; genotoxicity induced by cyclophosphamide.	Mice	Patel, Bigoniya, Singh, & Patel (2013)
–	Chloroform	Anti-feedant	–	Insects	Sivasubramanian, Narasimha, Rathnasamy, & Campos (2013)
–	–	Ameliorative	Aflatoxin-induced nephrotoxicity	Mice	Gupta & Sharma (2011)
Stem	n-Butanolic fraction of ethanolic extract	Nootropic	Elevated plus-maze	Mice	Une, Ejaj, & Tarde (2014)
Stem	Isoquinoline alkaloid rich fraction	Hypoglycemic	<i>In vitro</i> and <i>in vivo</i> Insulin-mimicking as well as releasing property.	Rats	Patel & Mishra (2011)
Stem	–	Hypoglycemic, anti-hyperglycemic	Decreased in body sugar level in normoglycemic rodents.	Mice	Sharma, Kumar, Ashok, Galib, Prajapati, & Ravishankar (2013)
Stem	Methanol	–	Alloxan induced diabetic rats	–	Sivakumar & Rajan (2011)
–	Aqueous ethanol	Antipsychotic	Amphetamine challenged model	Mice	Jain, Jain, & Shete (2010)
Fresh leaves	–	Antidepressant	Tail suspension method and forced swim test.	Albino mice	Kalabharathi, Vaibhavi, Naidu, Pushpa, & Shruthi (2014)
Stem	70% methanolic	Antifertility	Sperm motility, sperm density.	<b>Male rats</b>	Gupta & Sharma (2003)
–	Alcohol	Antitumor	Tumor-associated macrophages.	Mice	Singh, Singh, & Shrivastava (2005)



**TABLE 10.3** (Continued)

Plant Part	Extract	Biological Activity	Experimental Model	Animal Model	References
–	50% methanolic extract of stem	–	<i>In vitro</i> cytotoxic activity.	Human breast cancer cell line MDA-MB-231 and normal Vero epithelial cell line.	Ahmad, Srivastava, & Khan (2015)
Stem	Ethanol	Antimalarial	Inhibited the propagation of <i>in vivo Plasmodium berghei</i> .	BALB/c mice	Singh & Banyal (2011)
–	Diterpenoid	Hepatocellular carcinoma	Diethylnitrosamine induced hepatocellular carcinoma rats.	Rats	Dhanasekaran et al. (2009)
–	100% ethanol	Antimicrobial	Brain–heart infusion agar medium.	<i>Streptococcus mutans</i>	Agarwal, Ramamurthy, Fernandes, Rath, & Sidhu (2019)
Stem	–	–	Disc diffusion assay.	Gram-negative, <i>Escherichia coli</i> ; Grampositive, <i>Staphylococcus aureus</i> .	Singh, Singh, Katiyar, & Srivastava (2003)
Stem	Aqueous, ethanol, and chloroform	Antibacterial	Disc diffusion assay	Gram-negative and gram-positive	Jeyachandran, Xavier, & Anand (2003)
–	Petroleum ether, chloroform, methanol, and aqueous by	Antibacterial	Agar well diffusion assay	<i>S. aureus</i> , <i>S. mutans</i> , <i>S. salivarius</i> , <i>Lactobacillus acidophilus</i> , <i>S. sanguinis</i>	Vermani, Navneet, & Gautam (2013)

Note: –: not known.

**TABLE 10.4** Clinical Trials of *Tinospora cordifolia* (Willd.) Miers

SL. No.	Formulations	Models Used	Applications	References
1.	<i>Carica papaya</i> with <i>Tinospora cordifolia</i> (Willd.) Miers leaf extract.	Randomized with 250 patients, orally received 5 ml of syrup twice for five days.	Enhanced the platelet count in the cancer patients.	Babu et al. (2017)
2.	<i>Tinospora cordifolia</i> (Willd.) Miers	30 individuals randomly assigned into placebo, TC ( <i>Tinospora cordifolia</i> ) 150 and TC 300. Physical stressors and physical performance analyzed.	TC 300 mg group revealed deduction in BP and HR comparable with placebo.	Salve, Tripathi, Petare, Raut, & Rege (2015)
3.	<i>Tinospora cordifolia</i> (Willd.) Miers extract	Randomized double-blind placebo-controlled trial for six months; 68 HIV (human immunodeficiency virus) positive participants.	Potentially reduced the eosinophil count and hemoglobin percentage.	Kalikar et al. (2008)
4.	<i>Tinospora cordifolia</i> (Willd.) Miers lotion	Randomized, controlled, pilot clinical study of sample investigated in 66 scabies-infected patients.	Reduced the mean evaluation score after 28 days of treatment.	Castillo et al. (2013)
5.	<i>Tinospora cordifolia</i> (Willd.) Miers herb	Around 30 volunteers (age 18–30 years) received 500 mg of <i>T. cordifolia</i> aqueous extract for 21 days in a double-blind, randomized controlled design.	Significant ( $p < 0.05$ ) increased the test scores for verbal learning and memory and logical memory.	Bairy, Rao, Das, & Kumar (2004)
6.	<i>Tinospora cordifolia</i> (Willd.) Miers herb	15 patients; 20 gms of <i>T. cordifolia</i> along with honey in tested group and Pearl millet flour with syrup in placebo group for around 8 weeks.	Significantly decreased the severity of mucositis in the tested group.	Amruthesh, Mubeen, Pramod, Venkatesh, & Ramesh (2010)
7.	<i>Tinospora cordifolia</i> (Willd.) Miers herb	30 volunteers aged 18–30 years randomized, double-blind controlled study evaluated for 21 days.	Found safe at a dose of 500 mg.	Karkal & Bairy (2007)

(Willd.) Miers, the sheath of the sclerenchymatous layer has broken into several scattered patches present in cortical regions; however, in *Tinospora sinensis*, these sheaths gets disintegrated into different regions followed by the vascular bundle and would remain till the secondary growth may occur. Calcium oxalate crystals are found absent in *Tinospora cordifolia* (Willd.) Miers whereas, in *Tinospora sinensis*, the lumen of each corks cells are present. *Tinospora cordifolia* (Willd.) Miers contains more number of mucilaginous cells when compared to *Tinospora sinensis*. The vascular strands are present in a fewer amount in *Tinospora cordifolia* (Willd.) Miers and a larger amount in *Tinospora sinensis*. In *Tinospora cordifolia* (Willd.) Miers, the vascular bundle contains well-developed xylem and it has not well developed in case of *Tinospora sinensis*. Pith consists of thin-walled narrow cells in *Tinospora cordifolia* (Willd.) Miers while in *Tinospora cordifolia* (Willd.) Miers it is in the broader form (Preeti, 2011; Sinha, Mishra, Singh, & Khanuja, 2004).

## 10.10 CONCLUSION

*Tinospora cordifolia* (Willd.) Miers is a medicinally important herb possessing the number of secondary metabolites such as steroids, lignans, alkaloids, glycosides, and terpenoids. The current manuscript has introduced its pharmacological applications including antifungal, antioxidant, antimicrobial, antibacterial, hypolipidemic property, hepatoprotective effect, anti-cancer, and anti-HIV effects. The herb has employed in Ayurvedic medicine from the ancient period. Additionally, the products of this herbal drug are economically utilized for therapeutic purposes. In this regard, furthermore, studies are required to explore various secondary metabolites of *T. cordifolia* (Willd.) Miers, so therefore it could be potentially used in preventing and treating life-threatening diseases. Even the content of this chapter will be found more helpful in the management of novel drug formulation(s).

## KEYWORDS

- **ethnomedicinal uses**
- **geographical source**
- **Guduchi**
- **herbs**
- **hypolipidemic property**
- **novel drug formulation**
- **pharmacological applications**
- **phytochemical screening**

## REFERENCES

- Abhijeet, R., & Mokhat, D., (2018). On vegetative propagation through stem cuttings in medicinally lucrative *Tinospora* species. *J. Pharmacogn. Phytochem.*, 2, 2313–2318.
- Agarwal, S., Ramamurthy, P. H., Fernandes, B., Rath, A., & Sidhu, P., (2019). Assessment of antimicrobial activity of different concentrations of *Tinospora cordifolia* against *Streptococcus mutans*: An *in vitro* study. *Dent. Res. J. (Isfahan)*, 16(1), 24–28.
- Ahmad, R., Srivastava, A. N., & Khan, M. A., (2015). Evaluation of *in vitro* anticancer activity of stem of *Tinospora cordifolia* against human breast cancer and Vero cell lines. *J. Med. Plants Stud.*, 3(4), 33–37.
- Alsuhailbani, S., & Khan, M. A., (2017). Immune-stimulatory and therapeutic activity of *Tinospora cordifolia*: Double-edged sword against *Salmonellosis*. *J. Immunol. Res.* Article ID 1787803.
- Amruthesh, S., Mubeen, Pramod, K. P. R., Venkatesh, B. A., & Ramesh, C., (2010). Evaluation of radioprotective effects of *Tinospora cordifolia* in patients on radiotherapy for squamous cell carcinoma of the head & neck - a pilot study. *Int. J. Contemp. Dent.*, 1(1), 24–30.
- Antoniamy, P., Dhanasekaran, M., Ignacimuthu, S., Duraipandian, V., Balthazar, J. D., Agastian, P., & Kim, J. H., (2014). Gastroprotective effect of epoxy clerodane diterpene isolated from *Tinospora cordifolia* Miers (Guduchi) on indomethacin-induced gastric ulcer in rats. *Phytomedicine*, 21(7), 966–969.
- Arul, V., Miyazaki, S., & Dhananjayan, R., (2005). Studies on the anti-inflammatory, antipyretic, and analgesic properties of the leaves of *Aegle marmelos* Corr. *J. Ethnopharmacol.*, 96, 159–163.
- Babu, R., Kubavat, S., Poulse, K. P., Kumar, S., Handae, S., Satyanarayan, Dhamodaran, V., & Elangovan, B., (2017). A randomized, double-blind, placebo-controlled, proof of concept study to assess the safety and efficacy of *Carica papaya* and *Tinospora cordifolia* leaf extract (thrombobliss) in subjects undergoing chemotherapy treatment and subjects with systemic microbial infection and subsequent reduction in platelet count. *Int. J. Clin. Tri.*, 4(3), 116–121.
- Badar, V. A., Thawani, V. R., Wakode, P. T., Shrivastava, M. P., Gharpure, K. J., Hingorani, L. L., & Khiyani, R. M., (2005). Efficacy of *Tinospora cordifolia* in allergic rhinitis. *J. Ethnopharmacol.*, 96(3), 445–449.
- Bairy, K. L., Rao, Y., Das, S. K., & Kumar, B., (2004). Efficacy of *Tinospora cordifolia* on learning and memory in healthy volunteers: A double-blind, randomized, placebo-controlled study. *Iran. J. Pharm. Res.*, 3(2), 57–60.
- Bhatt, R. K., & Sabata, B. K., (1989). A furanoid diterpene glucoside from *Tinospora cordifolia*. *Phytochemistry*, 28, 2419–2422.
- Bhatt, R. K., Hanuman, J. B., & Sabata, B. K., (1988). A new clerodane derivative from *Tinospora cordifolia*. *Phytochemistry*, 27, 1212–1216.
- Bhatt, R. P., & Sabnis, S. D., (1987). Contribution to the ethnobotany of Khedbrahma region of North Gujarat. *J. Econ. Taxon. Bot.*, 9, 139.
- Bisset, N. G., & Nwaiwu, J., (1983). Quaternary alkaloids of *Tinospora* species. *Planta Med.*, 48, 275–279.
- Castillo, A. L., Osi, M. O., Ramos, J. D. A., De Francia, J. L., Dujunco, M. U., & Quilala, P. F., (2013). Efficacy and safety of *Tinospora cordifolia* lotion in *Sarcoptes scabiei* var *hominis*-infected pediatric patients: A single blind, randomized controlled trial. *J. Pharmacol. Pharmacother.*, 4(1), 39–46.

- Chandan, N. G., Deb, T., & Bhargavi, S. M., (2013). Evaluation of anti-ulcer activity of *Tinospora cordifolia* in albino rats. *Int. J. Pharm. Bio. Sci.*, 4(2), 78–85.
- Chaudhary, N., Siddiqui, M. B., & Khatoon, S., (2014). Pharmacognostical evaluation of *Tinospora cordifolia* (willd) Meirs and identification of biomarkers. *J. Res. Indian Med.*, 13, 543–550.
- Chi, S., She, G., Han, D., Wang, W., Liu, Z., & Liu, B., (2016). Genus *Tinospora*: Ethnopharmacology, phytochemistry, and pharmacology. *Evid. Based Complementary Altern. Med.* Article ID 9232593.
- Chintalwar, G., Jain, A., Sipahimalani, A., Banerji, A., Sumariwalla, P., Ramakrishnan, R., & Sainis, K., (1999). An immunologically active arabinogalactan from *Tinospora cordifolia*. *Phytochemistry*, 52, 1089–1093.
- Chopra, A., Saluja, M., Tillu, G., Venugopalan, A., Narsimulu, G., Handa, R., Bichile, L., et al., (2012). Comparable efficacy of standardized ayurveda formulation and hydroxychloroquine sulfate (HCQS) in the treatment of rheumatoid arthritis (RA): A randomized investigator-blind controlled study. *Clin. Rheumatol.*, 31(2), 259–269.
- Choudhary, N., Siddiqui, M. B., Azmat, S., & Khatoon, S., (2013). *Tinospora cordifolia*: Ethnobotany, phytopharmacology, and phytochemistry aspects. *Int. Pharm. Sci. Res.*, 4, 891.
- Dhanasekaran, M., Baskar, A. A., Ignacimuthu, S., Agastian, P., & Duraipandiyan, V., (2009). Chemopreventive potential of epoxy clerodane diterpene from *Tinospora cordifolia* against diethylnitrosamine-induced hepatocellular carcinoma. *Invest. New Drugs*, 27(4), 347–355.
- Dixit, S. N., & Khosa, R. L., (1971). Chemical investigations on *Tinospora cordifolia* (wild.) Miers. *Indian. J. Appl. Chem.*, 34, 46–47.
- Gagan, V. D., Pradhan, P., Sipahimalan, A. T., Banerji, A., & Palmatosides, C. F., (1996). Diterpene furan glucosides from *Tinospora cordifolia* – structural elucidation by 2D NMR spectroscopy. *Indian J. Chem.*, 35B, 630–634.
- Gangan, V. D., Arjun, P. P., Sipahimalani, A. T., & Banerji, A., (1995). Norditerpene furon glucoside from *Tinospora cordifolia*. *Phytochemistry*, 39, 1139–1142.
- Gangan, V. D., Arjun, P. P., Sipahimalani, T. A., & Banerji, A., (1994). Cardifolisides A, B, C: Norditerpene furon glucoside from *Tinospora cordifolia*. *Phytochemistry*, 37, 781–786.
- Goel, B., Pathak, N., Nim, N. K., Singh, S. K., Dixit, R. K., & Chaurasia, R., (2014). Clinical evaluation of analgesic activity of guduchi (*Tinospora cordifolia*) using animal model. *J. Clin. Diagn. Res.*, 8(8), HC01–HC04.
- Goel, H. C., Prasad, J., Singh, S., Sagar, R. K., Agrawala, P. K., Bala, M., Sinha, A. K., & Dogra, R., (2004). Radioprotective potential of an herbal extract of *Tinospora cordifolia*. *J. Radiat. Res.*, 45, 61–68.
- Gupta, R. S., & Sharma, A., (2003). Antifertility effect of *Tinospora cordifolia* (Willd.) stem extract in male rats. *Indian J. Exp. Biol.*, 41(8), 885–889.
- Gupta, R., & Sharma, V., (2011). Ameliorative effects of *Tinospora cordifolia* root extract on histopathological and biochemical changes induced by aflatoxin-b1 in mice kidney. *Toxicol. Int.*, 18(2), 94–98.
- Hanuman, J. B., Bhatt, R. K., & Sabata, B. K., (1986). A diterpenoid furanolactone from *Tinospora cordifolia*. *Phytochemistry*, 25, 1677–1680.
- Hanuman, J. B., Bhatt, R. K., & Sabata, B., (1988). A clerodane furano-diterpene from *Tinospora cordifolia*. *J. Nat. Prod.*, 51, 197–201.
- Hanuman, J. B., Mishra, A. K., & Sabata, B., (1986). A natural phenolic lignan from *Tinospora cordifolia* Miers. *J. Chem. Soc.*, 1181–1185.

- Hussain, L., Akash, M. S., Ain, N. U., Rehman, K., & Ibrahim, M., (2015). The analgesic, anti-inflammatory, and anti-pyretic activities of *Tinospora cordifolia*. *Adv. Clin. Exp. Med.*, 24(6), 957–964.
- Jain, B. N. G., Jain, V. K., & Shete, A., (2010). Antipsychotic activity of aqueous ethanolic extract of *Tinospora cordifolia* in amphetamine challenged mice model. *J. Adv. Pharm. Technol. Res.*, 1(1), 30–33.
- Jeyachandran, R., Xavier, T. F., & Anand, S. P., (2003). Antibacterial activity of stem extracts of *Tinospora cordifolia* (Willd) Hook. F & Thomson. *Anc. Sci. Life.*, 3(1), 40–43.
- Joshi, G., & Kaur, R., (2016). *Tinospora cordifolia*: A phytopharmacological review. *Int. J. Pharm. Sci. Res.*, 7(3), 890–897.
- Kalabharathi, H. L., Vaibhavi, P. S., Naidu, S., Pushpa, V. H., & Shruthi, S. L., (2014). **Anti-depressant activity of fresh leaves of *Tinospora cordifolia* miers (amruthaballi) in albino mice.** *Int. J. Pharm. Sci. Res.*, 5(12), 5420–5424.
- Kalikar, M. V., Thawani, V. R., Varadpande, U. K., Sontakke, S. D., Singh, R. P., & Khiyani, R. K., (2008). Immunomodulatory effect of *Tinospora cordifolia* extract in human immunodeficiency virus positive patients. *Indian J. Pharmacol.*, 40(3), 107–110.
- Karkal, Y. R., & Bairy, L. K., (2007). Safety of aqueous extract of *Tinospora cordifolia* (Tc) in healthy volunteers: A double blind randomized placebo controlled. *Iran. J. Pharm. Therapeu.*, 6(1), 59–61.
- Kaur, M., Singh, A., & Kumar, B., (2014). Comparative anti-diarrheal and anti-ulcer effect of the aqueous and ethanolic stem bark extracts of *Tinospora cordifolia* in rats. *J. Adv. Pharm. Technol. Res.*, 5(3), 122–128.
- Khaleque, A., Maith, M. A. W., & Huq, M. S., (1971). *Tinospora cordifolia* III. Isolation of tinosporine, heptacosanol,  $\beta$  sitosterol. *Pakistan J. Sci. Industry Res.*, 14, 481–483.
- Khaleque, A., Maith, M. A. W., Huq, M. S., & Abul, B. K., (1970). *Tinospora cordifolia* IV: Isolation of heptacosanol,  $\beta$  sitosterol and three other compounds tinosporine, cordifol, and cordifolone. *Pakistan J. Sci. Industry Res.*, 14, 481–483.
- Khan, M. A., Gray, I. A., & Waterman, P. G., (1989). Tinosporaside an 18-norclerodane glucoside from *Tinospora cordifolia*. *Phytochemistry.*, 28, 273–275.
- Khan, M. M., Dul Haque, M. S., & Chowdhury, M. S., (2016). Medicinal use of the unique plant *Tinospora cordifolia*: Evidence from the traditional medicine and recent research. *Asian J. Med. Biol. Res.*, 2, 508–512.
- Khuda, M. Q. I., Khaleque, A., & Ray, N., (1964). *Tinospora cordifolia* constituents of plants fresh from the field. *Sci. Res.*, 1, 177–183.
- Khuda, M. Q., Khaleque, A., Basar, K. A., Rouf, M. A., Khan, M. A., & Roy, N., (1966). Studies on *Tinospora cordifolia* II: Isolation of tinosporine, tinosporic acid and tinosporol from the fresh creeper. *Sci. Res.*, 3, 9–12.
- Kidwai, A. R., Salooja, K. C., Sharma, V. N., & Siddiqui, S., (1949). Chemical examination of *Tinospora cordifolia*. *J. Sci. Indian Res.*, 8, 115–118.
- Kirtikar, K. R., & Basu, B. D., (1933). *Indian Medicinal Plants* (Vol. 2). Lalit Mohan Basu, Leader Road, Allahabad.
- Kokate, C. K., Purohit, A. P., & Gokhale, S. B., (2010). *Pharmacognosy* (46<sup>th</sup> edn.) Nirali Prakashan, New Delhi.
- Kosaraju, J., Chinni, S., Roy, P. D., Kannan, E., Antony, A. S., & Kumar, M. N. S., (2014). Neuroprotective effect of *Tinospora cordifolia* ethanol extract on 6-hydroxy dopamine induced parkinsonism. *Indian J. Pharmacol.*, 46(2), 176–180.

- Kumar, V., (2015). Antidyslipidemic and antioxidant activities of *Tinospora cordifolia* stem extract in alloxan induced diabetic rats. *Indian J. Clin. Biochem.*, 30, 473–478.
- Mahajan, V. R., Jolly, C. I., & Kundnani, K. M., (1985). A new hypoglycaemic agent from *Tinospora cordifolia*. *Indian Drugs*, 23, 119–120.
- Mandal, P., Das, A. K., Mandal, A., & Biswas, T. K., (2020). A study to evaluate efficacy of *Tinospora cordifolia* (Guduchi) as analgesic agent using albino Wistar rats as an experimental animal model. *Int. J. Basic. Clin. Pharmacol.*, 9(2), 242–246.
- Maurya, R., & Handa, S. S., (1998). Tinocordifolin, a sesquiterpene from *Tinospora cordifolia*. *Phytochemistry*, 44, 1343–1345.
- Maurya, R., Manhas, L. R., Gupta, P., Mishra, P. K., Singh, G., & Yadav, P. P., (2004). Amritosides A, B, C, and D: Clerodane furano diterpene glucosides from *Tinospora cordifolia*. *Phytochemistry*, 5, 2051–2055.
- Maurya, R., Wazir, V., Tyagi, A., & Kapil, R. S., (1995). Clerodane diterpene from *Tinospora cordifolia*. *Phytochemistry*, 38, 659–666.
- Meena, A. K., Singh, A., Panda, P., Mishra, S., & Rao, M. M., (2010). *Tinospora cordifolia*: Its bioactivities & evaluation of physicochemical properties. *Int. J. Pharmacognosy and Phytochem. Res.*, 2, 50–55.
- More, P., & Pai, K., (2011). Immunomodulatory effects of *Tinospora cordifolia* (Guduchi) on macrophage activation. *Biol. Med.*, 3(2), 134–140.
- Panchabhai, T. S., Kulkarni, U. P., & Rege, N. N., (2008). Validation of therapeutic claims of *Tinospora cordifolia*: A review. *Phytother. Res.*, 22(4), 425–441.
- Patel, A., Bigoniya, P., Singh, C. S., & Patel, N. S., (2013). Radioprotective and cytoprotective activity of *Tinospora cordifolia* stem enriched extract containing cordifolioside-A. *Indian J. Pharmacol.*, 45(3), 237–243.
- Patel, M. K. B., & Mishra, S., (2011). Hypoglycemic activity of alkaloidal fraction of *Tinospora cordifolia*. *Phytomedicine*, 18(12), 1045–1052.
- Patgiri, B., Umretia, B. L., Vaishnav, P. U., Prajapati, P. K., Shukla, V. J., & Ravishankar, B., (2014). Anti-inflammatory activity of Guduchi Ghana (aqueous extract of *Tinospora Cordifolia* Miers). *Ayu*, 35(1), 108–110.
- Pathak, A. K., Agarwal, A. K., Jain, D. C., Sharma, R. P., & Howarth, O. W., (1995). NMR studies of 20 hydroxy ecdysones, a steroid isolated from *Tinospora cordifolia*. *Indian J. Chem.*, 34, 674–676.
- Pathak, A. K., Jain, D. C., & Sharma, P. R., (1995). Chemistry and biological activities of the genus *Tinospora*. *Int. J. Pharmacogn.*, 33, 277–287.
- Pradhan, P., Gangan, V. D., Sipahimalani, A. T., & Banerji, A., (1997). Two phytoecdysones from *Tinospora cordifolia*: Structural assignment by 2D NMR spectroscopy. *Indian J. Chem.*, 36B, 958–962.
- Preeti, S., (2011). *Tinospora cordifolia* (Amrita)-a miracle herb and lifeline too many diseases. *Int. J. Med. Aromat. Plants.*, 1(2), 57–61.
- Purandare, H., & Supe, A., (2007). Immunomodulatory role of *Tinospora cordifolia* as an adjuvant in surgical treatment of diabetic foot ulcers: A prospective randomized controlled study. *Indian J. Med. Sci.*, 61(6), 347–355.
- Saha, S., & Ghosh, S., (2012). *Tinospora cordifolia*: One plant, many roles. *Ancient. Sci. Life.*, 31, 151–159.
- Salkar, K., Chotalia, C., & Salvi, R., (2017). *Tinospora cordifolia*: An antimicrobial and immunity enhancer plant. *Int. J. Sci. Res.*, 6, 1603–1607.

- Salve, B. A., Tripathi, R. K., Petare, A. U., Raut, A. A., & Rege, N. N., (2015). Effect of *Tinospora cordifolia* on physical and cardiovascular performance induced by physical stress in healthy human volunteers. *Ayu*, 36(3), 265–270.
- Savrikar, S. S., Dole, V., Ravishankar, B., & Shukla, V. J., (2010). A comparative pharmacological investigation of three samples of 'Guduchi ghrita' for adaptogenic activity against forced swimming induced gastric ulceration and hematological changes in albino rats. *Int. J. Ayurveda Res.*, 1(2), 67–72.
- Shah, G. L., (1984). Some economically important plants of Salsette Island near Bombay. *J. Econ. Taxon. Bot.*, 5, 753.
- Sharma, A. K., Kishore, K., Sharma, D., Srinivasan, B. P., Agarwal, S. S., Sharma, A., Singh, S. K., et al., (2011). Cardioprotective activity of alcoholic extract of *Tinospora cordifolia* (Willd.) Miers in calcium chloride-induced cardiac arrhythmia in rats. *J. Biomed. Res.*, 25(4), 280–286.
- Sharma, D. N. K., Khosa, R. L., Chansauria, J. P. N., & Ray, A. K., (1995). The effect of *Tinospora cordifolia* on brain neurotransmitters in the stressed rat. *Fitoterapia.*, 66, 421–422.
- Sharma, D. N. K., Khosa, R. L., Chansauria, J. P. N., & Sahai, M., (1995). Antiulcer activity of *Tinospora cordifolia* Miers and *Centella asiatica* Linn extracts. *Phytother. Res.*, 9(8), 589–590.
- Sharma, R., Kumar, V., Ashok, B. K., Galib, R., Prajapati, P. K., & Ravishankar, B., (2013). Hypoglycemic and anti-hyperglycemic activity of *Guduchi Satva* in experimental animals. *Ayu.*, 34(4), 417–420.
- Sharma, U., Bala, M., Kumar, N., Singh, B., Munshi, R. K., & Bhalerao, S., (2012). Immunomodulatory active compounds from *Tinospora cordifolia*. *J. Ethnopharmacol.*, 141, 918–926.
- Sharma, U., Bala, M., Kumar, N., Singh, B., Munshi, R. K., & Bhalerao, S., (2012). Immunomodulatory active compounds from *Tinospora cordifolia*. *J. Ethnopharmacol.*, 141(3), 918–926.
- Singh, K. K., & Maheshwari, J. K., (1983). Traditional phytotherapy amongst the tribals of Varanasi district, U.P. *J. Econ. Taxon. Bot.*, 4, 829.
- Singh, N., Singh, S. M., & Shrivastava, P., (2005). Effect of *Tinospora cordifolia* on the antitumor activity of tumor-associated macrophages-derived dendritic cells. *Immunopharmacol. Immunotoxicol.*, 27(1), 1–14.
- Singh, P., Singh, B., Katiyar, D., & Srivastava, A., (2003). Antimicrobial activity of *Tinospora cordifolia* extracts against urinary tract infections causing bacteria. *Int. J. Pharma and Bio Sci.*, 6(3), B571–B577.
- Singh, S., Birla, H., Rai, S., Zahra, W., & Singh, S., (2018). Neuroprotective role of *Tinospora cordifolia* in MPTP induced parkinsonian mouse model. *Proceeding of the 2018 International Congress*. Hong Kong.
- Singh, V., & Banyal, H. S., (2011). Antimalarial effect of *Tinospora cordifolia* (Willd.) Hook. F. & Thoms and *Cissampelos pareira* L. on *Plasmodium berghei*. *Curr. Sci.*, 101(10), 1356–1358.
- Sinha, K., Mishra, N. P., Singh, J., & Khanuja, S. P. S., (2004). *Tinospora cordifolia* (Guduchi) a reservoir plant for therapeutic applications. *Indian J. Tradit. Knowle.*, 3, 257–270.
- Sivakumar, V., & Rajan, M. S. D., (2011). Hypoglycemic and antioxidant activity of *Tinospora cordifolia* in experimental diabetes. *Int. J. Pharm. Sci. Res.*, 2(3), 608–613.



- Sivasubramanian, A., Narasimha, K. K. G., Rathnasamy, R., & Campos, A. M. F. O., (2013). A new antifeedant clerodane diterpenoid from *Tinospora cordifolia*. *Nat. Prod. Res.*, 27(16), 1431–1436.
- Sohni, Y. R., & Bhatt, R. M., (1996). Activity of a crude extract formulation in experimental hepatic amoebiasis and in immunomodulation studies. *J. Ethnopharmacol.*, 54(2, 3), 119–124.
- Sohni, Y. R., Kaimal, P., & Bhatt, R. M., (1995). The antiamebic effect of a crude drug formulation of herbal extracts against *Entamoeba histolytica* *in vitro* and *in vivo*. *J. Ethnopharmacol.*, 45(1), 43–52.
- Spandana, U., Liakhat, A. S. L., Nirmala, T., Santhi, M., & Babu, S. D., (2013). A review on *Tinospora cordifolia*. *Int. J. Curr. Pharm. Res.*, 4, 61–68.
- Sumanlata, Suman, A., Sharma, R. K., & Khan, A., (2019). Evaluation of anti-inflammatory and antipyretic effect of aqueous extract of *Tinospora cordifolia* in rats. *Int. J. Res. Rev.*, 6(8), 340–347.
- Sumanlata, Suman, A., Sharma, R. K., Jindal, M., & Khan, A., (2019). Evaluation of the analgesic activity of the water-soluble extract of stem of *Tinospora cordifolia* in experimentally induced pain in albino rats. *Int. J. Res. Med. Sci.*, 7(3), 938–942.
- Sumran, G., & Aggarwal, A., (2019). Prospect of Indian herbs as sources of antioxidants in combating oxidative stress. *Chem. Biol. Interface.*, 9, 1–20.
- Tasaduq, S. A., Singh, K., Sethi, S., Sharma, S. C., Bedi, K. L., Singh, J., Jaggi, B. S., & Johri, R. K., (2003). Hepatocurative and antioxidant profile of HP-1, a polyherbal phytomedicine. *Hum. Exp. Toxicol.*, 22(12), 639–645.
- The Ayurvedic Pharmacopoeia of India*, (2003). Government of India Ministry of Health and Family Welfare Department of Ayush, Part 1.
- Tiwari, P., Nayak, P., Prusty, S. K., & Sahu, P. K., (2018). Phytochemistry and pharmacology of *Tinospora cordifolia*. *Syst. Rev. Pharm.*, 9, 70–78.
- Une, H. D., Ejaj, M. A., & Tarde, V. A., (2014). Nootropic activity of saponins obtained from *Tinospora Cordifolia* stem in scopolamine induced amnesia. *Int. J. Pharma Res. Rev.*, 3(2), 28–35.
- Upadhyay, A. K., Kumar, K., Kumar, A., & Mishra, H. S., (2010). *Tinospora cordifolia* (Willd.) Hook. F. and Thoms. (Guduchi) -validation of the ayurvedic pharmacology through experimental and clinical studies. *Int. J. Ayurveda Res.*, 1, 112–121.
- Upreti, P., & Chauhan, R. S., (2018). Effect of leaf powder of giloy (*Tinospora cordifolia*) in fish feed on survival and growth of post larvae of *Catla catla*. *J. Appl. Nat. Sci.*, 10, 144–148.
- Vermani, A., Navneet, & Gautam, S. S., (2013). Screening of antibacterial activity of *Tinospora cordifolia* Miers. extracts against dental pathogens. *J. Pharmacol Toxicol.*, 8, 28–34.
- Wani, J. A., Achur, R. N., & Nema, R. K., (2011). Phytochemical screening and aphrodisiac property of *Tinospora cordifolia*. *Int. J. Pharm. Clin. Res.*, 3(2), 21–26.
- Wazir, V., Maurya, R., & Kapil, R. S., (1995). A clerodane furano diterpene glucoside from *Tinospora cordifolia*. *Phytochemistry*, 38, 447–449.



Taylor & Francis

Taylor & Francis Group

<http://taylorandfrancis.com>

## CHAPTER 11

---

# White Tea: An Emerging Gift of Nature and Bioprospection Towards the Development of Novel Herbal Formulations, Nutraceuticals, and Cosmetics

DHRUBOJYOTI MUKHERJEE,<sup>1</sup> PARTHA PALIT,<sup>2</sup>  
SHUBHADEEP ROYCHOUDHURY,<sup>3</sup> SHUBHAJIT HALDER,<sup>4</sup> and  
SUBHASH C. MANDAL<sup>1</sup>

<sup>1</sup>*Pharmacognosy and Phytotherapy Research Laboratory,  
Division of Pharmacognosy, Department of Pharmaceutical Technology,  
Jadavpur University, Kolkata, West Bengal, India*

<sup>2</sup>*Department of Pharmaceutical Sciences, Drug Discovery Research  
Laboratory, Division of Pharmacognosy, Assam University  
(A Central University), Silchar, Assam, India*

<sup>3</sup>*Department of Life Science and Bioinformatics, Assam University  
(A Central University), Silchar, Assam, India*

<sup>4</sup>*Department of Chemistry, Hislop College, Nagpur, Maharashtra, India*

---

### ABSTRACT

Tea is a good friend of the human being as a Nutraceuticals, health drink, and medicinal agent. Different varieties of tea are derived from the pioneer herb, *Camellia sinensis*. Apart from black and green tea, the silver needle white tea, derived from young leave buds possesses amazing high quality and unique aroma. It is enriched with value-added Phyto marker compounds

that elicit multiple health benefits including disease prevention and management of cancer, inflammation, microbial infection and immunodeficiency, and CNS disorders. This is also known as de-stress tea, an ideal drink to refresh the consumers at the optimum level. This silver needle white tea is an antioxidant powerhouse, as well. Among all tea varieties, rarest white tea is the most bioactive health beverage. However, its health benefits and pharmacological activity have not been explored properly, to date. The phytoconstituents variety found to be better than green tea in the context of polyphenols, flavonoids, and saponin contents. Moreover, the yield of bioactive condensed or non-hydrolysable tannin is higher in white tea compared to green tea aqueous extract. Its process of production from young tea leave buds is very emerging. In this regard, the current study will be explored on the importance, area of production, market value, phytopharmaceutical activity on drug and cosmetics aspect, botanical, and taxonomical characterization, production methodology, processing, etc. The study also will be focused on the impact of soil quality, the climate of the cultivating zone and its changing scenario on the production and phytoconstituents yield and composition. This review will also highlight the tissue culture prospect, planting, and nutrient management system of the cultivating area, safe pest management system, processing techniques for extraction of phytoconstituents and their phytochemical characterization by HPLC study, bioprospection of phytopharmacological investigation, pharmaceutical formation development for effective drug delivery especially emphasizing on nanotechnology. The above-cited illustrated items may guide to the researchers and academicians or commercial chemist to develop some potential Phyto pharmaceutically value-added effective herbal drugs and cosmetics formulation and nutraceuticals with great safety and eco-friendly manner.

### **11.1 GENERAL INTRODUCTION**

Tea, a promising herb, is used extensively in daily life as a value-added health drink to supplement nutrients, boost immunity and energy. Its application for managing cancer, inflammation, arthritis, neurodegenerative disorders, cardiac disorders, obesity, and diabetes is promising. It has also been applied as health-protective nutraceuticals (Saldanha et al., 2015; Chen et al., 2015). L-theanine and other healthy nutrients amino acids, minerals may contribute to dietary supplements and nutraceuticals formulation developments. The impact of tea in the cosmetic industry as active ingredients or excipients is also remarkable (Juhász et al., 2018).

However, several varieties of tea are available, which are processed from *Camellia sinensis* leaves and early buds. They vary from each other concerning phytoconstituents and processing differences. Among 5 varieties of tea such as Black, Pu-erh, Oolong, Green, and White tea. All though, green, **and** white tea are less processed and fermented without oxidation (Hilal et al., 2007; Dai et al., 2017). They are dried quickly with steaming and withering to protect bioactive anti-oxidant polyphenols and flavonoids from polyphenol oxidase induced oxidation. White tea is manufactured by long-time withering and drying via pan-frying enriched with high yielded aromatic anti-oxidant polyphenols and flavonols among all tea varieties (Chen et al., 2019). It is regarded as de-stress tea and powerhouse of anti-oxidant molecules devoiding of caffeine, Therefore, chances of free-radical induced cardiovascular, neurodegenerative, inflammatory arthritis, nociceptive pain, and cancer would be minimized (Shahidi, 2000).

The white tea is widely cultivated and processed in Assam, China, Darjeeling, Thailand, Srilanka, Nilgiri. Reports also exists regarding the usage of white tea in ancient China, majorly in powdered form whisked in ceramic bowls via sun drying and pan-frying techniques. This process gave the tea leaves promising flavor and whitish-yellow colored delicate silver like needle crystal.

A prehistoric document of 1107 AD drafted by Chinese Emperor Huizong, known as 'Treatise on Tea' depicts the traditional tea ceremony of China. Moreover, he has cited his fondness for Bai Cha (Bai meaning white and Cha meaning tea), which is evident as possibly the first historical demonstration of an unprocessed tea that appears as white tea ([www.ndtv.com](http://www.ndtv.com)).

This type of rare and value-added tea variety is processed from young tea leave buds in the autumn season. The literature supports that the conventional bioactive catechins anti-oxidant molecules are available in higher content compared to green tea due to the manufacturing process specificity of sun drying, less oxidation, fermentation. Moreover, harvesting and processing are time-consuming. Plucking of leave buds is only done in a particular seasonal time in a year. That is why the market price of this variety of tea is a little bit higher rather than green tea. However, the prime objective of the present review chapter is to explore its pharmaceutical, cosmeceuticals value, and health benefits in public attention. Herein, the scope, benefits, present status and future goal of pharmaceutical formulation development of white tea will be discussed for a better understanding of the significance of white tea will

be critically evaluated. The main theme of this topic is also to highlight the importance of white tea as a key active ingredient of herbal formulation development. The review will also be forecasted by how the safe, value-added, and cost-effective low-cost white tea herbal formulation could be formulated.

## 11.2 AREA AND PRODUCTION

The area of harvesting and cultivation of white tea is very limited in the world. This type of tea is very rare and unique. The process of production of white tea is very sensitive. White tea is carefully produced from the young tea leaf buds before growing and development of mature tea leaves. When young unopened tea leaf buds are covered with white-colored hairy trichomes, then it is usually plucked for the development of precious and unique white tea. White tea is generally cultivated from the young buds of *Camellia sinensis* medicinal plants in China, India (Assam and Darjeeling), Korea of south Asian country.

History reveals that the development of white tea custom was executed in early era of Chinese imperial dynasties (During Emperor Huizong's rule of the Song Dynasty (960–1297) between 600 and 1,300) especially when the culture of tea consumption was flourishing across the country.

This majestic tea was naturally derived from the youngest and most delicate buds of finest tea plants during spring by manual hand processing. Hence, the white tea is very famous for its delicate and soothing aroma and flavor. Gradually India, Korea, Srilanka have adopted this methodology for the production of white tea on large scale. All those country's tea manufacturers are producing this rare and valuable tea species from the native tea plant's buds and unopened tea leaves. Till this date, there are no clear reports on the country-wise annual production rate of white tea from literature and commercial sources ([www.teatulia.com](http://www.teatulia.com); [www.thespruceeats.com](http://www.thespruceeats.com)).

## 11.3 MARKETING AND TRADE

To date, his variety of tea is not so much gathered public attention. The beneficial health benefit is not known to the common people. So, its public marketing and trade level production rate is unclear to us. We are trying

to explore its health benefit, the methodology of production and its potential safe biomarker compounds characterization and identification in this present review, so tea industry marketing executive will come forward to convince it's beneficial and efficacy towards the common people. If the significant buyers of this tea will increase, then the production cost would be decreased for common interest for better accessibility.

#### **11.4 COMPOSITION AND USES**

Both green and white tea consist of polyphenols and flavanols including catechins, (–)-epigallocatechin-3-gallate (EGCG), (–)-epicatechin gallate (ECG), (–)-epicatechin (EC), (–)-epigallocatechin (EGC). Health strength and profits associated with tea consumption are concerned with its potential free radical-scavenging and anti-aging action (Kilmartin & Hsu, 2003). But least processed white tea yields a higher percentage of total polyphenols and flavonoids than green tea (Dai et al., 2017). Non-hydrolysable tannin and saponin contents are present in white tea in higher yield value in comparison to green tea and other variety of tea including black tea (unpublished data). However, caffeine contents are lesser in white tea compared to green tea and black tea. Polyphenolic and flavonoid glycoside is present in higher yield in comparison to green tea (Uchenna et al., 2015). Furthermore, amino acids and essential oil-based glycosides contribute enormously to form the delicate aroma, sweetness, and flavor of white tea. Long withering and drying without fermentation and oxidation are responsible for retaining the bioactive and flavoring constituents like flavonoids, amino acids, and polyphenols and volatile oil (Chen et al., 2019). Flavonol glycoside's contents and numbers are comparatively higher in white tea rather than green tea. The total yield of bioactive marker compounds is higher in white tea rather than green tea as depicted in Table 11.1 (Hilal et al., 2007). During processing (Figure 11.1) of white tea, the application of steaming and withering inactivates the enzymatic activity of polyphenol oxidase resulting in the higher yield of flavonoids and polyphenol catechin contents as described in Figure 11.1. That is why, an earlier report (Sanlier et al., 2018) suggests that drinking of white tea significantly control and prevent disease progression and its severity.

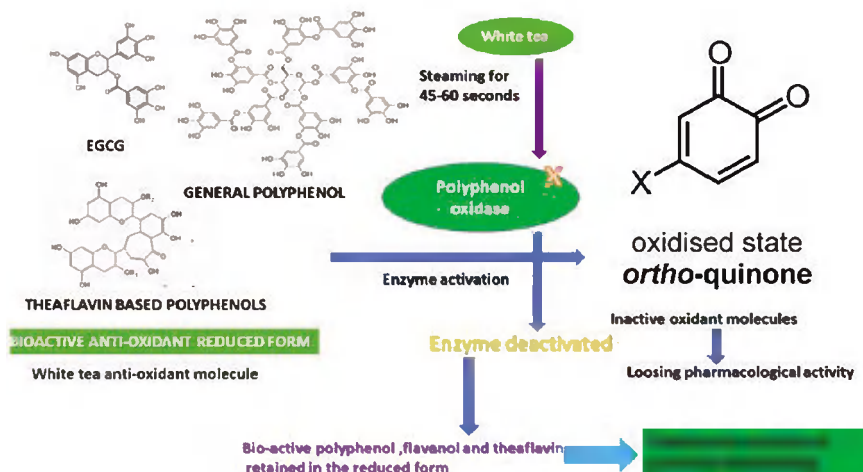
**TABLE 11.1** Comparative Yield of Different Phyto-Pharmacologically Bioactive Secondary Metabolites from Reported Literatures and Undertaken Research

<b>Name of the Bio-Active Phytopharmaceuticals</b>	<b>Average Quantity (g/Kg) in White Tea</b>	<b>Quantity Average (g/Kg) in Green Tea</b>
Total polyphenols	21.54	19.18
Catechins	13.22	12.95
Caffeine	4.85	2.90
Theogallin	1.4	1.0
Gallic acid	0.09	0.26
L-Theanine	6.56 mg/gm	6.30 mg/gm
epigallocatechin gallate	8.00	6.75
Total saponins (unpublished data)	8.5 mg/gm	7.56 mg/gm

White tea is used as a powerhouse of anti-oxidant molecule leading to prevent overall aging by free radical induced cell damage following the DNA fragmentation to boost energy in the human body. It supplies the armaments to the human body to fight against cancer cell growth and proliferation. It also helps to lower the bad cholesterol and increase the good cholesterol to attenuate the chances of cardiac artery block. Different types of catechin derivatives present in the white tea render the anti-inflammatory property to control the inflammation and regulate the immunity to resist microbial infection. White tea also progresses digestion, particularly when people are suffering from stomach cramps or nausea. It aids to circumvent constipation. White tea comprises of a large number of polyphenols, micronutrients essential minerals manganese, zinc, and selenium which could attenuate dementia and improves concentration reducing brain fatigue. L-theanine, another important nutrient in white tea, may help to produce a feeling of alertness and augment mental alertness. This theanine shows anti-stress property by calming frayed nerve. Daily intake of white tea aqueous extract alleviates the environmental pollutants and toxin-mediated skin wrinkles, dullness, spots, and premature aging leading to revitalizing the skin (Santana *et al.*, 2001; Cooper, 2012).

Basically, the young unopened tea leave buds and young tea leaves are usually utilized for the manufacturing of white tea needle-like crystals. But herbal medicine development from these rare parts makes the process costly. However, if the tea industry worker keeps the unopened tea leaf bud during the conventional tea leaf plucking in reserve for the preparation of white tea, then the production cost and rate would be higher in the white tea trade market.





b.

a.



**FIGURE 11.1** (a) Generalized methodology of white tea needle production from the garden young tea leave buds. (b) Schematic overview on the role of steaming on the antioxidant compound degrading enzyme (polyphenol oxidase) for retaining the bio-activity of white tea polyphenols.

## 11.5 BOTANY AND TAXONOMY

White tea has a distinguishing aroma, flavor, and pleasant sweetness and astringent taste. The macroscopic investigation of the leaf comprises of botanicals characteristic observation. However, the microscopic inspection was conducted with young unopened leaf or specific part fragment of leaf powder. The objective of this finding is to study specific parts contained in the organs of plants used. Macroscopic characteristics of *white tea* displayed that the leaves are silky dark green, alternate, short-petiole, coriaceous, lanceolate or elongated-ovate, and roughly serrate. The leaf blade is 6–18 cm long, 2–6 cm wide, short-stemmed, alternate layout, stiff leaves, elongated ellipse-shaped with finely toothed edges, and pinnately netted venation. While young leaves seem silver because of the covering of short downy hair on the underside. White tea leaves are as same as the *Camellia sinensis* (L.) Kuntze leaves but rolled up, oval, like a needle with a length of 1.5–3 cm, diameter 1–2 mm, as well and the superficial is enclosed with very subtle hairs color of dried white tea leaves is silvery-white (Ekayanti et al., 2017).

## 11.6 VARIETIES AND CULTIVARS

Da Bai and Da Hao are the two plant varieties from which white tea was first commercially produced in China's Fujian province in the year 1700s. Loose-leaf version was developed from the young leaf buds, as because these variety of tea was negligibly processed and moreover the rare teas from the young buds were difficult in respect to logistic issues like stocking and conveyance without degradation.

Nowadays, white tea production methods have been amended, with the advent of a greater number of methods not only limited to Fujian province but also other parts of the world. Apart from China, today several of countries like India, Korea, Srilanka, etc., are also engaged in cultivation of indigenous white tea from various species of tea plants. Generally, there are 3 varieties of white tea are available as follows ([www.teagalaxy.com](http://www.teagalaxy.com); [www.teatulia.com/tea-varieties](http://www.teatulia.com/tea-varieties))

### 11.6.1 SILVER NEEDLE (BAI HAO YIN ZHEN)

One of the scariest and most exclusive tea. Traditionally Dabai cultivar Fujian, China, produces only this tea. This finest tea leaf buds are plucked to take more than 4,500 hand-sorted leaves to make a pound of this tea. It is manufactured especially from the full-grown buds with white protective silky

hairs which gives the texture of silver color, thus known as Silver Needle variety which is recognized for its powerful health assistance because the bud is where the tea plant stores most of its antioxidants and other beneficial compounds (catechins, caffeine, and l-theanine).

### **11.6.2 BAI MUDAN (WHITE PEONY)**

This type of variety of white tea is cultivated in China and other countries around the world. It usually includes some buds blended with unfurled or barely opened young tea leaves. It is processed from both leaves and buds of the tea plant, generally picked later than Silver Needle. The leaves possess multiple colors in connection to varying degrees of oxidation – brown, green, gray, and silvery bud. It is very much popular as white tea blends. The flavor of this tea seems like peony flowers with a sweet taste.

### **11.6.3 SHOU MEI (CHINESE NAME: LONGEVITY EYEBROWS)**

This variety of Shou Mei often has three leaves plucked, making it darker and coarser. The flavor and aroma of this tea are like a lighter oolong tea. This tea is less expensive than the other teas. Shou Mei variety contains the lowest amount of caffeine of all white teas, too.

### **11.6.4 ASSAM VARIETY**

This is cultivated in India, Assam province, North-Eastern part of India from a unique environment around hillocks. The young middle un-opened leaf buds are the source of precious white tea production involving long withering, pan firing without oxidation. The saponin and condensed tannin contents are higher than the green tea.

### **11.6.5 DARJEELING WHITE TEA**

This famous tea plants are native to the Darjeeling region of India. Although this variety of tea is not derived from original Chinese white tea plant, but the processing method is quite comparable to the Fujian white tea, however, the flavor seems to be much better than other species.

### 11.7 SOIL AND CLIMATE

Soil quality such as soil composition, i.e., how much nutrients and heavy metals are present that also trigger the growth of the tea plants. Ultimately these soil constituents influence the plant phytoconstituents composition and yield by modulating the metabolic enzymes and gene in the shikimic acid and mevalonic acid pathway (Zhang et al., 2019). Cultivating soil are also the most important factor for an increasing rate of cultivation and growth for the medicinal plant (Bernath, 1997). The soil nutrients composition and groundwater content are varied by changing of cultivating zone. Therefore, the same species plant may change their phytochemical composition, anabolism, and accumulation of secondary metabolites, if it grows in different geographical cultivating zone across the world (Radusiene et al., 2012).

Therefore, bioactive secondary metabolites such as catechins, caffeine, polyphenols, flavonoids, glycosides, and saponin contents of the white tea are also influenced by the soil quality and composition. Because plants produce active metabolites in their tissues via shikimic acid and mevalonic acid pathway. In order to bio-synthesize successfully, those several bioactive metabolites via biochemical reaction, plants need to be exposed into the ideal weather condition such as favorable rainfall, humidity, air temperature, atmospheric vapor pressure, precipitation, and sunshine duration, etc. (Verma & Shukla, 2015; He et al., 2013; Liu et al., 2011). Furthermore, the weather condition of the same place nowadays has been drastically altered in comparison to the earlier time (Li et al., 2019). This phenomenon may modify the reproducibility of the percentage of total extractive matter comprising of bioactive phytoconstituents from traditional medicinal plants. That is why the same white tea species' biological and health benefits differ from Chinese, Indian, and Korean variety. Because the catechin contents of Chinese variety white tea are higher than the Sri Lankan and Korean variety. Assam variety white tea consists of a higher quantity of condensed tannins and saponin among all white tea varieties of another country. Darjeeling white tea variety contains the very delicate amount of flavoring volatile oil and bioactive amino acids compared to other country's white tea variety. In context to the above variation of the phytochemical composition in white tea, may be responsible for the variation of biological health benefits and therapeutic efficacy. Apart from this climate, the altitude of the cultivating area, rainfall is also the influencing factor for the growth of optimum white tea young leaves and unopened buds. That is why the biological effect like anticancer effect and anti-stress activity of Indian variety of white tea was found to differ from Chinese variety (Hajiaghaalipour et al., 2015; unpublished data). Therefore,

we need to be careful regarding the proper standardization of the white tea samples before using as medicine, nutraceuticals, and food flavoring agent. Moreover, the white sample should be characterized by macroscopically and chemically before packaging, with respect to the origin of production of the country and native place. This standardized data should be kept as reference standard data for future assessment of quality control and assurance of white tea from different batches. Thus, the optimized white tea processed packet could be marketed for pioneer health drinks, nutraceuticals or therapeutic purposes.

### **11.8 PROPAGATION**

A commercially very precious variety of white tea is Needle shaped crystal young teal leaf buds which are usually collected during Spring from the premature leaf. This type of silver needle white tea is very rare and produced at a low rate in a year. Therefore, its cost is so high.

So far literature concern to date, there are no reports on the tissue culture of white tea deriving tea plants. However, we need to focus on its production and regeneration from callus of young teal leaf buds through tissue culture by the cost-effective manner by standardizing the influencing growth factors and related triggering factors. This approach will reduce the cost of rare white tea enriched with bioactive antioxidant polyphenols, saponins, amino-acids, etc.

### **11.9 PLANTING, IRRIGATION, AND NUTRIENT MANAGEMENT**

In order to optimum tea crops production with high nutrients and anti-oxidant molecules, the irrigation system should be improved in such a way that the cultivating soil quality are fertilized with the high amount of essential nutrients, hormone. There should be applying of organic fertilizer may enhance the effective tea crops. But in connection to white tea production, there is no such scientific irrigation system and nutrient management policy reported so far. During drought, scarcity of water deficit may hamper the soil nutrients, which may indirectly hamper the tea crop quality along with potential phytoconstituents. Moreover, a heavy rainfall mediated water logging system causes Nutrients leaching and run-off via deep percolation. This deficiency may hamper the tea quality production. Therefore, the optimum nutrient composition of the soil needs to be managed by choosing a relevant cultivating place like the lap of hillocks of the valley via drip irrigation of tea plant roots, where the soil is enriched with so many essential

nutrients. The rainwater is not logged surrounding soil of tea plant roots ([www.indiatea.org](http://www.indiatea.org)).

### **11.10 CHARACTERIZATION OF PHYTOCONSTITUENTS OF WHITE TEA**

Irrespective of cultivating zone and climatic variation, white tea is enriched with antioxidant polyphenolic catechins and tannins. It also contains the flavonoid glycosides and saponin contents as depicted in Table 11.1 (Ekayanti et al., 2017; Hilal et al., 2007; Ning et al., 2016). These bioactive secondary metabolites are mainly responsible for pharmacological activity against different types of disorders like cancer, arthritis, diabetes, and various types of CNS disorders.

### **11.11 VALUE ADDITIONS OF WHITE TEA**

The value of white tea is gradually increasing in the global market. The needle-shaped white tea derived from the young unopened teal leaves and buds are explored entire South Asia, London, and America. Their demand for global customers is uprising beyond the expectation in spite of their high-cost. This highly demanding silver needle variety of white tea is acceptable to all customer due to their value-added phytometabolites and phytonutrients (Li et al., 2020), for which can be highlighted for prophylactic and therapeutic agents for the management of various type of non-communicable lifestyle diseases (Pastoriza et al., 2017). Value of this white tea further needs to be explored as health drink may due to its nutraceutical value, taste, and aroma.

### **11.12 BIO-PROSPECTION OF WHITE TEA**

There is no doubt that white tea could be a very promising bio-prospective agent. Because it elicits a variety of bioactivity against different disease models. It is enriched with a high level of antioxidants (Espinosa et al., 2012). It improves oral Health, amps up body fat diffusion, kills cancer cells, attenuates the reproductive health, enriches brain cognitive health (Almajano et al., 2011), improves the hyperglycemic status of the diabetic patient, downregulates the bad cholesterol level of the body (Pastoriza et al., 2017). Various health-protective activity rendered by white tea may need to be further extended for the clinical level to establish its therapeutic potentiality for drug development in the market.

### **11.13 PROCESSING TECHNIQUES IN PHARMACEUTICALS**

Till date, there are no reports on Nanotechnology-based pharmaceutical formulation or nutraceuticals development from white tea available. But the prospect of this white tea derived bioactivity guided Phyto-fractions and other potentially bioactive compounds are enormous and emerging. All those phytocompounds and nutrient molecules like amino acids could be focused against numerous lifestyle disorders and infective microbes based on *in-silico* bio-informatics based validation and evaluation. Thereafter, those fractions and nutrients and essential oil can be formulated pharmaceutically for drugs, nutraceuticals, and cosmetics development.

### **11.14 POTENTIAL BIOMOLECULES AND CLINICAL TRIALS RELATED TO WHITE TEA**

Clinical studies on anti-oxidant potentiality have been carried out with green tea (1–6 cup/day) in the human model, where plasma antioxidant capacity was found to be significant. The post-consumptions of tea blood anti-oxidant enzymatic activity was significantly increased to protect the cell DNA damage and lipid peroxidation. Thus, tea has been established as a promising anti-oxidant health drink for protection against several free radicals, toxin-induced cellular damage and subsequent several inflammatory disorders. The bio-active molecules like catechins, flavonoids, condensed polyphenols (Tenore et al., 2015), L-theanine have been contributed to demonstrate such emerging anti-oxidant capacity (Rietveld, 2013). However, there are no clinical reports on the anti-oxidant activity of white tea available. We need to focus on its clinical validation against free radical, pollutants, oxidant-induced cell-damaging, anti-aging effects. This evaluation should be compared with green-tea potentiality. The saponins and glycosides and some essential oils need to be identified followed by characterization from white tea for evaluation of anti-microbial, anti-cancer, and anti-arthritic, neuroprotective activity both in preclinical and clinical level, near future.

### **11.15 COMMERCIAL/PHARMACEUTICAL PRODUCTS AVAILABLE**

Commercially Pharmaceutical formulation of white tea is not available, till now. The white tea nano formulation for efficient therapy can be processed subjected to their clinical validation.

## 11.16 CONCLUSION

The above-cited literature-based reports suggesting that the white tea could be the emerging therapeutic, prophylactic, nutraceutical agent and cosmetics tool. The maximum content of polyphenols catechin, saponins, and condensed tannins in the white tea aqueous extract can be used for bioactive therapeutic drug formulations against numerous lifestyle disorders like stroke, cardiac disorders, cancer, and diabetes, etc. Polyphenols enriched white tea infusion may be explored for nutraceuticals development. Furthermore, many health-protective minerals and amino-acids nutrients of this variety may help to formulate the development of the promising nutraceutical. The essential volatile oils of this tea could be the potential ingredient for cosmetic formulations. The above-cited active ingredients are present in the white tea in greater amounts rather than green tea, so white tea may hold emerging promise towards the development of food, drugs, nutraceuticals, and cosmetics in an effective manner among all types of tea. However, the needle-shaped white tea production cost is high due to its scarcity of amount and manual processing. In order to circumvent such limitations and reduce the production cost, the tissue callus culture of the young unopened tea leaves and buds can be implemented. This approach may increase the quantity of white tea production in cheapest price to fulfill the demand of the customer.

## KEYWORDS

- **anti-inflammatory**
- **anti-oxidant**
- **bio-activity**
- **bio-prospection**
- **pharmaceutical products**
- **phytoconstituents**
- **phytopharmaceutical**
- **polyphenols**
- **white tea**



## REFERENCES

- 10 *Impressive Benefits of White Tea*. healthline.com (accessed on 13 October 2023).
- 17 *Proven White Tea Benefits That Will Surprise You*. stylecraze.com (accessed on 13 October 2023).
- Almajano, M. P., Vila, I., & Ginés, S., (2011). Neuroprotective effects of white tea against oxidative stress-induced toxicity in striatal cells. *Neurotoxicity Research*, 20(4), 372–378.
- Bernath, J., (1997). Cultivation of valerian. In: Houghton, P. J., (ed.), *Valerian—The Genus Valeriana* (pp. 77–100). UK: Harwood Academic Publishers.
- Chen, Q., Zhu, Y., Dai, W., Lv, H., Mu, B., Li, P., & Lin, Z., (2019). Aroma formation and dynamic changes during white tea processing. *Food chemistry*, 274, 915–924.
- Chen, Z. M., & Lin, Z., (2015). Tea and human health: Biomedical functions of tea active components and current issues. *Journal of Zhejiang University-Science B*, 16(2), 87–102.
- Cooper, R., (2012). Green tea and theanine: Health benefits. *International Journal of Food Sciences and Nutrition*, 63(sup1), 90–97.
- Dai, W., Xie, D., Lu, M., Li, P., Lv, H., Yang, C., & Tan, J., (2017). Characterization of white tea metabolome: Comparison against green and black tea by a nontargeted metabolomics approach. *Food Research International*, 96, 40–45.
- Ekeyanti, M., Ardiana, L., Najib, S. Z., Sauriasari, R., & Elya, B., (2017). Pharmacognostic and phytochemical standardization of white tea leaf (*Camellia sinensis* L. Kuntze) ethanolic extracts. *Pharmacognosy Journal*, 9(2).
- Espinosa, C., López-Jiménez, J. Á., Cabrera, L., Larqué, E., Almajano, M. P., Arnao, M. B., & Pérez-Llamas, F., (2012). Protective effect of white tea extract against acute oxidative injury caused by Adriamycin in different tissues. *Food Chemistry*, 134(4), 1780–1785.
- Hajiaghaliipour, F., Kanthimathi, M. S., Sanusi, J., & Rajarajeswaran, J., (2015). White tea (*Camellia sinensis*) inhibits proliferation of the colon cancer cell line, HT-29, activates caspases and protects DNA of normal cells against oxidative damage. *Food Chemistry*, 169, 401–410.
- He, C. E., et al., (2013). Effects of nitrogen on root development and contents of bioactive compounds in *Salvia miltiorrhiza* Bunge. *Crop Science*, 53, 2028–2039.
- Hilal, Y., & Engelhardt, U., (2007). *Characterization of White Tea – Comparison to Green and Black Tea (PDF)*. www.tu-braunschweig.de (accessed on 02 September 2023).
- Juhász, M. L., Levin, M. K., & Marmur, E. S., (2018). The use of natural ingredients in innovative Korean cosmeceuticals. *Journal of Cosmetic Dermatology*, 17(3), 305–312.
- Kilmartin, P. A., & Hsu, C. F., (2003). Characterization of polyphenols in green, oolong, and black teas, and in coffee, using cyclic voltammetry. *Food Chemistry*, 82, 501–512.
- Li, C., Zong, B., Guo, H., Luo, Z., He, P., Gong, S., & Fan, F., (2020). Discrimination of white teas produced from fresh leaves with different maturity by near-infrared spectroscopy. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, 227, 117697.
- Li, J., (2019). Simulating the effects of climate change across the geographical distribution of two medicinal plants in the genus *Nardostachys*. *PeerJ*, 7, e6730.
- Liu, H. Y., et al., (2011). Effect of drought stress on growth and accumulation of active constituents in *Salvia miltiorrhiza* Bunge. *Industrial Crops & Products*, 33, 84–88.
- Ning, J. M., Ding, D., Song, Y. S., Zhang, Z. Z., Luo, X., & Wan, X. C., (2016). Chemical constituents analysis of white tea of different qualities and different storage times. *European Food Research and Technology*, 242(12), 2093–2104.

- Pastoriza, S., Mesias, M., Cabrera, C., & Rufián-Henares, J. A., (2017). Healthy properties of green and white teas: An update. *Food & Function*, 8(8), 2650–2662.
- Radusiene, J., Karpaviciene, B., & Stanius, Z., (2012). Effect of external and internal factors on secondary metabolites accumulation in St. John's wort. *Bot. Lithuanica*, 18, 101–108.
- Rietveld, A., & Wiseman, S., (2003). Antioxidant effects of tea: Evidence from human clinical trials. *The Journal of Nutrition*, 133(10), 3285S–3292S.
- Saldanha, L., Dwyer, J., Andrews, K., Betz, J., Harnly, J., Pehrsson, P., & Savarala, S., (2015). Feasibility of including green tea products for an analytically verified dietary supplement database. *Journal of Food Science*, 80(4), H883–H888.
- Sanlier, N., Gokcen, B. B., & Altuğ, M., (2018). White tea consumption and disease correlations. *Trends in Food Science & Technology*, 78, 95–106.
- Santana-Rios, G., Orner, G. A., Amantana, A., Provost, C., Wu, S. Y., & Dashwood, R. H., (2001). Potent antimutagenic activity of white tea in comparison with green tea in the *Salmonella* assay. *Mutation Research/Genetic Toxicology and Environmental Mutagenesis*, 495(1, 2), 61–74.
- Shahidi, F., (2000). Antioxidant factors in plant foods and selected oilseeds. *Biofactors*, 13, 179–185.
- Tenore, G. C., Campiglia, P., Giannetti, D., & Novellino, E., (2015). Simulated gastrointestinal digestion, intestinal permeation and plasma protein interaction of white, green, and black tea polyphenols. *Food Chemistry*, 169, 320–326.
- Uchenna, J. U., Selena, A., Adam, K., James, T. L., & Edward, J. K., (2010). White and green teas (*Camellia sinensis* var. *sinensis*): Variation in phenolic, methylxanthine, and antioxidant profiles. *J. Food Sci.*, 75(6), C541–C548.
- Verma, N., & Shukla, S., (2015). Impact of various factors responsible for fluctuation in plant secondary metabolites. *Journal of Applied Research on Medicinal & Aromatic Plants*, 2, 105–113.
- [www.indiatea.org/uploads/downloads](http://www.indiatea.org/uploads/downloads) (accessed on 02 September 2023).
- [www.teagalaxy.com/white-tea/3-common-varieties-of-white-tea/](http://www.teagalaxy.com/white-tea/3-common-varieties-of-white-tea/) (accessed on 02 September 2023).
- [www.teatulia.com/tea-varieties/what-is-white-tea.htm](http://www.teatulia.com/tea-varieties/what-is-white-tea.htm) (accessed on 02 September 2023).
- [www.thespruceeats.com/what-is-white-tea-766437](http://www.thespruceeats.com/what-is-white-tea-766437) (accessed on 02 September 2023).
- Zhang, C., et al., (2019). Climatic factors control the geospatial distribution of active ingredients in *Salvia miltiorrhiza* Bunge in China. *Scientific Reports*, 9.

# Index

---

## $\alpha$

$\alpha$ -bulnesene, 137, 141  
 $\alpha$ -glucosidase, 146  
 $\alpha$ -guaiene, 137, 138, 141  
 $\alpha$ -humulene, 137  
 $\alpha$ -patchoulene, 137, 138, 141  
 $\alpha$ -pinene, 23, 24, 30, 357, 368  
 $\alpha$ -selinene, 137, 141  
 $\alpha$ -terpineol, 23

## $\beta$

$\beta$ -caryophyllene, 23, 24, 28, 30, 138  
 $\beta$ -elemene, 137  
 $\beta$ -endorphin, 36  
 $\beta$ -myrcene, 23, 27  
 $\beta$ -patchoulene, 132, 137–139  
 $\beta$ -phellandrene, 351, 353  
 $\beta$ -pinene, 23, 24, 357, 370  
 $\beta$ -sitosterol, 70, 109, 139, 359

## $\gamma$

$\gamma$ -guaislene, 132  
 $\gamma$ -patchoulene, 137  
 $\gamma$ -pinene, 357  
 $\gamma$ -terpene, 358  
 $\gamma$ -terpinene, 355, 357

## $\delta$

$\delta$ -elemene, 137, 141, 172  
 $\delta$ -guaiene, 137, 138, 141  
 $\delta$ -patchoulene, 137, 141

## A

Abdominal pain, 359, 362  
Aberrant crypt foci (ACF), 97, 98  
Abeyance, 306  
Acaricidal  
  activity, 37, 45  
  properties, 30

Acetone, 23, 32, 139, 146, 256  
Acetylated mannans, 299, 330  
Acre, 244, 252, 311, 314  
Active ingredient (Ai), 55, 57, 65, 67, 68,  
  71, 75, 77, 78, 96, 99, 100, 102, 148, 250,  
  257, 360, 370, 404, 406, 416  
Adaptogenic potency, 337  
Adenosine triphosphate (ATP), 148, 356,  
  361, 368  
Adrenal gland  
  hypertrophy, 337  
  weight, 336  
Adriamycin, 191, 192  
Adulterants, 389  
Adulteration, 228  
Adulticidal activity, 187  
Aerial sowing methods, 83  
Afforestation, 112  
Agro-climates, 11  
Agro-forestry, 83  
*Agromore foliar*, 65  
*Agro-neem*, 64  
Ailments, 3, 13, 14, 39, 56, 57, 225, 245,  
  306, 307, 382  
Air penetration, 313  
Ajmodadichurna (AJC), 206  
Ajwain, 17, 356–363, 366, 370  
  essential oil, 357, 362  
  seeds, 352–359, 361, 362  
Alanine transferase, 360, 364  
Alanine transaminase (ALT), 108, 360, 364  
Alcohol, 131, 148–150, 239, 284–286, 288,  
  332, 362  
Aliphatic  
  components, 386  
  compounds, 24, 382  
Alkaline  
  phosphatase (ALP), 99, 194, 360, 364  
  soils, 228

- Alkaloid, 23, 29, 34, 59, 95, 163, 170, 188, 189, 208, 224, 225, 227, 237, 300, 302, 315, 355, 386, 395  
compounds, 29  
piperine, 170
- Alloxan, 109, 328
- Alpha-melanocyteenhancing hormone, 194
- Alternipetalous, 357
- Aluminum, 352
- Amino acids, 106, 237, 278, 404, 407, 412, 413, 415, 416
- Amplified fragment length polymorphism (AFLP), 56, 111
- Analgesic, 1, 39, 68, 73, 107, 133, 164, 165, 187, 265, 289, 291, 363, 367, 370, 382  
activity, 187  
effect, 363
- Ancient oriental therapy, 316
- Anorexia, 38, 68, 108
- Ant-fertility activity, 189
- Anthericum, 302
- Anthers, 110, 136, 308
- Anthraquinone, 241, 243, 245, 254, 257  
fraction, 70
- Antiaflatoxic activity, 36
- Anti-allergic, 1, 3, 35, 105, 389  
activity, 1, 3, 35, 147
- Antiamoebic activity, 187
- Anti-angiogenic effect, 1, 3, 35
- Antiarthritic, 70, 300  
properties, 389
- Antiarthritis, 367
- Anti-asthmatic effect, 1, 3, 34, 45
- Antibacterial, 1, 3, 30–32, 37, 44, 59, 68, 70, 72, 96, 97, 109, 133, 149, 187, 224, 238, 264, 288, 333, 361, 367, 368, 370, 395  
activity, 31, 96, 97, 149, 187, 333
- Anticancer, 3, 34, 44, 55, 100–102, 150, 188, 237, 243, 300, 318, 331, 372, 395, 412, 415  
activity, 149, 188, 330
- Anti-cancerous  
agent, 355  
impact, 98, 101
- Anti-candida activity, 146
- Anti-carcinogenic, 97
- Anti-complement property, 68
- Anticonvulsant, 360
- Anti-depressant activity, 133, 147, 165, 188, 195, 270, 291
- Antidiabetic  
activity, 104, 107, 165, 241, 243, 256, 264, 288, 291, 316, 333, 389  
evaluation, 104  
potential, 316
- Anti-diarrheal activity, 362, 367
- Antiemetic activity, 146
- Antiepileptic property, 360
- Antifeedant, 59, 68, 74, 75, 77, 78, 94, 106, 109
- Antifertility, 68, 75, 107, 109
- Antifungal activity, 1, 3, 30, 32, 33, 44, 59, 68, 70, 94, 96, 97, 107, 133, 140, 146, 155, 165, 189, 239, 243, 245, 359, 361, 367, 370, 395
- Antigasteric ulcer, 70
- Antigen, 99, 102, 103, 329  
presenting cells (APC), 102
- Anti-hyperlipidemic  
action, 189  
activity, 189
- Anti-inflammatory  
actions, 1, 3, 30, 33, 37, 39, 44, 68, 70, 73, 107, 109, 148, 163, 189, 206, 225, 241, 256, 264, 270, 289, 291, 356, 360, 362, 365, 367, 382, 389, 408, 416  
activity, 33, 163, 189, 362, 365  
agent, 33, 356
- Anti-malarial properties, 68
- Anti-microbial, 3, 43, 389, 415  
activity, 32, 190, 370  
effects, 31, 149, 190
- Anti-mutagenic  
activity, 146, 155  
effect, 97
- Anti-nociceptive  
activity, 147  
effect, 147
- Antiobesity activity, 190
- Antioxidant, 31, 105, 225, 239, 290, 359, 360, 367, 411, 415  
activity, 1, 3, 30, 31, 44, 70, 94, 98, 99, 108, 109, 133, 148, 149, 155, 165, 190–193, 206, 207, 236–238, 243, 245, 256, 264, 270, 288, 290, 291, 300, 318, 329, 332, 333, 355, 357, 359, 360, 363, 365, 367, 372, 395, 404, 405, 408, 409, 413–416  
molecules, 405  
properties, 94, 236, 238, 290, 332

- Antiplatelet activity, 35, 191  
 Antiproliferative action, 330, 364  
 Antiradical, 290  
 Anti-snake venom, 191, 209  
 Antistress  
   activity, 332  
   effect, 36  
 Anti-tubercular activity, 188  
 Antitumor, 44, 55, 68, 70, 98, 101, 103, 107,  
   165, 241, 243, 256, 331  
 Antitussive, 264, 288, 359  
   properties, 357  
 Antiulcer, 68, 94, 107, 163, 187, 109, 191, 332  
   activity, 332  
 Antiulcerogenic  
   actions, 36  
   activity, 1, 3, 35  
 Anti-venom product, 209  
 Antiviral, 30, 33, 37, 68, 72, 107, 238, 239,  
   241, 256, 333  
   activity, 33, 107, 148  
   agents, 72  
 Antonyms, 166  
 Aphrodisiac  
   activity, 195, 270, 306, 316, 318, 324,  
     327–329, 356  
   analysis, 328  
   drug, 328  
   potency, 327–329  
   potential, 327  
*Apiaceae*, 355, 356  
 Apigenin, 29, 138, 139  
 Apoptosis, 99–101, 103, 150, 330  
 Appetite, 71, 78, 271, 385  
 Apple mosaic virus (ApMV), 281  
 Aqua extract, 331, 332  
 Aqueous, 29, 33, 34, 43, 97, 98, 103–105,  
   107, 108, 146, 149, 187, 289, 327–332,  
   356, 358, 363, 368, 404, 408, 416  
   extract, 68, 330, 365  
 Arabis mosaic virus (ArMV), 281  
 Arachidonic acid  
   metabolism, 35  
   metabolite thromboxane, 35  
 Arid forest research institute (AFRI), 62, 85,  
   110, 114, 115  
 Aroma, 9, 37, 40, 131, 132, 150, 168, 288,  
   357, 403, 406, 407, 410, 411, 414  
   Aromatherapeutic usage, 288  
 Aromatic, 1, 2, 9, 30, 131, 133, 135, 150,  
   164, 168, 207, 208, 220, 229, 267, 284,  
   287, 355  
   anti-oxidant polyphenols, 405  
   glucosides, 358  
   glucosidic compound, 358  
   hydrocarbons, 358  
   plants, 284, 285, 288  
 Arthritis, 33, 39, 58, 306, 329, 355, 356,  
   360, 362, 368, 382, 404, 405, 414  
 Ascorbic acid, 31, 105, 237  
*Asparagaceae*, 299, 300, 307, 309, 344  
 Aspartate aminotransferase (AST), 99, 108,  
   360, 364  
*Aspergillus niger*, 32, 94, 190  
 Asthma, 34, 38, 106, 163, 187, 195, 206,  
   207, 306, 356, 359, 370  
 Astringent, 219, 224, 225, 241, 243, 247,  
   256, 264, 270, 271, 290, 305, 410  
 Atherosclerosis, 329  
 Ayurveda depicts, 305  
 Ayurvedic  
   erudition, 299  
   herbs, 305  
   medicinal systems, 305  
   medicine, 195, 206, 210, 271, 381, 395  
   system, 195  
*Azadirachta indica*, 94, 105  
 Azadirachtin (AI/AZ), 56, 57, 63, 64,  
   66–69, 71, 72, 75, 77–79, 85, 87, 88, 95,  
   96, 99, 98, 106, 109, 113–117  
   treatments, 79  
 Azathioprine, 329
- ## B
- Bacillus*  
   *cereus*, 32  
   *subtilis*, 31, 32, 95, 361  
 Bacterial  
   inhibition, 356, 365  
   pathogens, 96  
 Bactericidal treatments, 280  
 Bark, 55, 56, 59, 63, 68–71, 76, 78, 80, 92,  
   99, 100, 106, 107, 221, 225–228, 233,  
   243, 273, 383, 386  
 Barring, 57, 58, 64, 67, 68, 72, 100, 108  
 Begomovirus disease, 19

- Belixasol, 15  
 Bilioussness, 68, 105, 108  
 Bioactive, 3, 20, 29, 32, 56, 133, 140,  
   149, 155, 237, 244–246, 250, 256, 290,  
   355–360, 362, 363, 366, 368, 369, 404,  
   405, 407, 412–416  
   compounds, 29, 32, 55, 56, 69, 133, 237,  
   244–256, 415  
   factors, 193  
   ingredients, 359  
   secondary metabolites, 20, 29, 412, 414  
   substances, 290  
 Bio-activity, 409, 416  
 Bio-adsorbent, 43  
 Bioavailability enhancers, 163, 187, 192  
 Biochemical  
   change, 239  
   compounds, 30, 109, 113  
   constituents, 68  
   markers, 112  
 Bio-constituents, 77, 94, 108, 116  
 Biofuel, 44, 57  
 Biological  
   activities, 30, 44, 59, 165, 170, 194, 243,  
   245  
   chemicals, 329  
   fitness, 79  
 Biomolecules menthol, 24  
 Biopesticides, 66  
 Bio-prospectation, 94  
 Bio-prospection, 256, 257, 288, 410, 412  
 Bioprospects, 237  
 Biosynthesis, 356, 358, 361, 362, 365, 368  
 Biotechnology, 150, 155  
   aspects, 208  
 Bisexual, 9, 82, 136, 357  
 Botanical, 2, 44, 133, 273, 299, 363, 368,  
   404  
   descriptions, 299  
   nomenclature, 133  
   taxonomical classification, 133, 166  
 Botany, 80, 247  
 Bowel movement, 362  
 Bracteate, 248, 273, 307, 309  
 Breeding, 70, 112, 115, 117  
   systems, 110  
 Broad exploration, 314  
 Butanol, 146, 187, 189, 323
- C**
- Cadinol, 358  
 Cadmium, 356  
 Caffeic acid, 29  
 Caffeine, 290, 405, 407, 411, 412  
 Calcareous, 83, 228, 275  
 Calcium oxalate crystals, 81, 383  
 Callus, 231, 413, 416  
*Camellia sinensis*, 403, 405, 406, 410  
 Camphor, 23, 27  
 Cancer cells, 101–103, 150, 246, 414  
*Candida albicans*, 32, 70, 95, 329  
*Cannabis sativa*, 33, 39  
 Carbohydrates, 34, 106, 255, 300, 302, 356  
 Carbon tetrachloride, 34, 193  
 Carcinoembryonic antigen (CEA), 102  
 Cardiac glycosides, 23, 29, 30  
 Cardio protective activity, 163, 187, 192  
 Cardiovascular  
   disease, 1, 35  
   effects, 359  
   problems, 356, 359, 370  
 Carminative, 1, 39, 163, 195, 305, 356, 366  
 Carvacrol, 357, 359, 360  
 Carvone, 23, 24, 358  
 Caryophyllene, 137, 140, 358  
 Casual organism, 15  
 Catabolism, 357, 359, 363, 368  
 Catalase (CAT), 149, 191, 331, 332, 360,  
   364, 368  
 Catechin, 68, 107, 405, 407, 408, 411, 412,  
   414–416  
 Causal organism, 16–20, 92  
 Cecum amebiasis, 187  
 Cell kinetics, 330  
 Cellular  
   acetylcholine level, 360  
   aflatoxin biosynthesis, 356  
   aspartate transferase, 360  
   enzymes, 355  
   immune functions, 329  
   lipoproteins, 368  
   nucleoside, 358  
   system, 359  
 Cellulose, 30, 44  
 Chemical  
   compound, 23, 33, 36, 56, 67, 68, 95,  
   106, 113, 137, 146

- constituents, 30, 34, 41, 65, 67, 68, 100,  
 114, 137, 358  
 moiety acts, 59  
 Chemomodulatory, 331  
 Chemo-preventive efficacy, 356  
 Chemotypic variation, 358  
 Chest pains, 1  
 Chick chorioallantoic membrane (CAM), 35  
 Chinese academy of forestry (CAF), 61  
 Chloroform extract, 68  
 Chlorophyll, 30, 277  
*Chlorophytum*  
   *borvillianum*, 299, 300, 309, 315, 344  
   genus, 307, 308  
   species, 300, 307, 316  
 Cholera, 97, 356  
 Cholesterol, 104, 225, 290, 311, 332, 359,  
 368, 408, 414  
 Cholinergic mediated mode, 363  
 Chromatographical steps, 323  
 Chromosome, 9, 331  
 Chronic  
   arthritis, 355  
   pain, 363, 365  
   stress, 332  
 Chronotropic effect, 359  
 Chrysin, 29  
 Circulatory system, 271  
 Cobalt, 356, 357  
 Cold pressed neem oil, 65  
 Coleoptera, 78, 79  
 Column chromatography (CC), 138, 139,  
 146, 254  
 Combating diseases, 95  
 Commercial, 3, 19, 56, 61, 63, 65, 67, 71,  
 77, 83, 133, 134, 138, 155, 208, 239, 243,  
 254, 257, 275, 280, 281, 357, 366, 381,  
 404, 406  
   dye, 226  
 Composition, 25, 39, 137, 209, 236, 257,  
 270, 291, 316, 369, 370, 404, 412, 413  
 Conductive climatic condition, 66  
 Conidia germination, 32  
 Contraceptive, 59, 66, 73, 108, 109  
   agents, 73  
 Cork tissues, 82  
 Corolla, 9, 136  
 Coronary vasodilation, 163, 187, 192  
 Corpora cavernosa, 328  
 Corrugated fiberboard (CFB), 235  
 Cortical cells, 383  
*Corticiumsalmonicolor*, 92  
 Corticosterone, 36, 332, 333  
*Corynespora cassiicola*, 16  
 Cosmetic, 1, 41, 43, 57, 58, 71, 73, 115, 131,  
 133, 164, 241, 242, 256, 257, 264, 269,  
 271, 286, 291, 307, 370, 404, 415, 416  
   industry, 43, 404  
 Cost-effective manner, 413  
 Cremocarps, 357, 358  
 Crop  
   maturity, 252  
   protection, 13, 115  
 Crude distillation process, 285  
 Cucumber mosaic virus (CMV), 19  
*Culex quinquefasciatus*, 193, 333  
 Culinary formulations, 307  
 Cultivar, 23, 24, 39, 110, 111, 220, 222,  
 229, 230, 234, 236, 248, 263, 264, 272,  
 274–277, 279, 281, 282, 292, 309, 410  
 Cultivation, 3, 5, 10, 11, 15, 19, 23, 39, 55,  
 61–63, 66, 67, 70, 82, 89, 111, 132, 137,  
 167, 207, 219–222, 228, 230, 236, 237,  
 244, 250, 252, 267, 272, 274, 310, 311,  
 314, 315, 358, 406, 410, 412  
 Culture, 231  
 Cup diffusion method, 333  
 Cut flowers, 265, 267, 268, 283  
 Cyclic trisulfide, 68  
 Cyclooxygenase, 35, 147, 190  
 Cytochrome oxidase, 355, 359  
 Cytotoxic T lymphocyte (CTL), 103  
 Cytotoxicity, 34, 102, 138, 149, 188, 324,  
 330  
   activity, 34
- ## D
- Days after anthesis (DAA), 85  
 Deadheading, 251, 257  
 Decennial, 306  
 Decoction, 71, 95, 106, 189, 224, 291, 366, 384  
 Deep  
   acidic, 228  
   eutectic solvent (DES), 29, 32  
 Defense Institute of Physiology and Allied  
 Sciences (DIPAS), 73

- Delayed-type hypersensitivity response (DTH), 329
- Dementia, 163, 408
- Dendrothoe falcata*, 93
- Dental
- health, 37
  - treatments, 73
- Deoxyribonucleic acid (DNA)
- based marker, 56, 117
  - fragmentation assay, 331
- Dephosphorylation, 355, 360, 364
- Dermatological uses*, 72
- Deteriorate, 2, 3
- Deterioration, 13, 253
- Diabetes, 57, 68, 109, 206, 238, 287, 306, 328, 329, 381, 404, 414, 416
- Diarrhea, 207, 362
- Diarrheal symptom, 362
- Dichloromethane, 146, 358
- Dietary
- fibers, 355
  - meals, 367
  - supplements, 239, 367, 404
- Digestive problems, 3, 287
- Diode array detection (DAD), 30, 138, 139
- Diptera, 78, 79
- Disc diffusion test, 33
- Disease, 1–3, 13, 14, 18, 44, 55–57, 64, 65, 73, 76, 92, 93, 95, 96, 98, 102, 105, 116, 163–165, 169, 195, 206, 232, 233, 238, 256, 265, 276, 279, 281, 287, 289, 381, 382, 395, 414
- management, 13, 15–18, 20, 252, 279
- Distilled biomass, 30, 44
- Diterpenoids, 68, 106, 107
- Diuretic properties, 68
- DMBA (7,12-dimethylbenz-(a)-anthracene), 331
- Dorsal surface, 81
- Dorsiventral, 81
- DPPH (1,1-diphenyl-2-picrylhydrazyl), 332
- Drastic reduction, 19, 327
- Dried
- flowers, 286
  - rose petals, 286, 287, 290
- Drug metabolizing enzymes, 98
- Duodenum histology, 36
- Dyspepsia, 71, 224, 225, 238, 243, 356, 359, 383
- ## E
- Eco-floristic regions, 223
- Eco-geographical regions, 111, 112
- Ecosystem, 58, 282
- Efficacy, 31, 32, 43, 57, 68, 72–75, 97, 101, 102, 105, 108, 111, 254, 255, 289, 332, 357, 360–362, 381, 407, 412
- Ejaculation, 305, 327, 328
- Electrospray ionization multistage mass spectrometry (ESI-MS<sup>n</sup>), 139
- Elemene, 137, 354
- Ellipsoid tubers, 302
- Emmenagogue, 39, 59, 70, 164
- Emulsifier, 64, 147
- Endospermic seeds, 308, 309
- Enterococcus faecalis*, 32
- Environmental
- management, 280
  - Protection Act (EPA), 63, 64
- Enzymatic method, 31
- Enzyme-linked immunosorbent assay (ELISA), 330
- Epicatechin (EC), 31, 68, 107, 387, 407
- gallate (ECG), 407
- Epidermal cells, 79
- Epigallocatechin (EGC), 407, 408
- 3-gallate (EGCG), 407
- Epilepsy, 243, 362, 365
- Epistaxis, 68, 108
- Erectile dysfunctions (ED), 33, 328
- Erythrocytes, 100, 318
- Escherichia coli*, 31, 32, 59, 96, 190, 361
- Essential oil (EO), 1–3, 9, 16–18, 20, 23, 24, 31–34, 36, 37, 39–41, 43–45, 131–133, 137, 138, 140, 147, 148, 150, 155, 164, 170, 187, 189, 208, 243, 270, 275, 283, 284, 286, 288, 291, 355–363, 365–370, 376, 382, 407, 415
- constituents, 20
- Ethanol, 23, 31, 32, 34, 35, 107, 146, 149, 187, 194, 288, 324, 329, 330
- Ethanolic
- extract, 33, 68, 94, 101, 361, 365
  - roots, 323
- Ethical trading initiative (ETI), 269



Ethiopian Horticulture Producer and Exporters Association (EHPEA), 269

### Ethno

- botanical use, 363
- medicinal properties, 356, 372
- uses, 366, 384, 395
- value, 369

### Ethyl

- acetate extracts, 35
- linolenate, 30

Ethylene, 234

Eudesmol, 359

Eugenol, 370

Exotic, 60, 93, 111, 114

Export potential, 67, 207

## F

Farm forestry plantations, 84

Farmyard manure (FYM), 74, 231, 232, 251, 313, 314

Fascicle, 308

Fatty acids, 285, 287, 317, 326, 356, 367, 382

Febrifuge, 59, 357

*Fecundity suppression*, 79

Fermentation, 85, 225, 405, 407

Fermented *M. arvensis* (FMA), 36

Fertilizers, 12, 64, 66, 74, 106, 314

Fibers, 226, 227, 302, 383

Fibrous, 302, 308

Flame-ionization detection (FID), 138

Flatulence, 38, 195, 246, 256

Flavonoid, 23, 29–31, 34–36, 44, 68, 70, 94, 96, 106, 138, 139, 146, 163, 170, 190, 192, 208, 237, 239, 242, 243, 245, 254, 255, 270, 285, 315, 357, 404, 405, 407, 412, 414, 415

Flavonols, 31, 285, 405

Flavoring agent, 133, 164, 286, 413

Folic acid, 220

Free radical, 405

- scavenging property, 31

Fructans, 299, 316, 334

Fructooligosaccharides (FOS), 299, 316, 333

Fructose, 237, 302, 316, 327

Fumigant, 3, 37, 75, 365, 366

### Fungal

- ailments, 14
- diseases, 280

Fungi, 2, 3, 13, 14, 44, 75, 95, 149, 189, 190, 279, 333, 361, 369

Fungicidal, 44, 189, 280, 365

Fungicides, 2, 13, 15, 16, 64, 72, 106

Fungitoxic effects, 356

Furostanol, 324, 326

- saponins, 324

*Fusarium oxysporum*, 16, 32, 92, 94, 96

## G

Galactogogue, 305, 356, 366

Galactose, 246, 302, 316, 324

Gallic acid, 68, 227, 285

Gas chromatography (GC), 23, 24, 29, 30, 137, 138, 324, 357

- mass spectrometry (GC-MS), 23, 24, 29, 30, 137, 357

### Gastric

acid, 359, 366

disturbances, 356

mucosa, 360

mucosal glycoproteins discharge, 191

problem, 1

Gastrointestinal, 264, 307, 355, 370

effects, 359

Gastro-protective activity, 146

Genetic, 155, 208, 230

variation, 112, 113

Genotype, 23

Genus, 1, 4, 5, 9, 20, 29, 43, 78, 163, 164, 241, 242, 267, 270, 272, 273, 285, 286, 289, 300, 302, 307, 308

chlorophytum, 302

### Geographical

areas, 11

distribution, 6, 165

source, 5, 134, 382, 395

variation, 110, 358

Germacrene-D, 23

Germination rate, 87, 311

Germplasm, 57, 208

Glabrous, 80, 248, 357

### Global

market, 10, 207, 414

response to DNA damage (SOS), 146

Glucose, 104, 107, 237, 246, 302, 315, 316, 324, 332, 333

Glutathione (GSH), 31, 99, 108, 149, 191, 194, 331, 332, 360, 364, 368  
 peroxidase, 99  
 Glycol preservation, 286  
 Glycoside, 34, 68, 96, 106, 139, 170, 208, 241–243, 245, 246, 270, 316, 318, 355, 357–359, 382, 386, 395, 407, 412, 414, 415  
 Gonorrhoea, 71, 306  
 Granulocyte colony-stimulating factor (GCSF), 98  
 Growth regulation, 78  
 Guduchi, 381, 383, 385, 395

## H

Hamster Buccal Pouch (HBP), 98  
 Harvesting, 23, 85, 88, 89, 137, 219, 220, 233–237, 239, 250, 252, 255, 282, 283, 401, 402  
 time, 252  
 Health disorders, 356, 358, 367, 372  
 Heavy-duty hand cleanser (HDHC), 39  
 Hectares, 10, 11, 41, 62, 66, 132, 268  
*Helicoverpa armigera*, 328  
 Hemicellulose, 30  
 Hemiptera, 78, 79, 91  
 Hepatic tissue, 360  
 Hepatitis, 385  
 Hepatoprotective, 1, 3, 34, 165, 192, 193, 245, 254, 256, 366, 395  
 activity, 34, 163, 187, 192, 193  
 Herbaceous, 9, 242, 246, 247, 307, 382  
 Herbal  
 drug, 344, 395  
 formulations, 328, 369, 389  
 juice, 384  
 teas, 37  
 Herpes simplex type-1 (HSV-1), 33  
 Hesperidin, 29  
*Heteroptera*, 79  
 Hexane fraction, 139, 187, 189  
 High  
 density lipoproteins (HDL), 359, 368  
 performance  
 liquid chromatography (HPLC), 29, 30, 36, 87, 138, 139, 254, 318, 404  
 thin layer chromatography (HPTLC), 316, 318

photosynthetic activity, 278  
 speed counter-current chromatography (HSCCC), 139  
 Higher light photosynthetic impact, 278  
 Himalaya, 11, 24, 40, 242, 243, 246, 247, 249, 257  
 Histamine, 33, 35, 362, 363, 365  
 Hormone accumulation, 314  
 Horticultural, 64, 66, 70, 74, 77, 267  
 products, 66  
 Host resistance, 2, 13  
 Human  
 breast cancer cell, 330  
 immunodeficiency virus (HIV), 70, 237, 264, 271, 288, 369, 395  
 infections, 271  
 pathogenic bacteria, 31  
 Humid  
 conditions, 280  
 environment, 135  
 weather, 310  
 Humuline, 359  
 Hydrochloric acid (HCl), 35  
 Hydro-distillation process, 23  
 Hydrogen peroxide, 31, 148  
 Hydrolytic enzymes, 368  
 Hydroxyanthraquinones, 254  
*Hymenoptera*, 79  
 Hypotensive, 68, 107, 357

## I

Ileum, 360  
 Immemorial, 55, 59, 72  
 Immune  
 stimulant, 68  
 system, 68, 103, 107, 305, 329  
 Immunity, 101–103, 105, 107, 209, 306, 329, 367, 404, 408  
 buster products, 209  
 Immunoadjuvant, 329  
 Immunomodulator, 300, 305, 316, 329  
 Immunomodulatory  
 action, 329  
 activity, 163, 187, 193, 329  
 effects, 329  
 Immunostimulant, 329, 330  
 Immunostimulatory effects, 329  
 Immunosuppressive properties, 329

- Implementation, 2, 366  
*In vitro*, 31, 32, 88, 97, 102, 108, 140, 149, 170, 187, 188, 193, 194, 231, 245, 277, 318, 324, 327, 330, 331  
*In vivo*, 32, 35, 80, 97, 102, 109, 170, 187, 189, 190, 193, 194, 245, 324, 327, 329–331, 369  
 Indian Council for Forest Research and Education (ICFRE), 67, 113  
 Indo-Gangetic plains, 3, 5, 10, 19  
 Indomethacin (IMC), 146, 360  
 Inducible NO (iNO), 99  
 Infestation, 19, 71, 91, 92, 233, 366  
 Infested, 13, 252  
 Inflammation, 362  
     activity, 68  
 Inflammatory arthritis, 405  
 Inflorescence, 1, 82, 93, 135, 247, 248, 302, 312, 357  
 Infrared (IR), 254  
 Inhibitor, 43, 328  
 Inhibitory action, 31, 149, 194, 356, 359, 363  
 Insect growth regulators (IGRs), 78  
*Insect pests*, 20, 44, 364, 369  
 Insecticidal, 1, 3, 30, 36, 44, 57, 67, 68, 209, 324, 325  
     activity, 3, 36, 44, 68, 325  
 Insecticide, 59, 64, 71  
 Insect-pest management (IPM), 77, 90  
 Insomnia, 1  
 Integrated  
     crop management (ICM), 77  
     disease management, 2, 13  
     plant nutrient management (IPNM), 238  
 Intercropping, 2, 13, 282, 312, 314  
     system, 251  
 Interculture, 251  
 Interferons (IFN), 100, 102  
 Interleukin-2, 329  
 International  
     neem network (INN), 111–114, 117  
     patent, 209  
     classification (IPC), 43  
     provenance trials, 112–114  
 Inter-nodal callus, 32  
 Intestinal worm, 68  
 Intracellular calcium ion level, 147  
 Intraplantar administration, 147  
 Intromission latency, 327  
 Invigorating meal, 306  
 Iodine, 352  
 Ionotropic movement, 355  
 Iron, 12, 31, 226, 270, 275, 353  
 Irrigation, 12, 75, 222, 231, 251, 278, 413  
     practices, 251  
 Ischemic heart disease, 35  
 Isolation, 88, 139, 253, 323  
 Iso-menthone, 23, 24
- J**
- Jaundice disease, 105  
 Joint venture, 66  
*Juncus*, 302
- K**
- Kenya flower council (KFC), 269  
 Khadi and Village Industries Commission (KVIC), 93  
 Kharif crop, 311, 344  
 Kinin, 362
- L**
- Lablab bean, 312  
 Lactate dehydrogenase, 355  
 Lactations, 306  
*Lamiaceae*, 2, 4, 9, 133–135  
*Lamiales*, 4, 134  
*Lamina*, 16, 81, 383  
 Lanceolate, 9, 80, 302, 308, 410  
 Land equivalent ratio (LER), 312  
 Large scale cultivation demands, 315  
 Larvicidal  
     action, 333  
     activity, 104, 163, 187, 193, 333, 344  
     features, 333  
 Latency, 147, 327  
 Laxative, 225, 243, 245, 247, 286, 362, 368  
 Leaf  
     defoliators, 90  
     midrib, 81  
     spot, 15, 40, 64, 92  
 Length, 81, 87, 111, 135, 248, 277, 302, 308, 309, 410  
 Lepidoptera, 78, 79  
 Leprosy, 58, 59, 68, 71, 76, 108, 109, 165, 225, 366, 381, 382

Lethargy, 305  
 Leucorrhoea, 71, 306  
 Leukopenia, 329  
 Lignin, 30  
*Liliaceae*, 299, 300, 307, 309, 344  
 Limonene, 23, 24, 40, 140, 358  
 Limonoids, 67, 70, 88, 100, 106  
 Linolenic acid, 30  
 Lipase, 359, 363  
 Lipid, 30, 64, 104, 106  
   Peroxidation (LPO), 99, 100, 109, 193,  
   194, 331, 332, 359, 363, 415  
 Lipopolysaccharide (LPS), 99, 148  
 Lipoproteins, 357, 368  
 Lipxygenase, 35, 109  
 Liquid chromatography–mass spectrometry  
 (LC-MS), 29, 94, 95  
 Liver protectant, 105  
 Loamy soil, 11  
 Lobe shape, 9  
 Local meteorological conditions, 112  
 Low-density lipoproteins (LDL), 332, 359, 368  
 L-threonine, 367  
 Lubricants, 74  
 Luteolin, 29, 30  
 Lymphoid cell stimulations, 329  
 Lysosomal hydrolytic enzymes, 357

## M

*M. arvensis* (MA), 1–3, 5, 6, 10–12, 16, 23,  
 24, 26, 29–37, 39, 40, 43, 44  
 Macrophages, 99, 193, 329  
 Macropropagation, 87  
 Macroscopic description, 80  
 Magnesium (Mg), 65  
*Magnoliophyta*, 4, 134, 166  
*Magnoliopsida*, 4, 134, 166  
 Malaria, 57, 59, 61, 73, 187, 356, 382  
 Maltodextrin, 147  
 Mammals, 91, 110  
 Mancozeb propiconazole, 15  
 Mannose, 246, 302, 316  
 Manuring, 232  
 Mass spectrometry (MS), 23, 30, 32, 33, 94,  
 137, 138, 231, 254  
 Matrix metalloproteinase (MMP), 148  
 Maturity indices, 239  
 Medical biology, 362  
 Medication, 291, 299, 300, 302, 305, 306,  
 314, 316  
 Medicinal, 1–3, 38, 44, 55, 56, 58–61, 106,  
 133, 150, 163–165, 167, 170, 207, 208,  
 210, 219, 238, 239, 242, 244, 245, 251,  
 254, 256, 263–265, 267, 269–271, 274,  
 284, 286, 289, 299, 305, 307, 309, 315,  
 328–330, 355–357, 366, 369, 370, 372,  
 381, 403, 406, 412  
   and aromatic plants (MAPs), 43  
   properties, 3, 59, 219, 242, 245, 251, 265,  
   267, 270, 299, 356  
   uses, 38, 44, 239, 299  
 Melanin-inhibiting activity, 194  
 Meliantriol, 67, 69  
 Membrane, 146, 360, 361, 364, 368  
 Menstrual disorders, 207  
 Menstruation, 207, 265, 355  
*Mentha*, 1–7, 9–14, 17, 18, 20, 21, 24, 25,  
 29–45  
   *arvensis*, 1, 4, 10, 14, 25, 32, 34, 39, 45  
   cultivation, 2, 11, 12  
   genus, 3, 5, 41, 44  
   oil, 1, 10, 41, 42  
   species, 2, 38  
 Menthol, 1, 3, 11, 16, 23, 24, 31–34, 36, 37,  
 40, 41, 43, 45  
   mint ethanolic extract, 30  
 Menthone, 23, 24, 33, 40, 43  
 Menthyl acetate, 23, 24  
 Mericarps, 357, 358  
 Meta-analysis, 290  
 Metabolic  
   effects, 290  
   process, 356  
 Metastatic cell proliferation, 356  
 Methanol, 23, 29, 35, 95, 146, 189, 256,  
 257, 318, 326, 328, 330, 331  
 Methanolic  
   extract, 29, 30, 34, 146, 358  
   leaf extract, 31  
 Methyl thiazolyldiphenyl-tetrazolium  
 bromide (MTT), 34, 324, 331  
 Methylendioxyamphetamine (MDA), 149  
 Micro-dilution method, 32, 361  
 Microflora, 74, 90  
 Micro-nutrients, 12, 74, 311, 313, 408  
 Micropropagation, 88, 231

Microscopic description, 81  
 Microscopical characters, 383  
 Midgut epithelial cells, 79  
 Mineral, 237, 238, 270, 271, 287, 300, 356, 404, 408, 416  
   constituents, 69  
 Minimum  
   bactericidal concentration (MBC), 32  
   inhibitory concentration (MIC), 32, 33  
 Minor diseases, 233  
 Mint  
   disease management techniques, 13  
   rust disease, 15  
 Mites, 37, 64, 75, 91, 96, 106  
 Modulatory action, 364  
 Molecular variation, 110  
*Mollusks*, 91, 96  
 Monocot, 344  
 Monoterpene alcohol, 3, 24  
 Monoterpenoid, 358  
 Morphological characters, 383  
 Morphology, 9, 114, 135, 221  
 Mosaic disease, 19  
 Mosquito species, 333  
 Mouse macrophage, 327  
 Mouth aphthae, 306  
 Mucilage, 227, 302, 316  
 Multi-commodity exchange (MCX), 41  
 Multilayered (5–6) spongy parenchyma cells, 81  
 Mu-opioid receptor expression, 147  
 Muscular  
   mass, 305  
   pain, 189  
 Musli's aphrodisiac potential, 324  
 Mycelial growth, 32, 36  
*Mycobacterium tuberculosis*, 59, 109  
 Mycotoxin, 367  
 Myelosuppression, 329  
 Myrcene, 24, 357  
 Mythological nymph, 5

## N

National  
   Commodity and Derivatives Exchange (NDEX), 41  
   Multi Commodity Exchange of India (NMCEIL), 41  
 Natural killer (NK), 103, 329, 330  
 Neem, 20, 55–117, 207  
   aura naturals, 65  
   cake, 57, 63–65, 74–76, 89, 96  
   co-operative, 65  
   cultivation technology, 61  
   extracts, 70, 72, 77, 78, 96–98, 101–106  
   facial moisturizing lotion, 65  
   fruit, 68, 71, 76, 81, 85, 88, 89, 93  
     extracts (NFEs), 109  
   herbal spray, 65  
   kernels, 62, 63, 69  
   leaf  
     extract (NLE), 57, 65, 69, 97–99, 101, 102, 105, 107, 108  
     glycoprotein (NLGP), 102, 103  
     tea, 76  
   oil, 57, 58, 60, 62–74, 78, 89, 96, 97, 104–106, 109, 117  
   potential, 65  
   raw materials, 61  
   seed extracts (NSE), 108, 109  
 Nematode, 2, 3, 13, 19, 20, 64, 74, 96, 279, 369  
 Neomenthol, 23, 24  
 Neophytadiene, 30  
 Nervous disorders, 1  
 Nervous system, 194, 271, 305, 364  
 Network program, 114  
 Neural system, 360, 370  
 Neurodegenerative, 239, 404, 405  
 Nicotinic acid, 356, 357  
 Nimbin, 67, 70, 95  
 Nimbolide, 70, 100, 101, 109  
 Nitrate reductase activity, 278  
 Nitric oxide/nitrous oxide (NO), 99, 103, 146, 327, 362, 364, 365, 368  
 Nitrogen, 12, 70, 74, 237, 251, 278, 282, 312  
 Nitrous oxide scavenging, 31  
 Nociceptive pain, 405  
 Non-enzymatic method, 31  
 Non-hydrolysable tannin, 404  
 Non-specific cellular immune system, 329  
 Non-thymol constituents, 357  
 Non-toxic, 66, 75, 77, 106, 330  
 Non-volatile chemical constituents, 29, 138, 155

Normo-glycemic control group, 328  
 Norpatchoulene, 131  
 Norpatchoulenol, 132  
 Novel drug formulation, 391  
 Nuclear magnetic resonance (NMR), 139, 254  
 Numerous systems, 1  
 Nutraceutical, 329, 403, 404, 413, 415, 416 value, 271, 414  
 Nutrient, 12, 64, 79, 257, 316, 404, 409, 413, 415  
   management, 231, 257, 277, 404, 413  
 Nutritional  
   benefits, 356, 367, 369, 372  
   excitant, 310

### O

Odor, 3, 39, 43, 67, 71, 80, 81, 106, 307, 312, 356, 383  
 Oligospermia, 305, 328  
 Oligozoospermic patients, 328  
 Ophthalmia, 59  
 Oral administration, 73, 99, 108, 332, 359–361  
 Orchard health management (OHM), 238  
 Organic  
   farming, 269, 279, 281, 282, 314  
   fertilizers, 66  
   matter, 11, 70, 168, 275  
   neem leaf extract, 65  
 Origin, 2, 55, 58, 60, 69, 111, 189, 220, 274, 282, 360, 413  
 Ornamental, 263  
   purposes, 267  
 Orthoptera, 78, 79  
 Osteo-arthritic pain, 290  
 Osteoarthritis, 33, 39, 237, 360, 364  
 Ovalbumin (OVA), 34, 147  
 Ovarian, 79  
 Ovary, 79, 110, 247, 248, 357  
 Ovate, 9, 80, 82, 221, 222, 229, 247, 248, 307, 308, 383, 410  
 Oviposition, 75, 77–79  
   repellency, 79  
 Oxidation, 98, 148, 331, 332, 401, 403, 411  
 Oxygenated  
   monoterpenes, 23, 34  
   sesquiterpenes, 24, 137

### P

Paclitaxel, 324  
 Pain relief, 73, 264, 289  
 Pancreatic  
   amylase, 359, 363  
   lipase, 355  
 Paracetamol, 108, 360  
 Paralleled venation, 308  
 Parasites, 18, 96, 108  
 Parasitic plants, 92  
 Parasiticide, 59  
 Parenchyma, 81, 383  
 Parenchymatous thin walled cells, 384  
 Patchouli, 131–135, 138, 140, 147, 148, 150, 155  
   alcohol (PA), 131, 138–140, 146–150  
   oil, 131, 132, 147, 149, 150, 155  
 Patchoulol, 132, 137–139  
 Patent, 39, 43, 63, 115, 150, 209, 238, 257, 291, 292, 344, 369, 370  
 Pathogens, 3, 14–18, 32, 44, 59, 69, 70, 96, 279, 280, 361, 362  
 Pedicillate, 309  
 Pediculicide, 59  
 Pediculosis, 105  
 Pentamerous, 82, 357  
 Perennial, 9, 13, 221, 242, 247, 248, 272  
 Perfumery industries, 132, 267, 269  
 Perianth, 247, 248, 308  
 Pericarp, 88, 221  
 Periongumine, 170  
 Peripheral blood mononuclear cells (PBMC), 100, 102, 330  
 Peritoneal macrophages, 329  
 Permeable soil, 310  
 Per-oxidation, 31  
 Pest  
   and disease management, 2, 11, 13, 45, 340  
   control treatment, 314  
 Pesticide, 2, 13, 57, 62, 66, 67, 72, 106, 116, 280  
 Petroleum ether, 23, 191, 256, 287  
   extracts, 23  
 Petroselinic acid, 358  
 Phagocytosis stimulations, 329

- Pharmaceutical, 1–3, 41, 43, 44, 67, 71, 133, 150, 164, 208, 238, 290, 291, 356, 372, 404, 405, 415, 416  
industry, 2, 41, 290, 291  
products, 43, 133, 290, 416
- Pharmacists, 2
- Pharmacognosy, 132, 403
- Pharmacologic benefits, 324
- Pharmacological, 2, 3, 30, 38, 45, 105, 106, 140, 155, 164, 170, 187, 188, 194, 195, 225, 245, 264, 288, 289, 292, 318, 357–359, 363, 367–370, 381, 382, 395, 404, 414  
activity, 30, 38, 106, 140, 187, 194, 289, 389, 404, 414  
applications, 395  
companies, 369  
effects, 195, 288, 289, 318, 359  
efficiency, 45  
profile, 170  
properties, 3, 194, 245, 292, 370  
report, 194
- Pharmacology, 45, 132, 210, 362, 372
- Pharmacopeia standards, 254
- Pharmacotherapeutic applicant, 188
- Phenol, 302
- Phenolic, 95, 237, 299  
acids, 254, 285, 315  
compounds, 34, 254
- Phenology, 221
- Phenols, 31, 44, 59, 190, 237, 255, 284
- Phenomenon, 278, 412
- Phenylethyl alcohol, 288
- Phenylpyruvic acid, 29
- Phloem, 81, 82, 379  
elements, 81, 82
- Phosphorous (Ph), 12, 65, 237, 251, 312, 356, 357, 386
- Phosphorylation, 148, 355, 357
- Photosynthetically active radiation (PAR), 312
- Physico-chemical properties, 255
- Phyto marker compounds, 401
- Phytochemical, 23, 29, 30, 36, 37, 39, 95, 44, 55, 106, 117, 170, 188, 210, 238, 243, 255, 270, 316, 330, 355, 357, 372, 395, 404, 412  
analysis, 356  
components, 29, 39, 188  
compounds, 30, 170  
profiling, 356  
screening, 95, 316, 395
- Phytochemistry, 2, 20, 45, 137, 155, 208, 210, 381, 386
- Phytoconstituents, 23, 106, 137, 236, 239, 243, 253, 254, 285, 299, 315, 344, 388, 404, 405, 412, 413, 416
- Phytol, 30
- Phytopharmaceutical, 404, 416
- Phytosterol, 359
- Pigeon pea, 312
- Piles, 68, 71, 76, 109, 206, 366
- Pinocembrin, 29
- Piper longum*, 163, 166–169, 171, 195, 196, 209, 210
- Piperaceae*, 210
- Piperine, 163–165, 170, 187–189, 191–193, 206, 207, 210
- Piperitone, 23, 24, 28
- Piperlonguminine, 165, 170, 189, 194, 209
- Pippali powder, 384
- Pistil, 308
- Pith, 395
- Plant  
growth promoting rhizobacteria (PGPRs), 20  
metabolites, 20
- Plantae*, 4, 82, 133, 166, 309
- Plantation  
growth, 84  
material, 311
- Planting  
root-shoot cuttings, 84  
system, 277  
techniques, 83
- Plantovax, 15
- Plasma  
cholesterol levels, 290, 332  
glucose levels, 332
- Pogostemon cablin* benth, 131, 133, 134, 138, 139, 143, 148, 151, 153, 155
- Pogostone, 137–139, 146, 149  
analogs, 146
- Polarity level, 23
- Poly-herbal formulation, 358, 360
- Polymorpho nuclear neutrophil (PNN), 107

- Polyphenol, 23, 242, 243, 289, 404, 405, 407–409, 412, 413, 415, 416  
   catechin, 407  
   oxidase, 405, 407, 409  
 Polyphenolic components, 386  
 Polypot planting, 83  
 Polysaccharides, 68, 100, 106, 107, 237, 246, 300, 302, 316, 330, 382, 386  
 Post  
   and pre-natal symptoms, 306  
   ejaculatory, 327  
   harvest  
     handling, 257, 283, 292  
     management practices, 252  
 Postharvest decay control, 44  
 Potpourris, 286  
 Powdery mildew, 15, 18, 40, 279, 280  
 Preclinical  
   examinations, 333  
   trials, 333  
 Premature  
   ejaculation, 328  
   leaf, 413  
 Premenstrual syndrome (PMS), 271, 364  
 Presumptuous, 192  
 Pricking, 83  
 Primary dysmenorrhea pain intensity, 289  
 Principal component analysis (PCA), 111  
 Production methodology, 404  
 Proliferating cell nuclear antigen (PCNA), 97, 98, 101, 102  
 Proliferation, 99–101, 103, 237, 281, 356, 361, 408  
 Propagation, 62, 85, 87, 88, 150, 208, 219, 230, 231, 250, 276, 277, 301, 413  
 Propagule, 251, 311  
   rate, 251  
 Prostaglandin E2 (PGE2), 99, 362  
 Proteins, 106, 271, 299, 300, 302, 315, 316, 356, 357, 368  
*Proteus vulgaris*, 31, 32  
 Prothoracicotropic hormone (PTTH), 78, 79  
 Provenance exploration, 111, 112  
 Proximate composition, 255  
 Pruning, 84, 229, 231, 232, 275, 276, 278  
 Prunus necrotic ring spot virus (PNRS), 281  
*Pseudomonas aeruginosa*, 31, 59, 70, 96, 190, 333, 361  
 Psychological disorder, 71  
 Pulegone, 23, 24, 40  
 Pungent, 247, 271, 356  
 Purity assessment, 255  
*Pythium aphanidermatum*, 17
- ## Q
- Qualitative, 2, 3, 65, 66, 74, 76, 316, 318  
   yield, 2  
 Quality  
   enhancement, 254  
   testing, 255  
 Quantitative  
   analysis, 30, 131, 138  
   evaluations, 65  
 Quercetin, 68, 70, 107, 285
- ## R
- Radioprotective, 3, 165, 194  
   activity, 194  
 Reactive oxygen species (ROS), 32, 99, 148  
 Reforestation, 112  
 Regional  
   research laboratory, 5, 315  
   therapy, 306  
 Rejuvenators, 329  
 Reproductive  
   biology, 112, 113  
   systems, 104, 305  
 Resin, 76, 170, 227, 302, 316  
 Retention index (RI), 23  
 Reverse peristalsis, 77  
 Rhamnose, 246, 324  
*Rheum*, 257  
   *moorcroftianum*, 242–244, 247, 248  
   species, 241–244, 246–249, 252–257  
 Rheumatism, 243, 306  
*Rhizoctonia*  
   *bataticolala*, 17  
   *solani*, 15, 33, 96, 117, 189  
 Rhizome, 17, 244, 250, 252, 257  
 Riboflavin, 357  
 Ridge, 83, 311  
   furrow, 83  
 Rind, 224, 226  
 Root  
   knot nematode, 19  
   lesion nematode, 20



Rootstock, 230, 247, 276, 277

*Rosa*

*canina*, 274, 276, 287, 289, 290, 292

*damascene*, 289, 292

Rose, 229, 252, 263–292

absolute, 264, 283, 288

concrete, 263, 283, 287, 288, 291

cryptic virus-1 (RCV-1), 281

essential oil, 263, 264, 267, 269, 279,  
282–286, 288, 290–292

export, 266

import, 266

oil

production, 285

vapor thermal therapy, 271

production, 265, 268

products, 283, 292

water, 264, 265, 270, 283, 285, 286, 291

Rosehips, 285, 287, 291

Rosmarinic acid, 29, 30, 36, 37

Royal forest department, 114

## S

Safed musli, 299–302, 305–309, 311–316,

318, 326, 329, 332, 344

tuberous root, 306

Saponin, 23, 29, 94, 96, 300–302, 315–318,

323, 324, 326, 331, 333, 355, 357, 404,  
407, 408, 411–416

Sclereids, 383

Sclerenchymatous layer, 395

Scrotal sacs, 327

Seasonal weeds, 13

Secondary metabolites, 29, 30, 59, 132, 137,

170, 255, 285, 316, 318, 381, 382, 386,  
387, 395, 412

Secretion, 78, 103, 105, 107, 359–364, 366

Sedative, 360

Seed

germination, 87, 250, 311

harvesting, 85

kernels, 67, 69, 85, 95, 96

physiology, 111, 113

sowing, 231

storage, 86, 113

Seizure model, 362

Senegal neem foundation [SNF], 61

Serological parameters, 329

Serotonin, 36, 362

level, 36

Serum glutamic oxaloacetic transaminase  
(SGOT), 360, 364

Sessile, 135, 302, 307, 308

Sexual propagation, 85

Sharp apex, 308

Sheep red blood cell (SRBC), 329

Silver needle, 410, 411

Single layered palisade cells, 81

Sitopaladichurna (STPLC), 206

Skeletal muscles, 33, 39

Skin diseases, 149, 256

Socio-economic, 220

Soil

acidity neutralization, 83

conditioner, 74, 75

pathogen, 20

quality, 311, 404, 412, 413

requirements, 275

supplement, 64

Solvent

dehydration, 286

extraction, 74, 264, 284, 285, 287

Sowing, 231, 250

Spasmolytic, 39, 68, 107

Spathulenol, 23, 29

Spectrum bacterial toxicity, 360

Sperm, 79, 327, 328

Spermatogenesis, 324

Spices industry, 208, 210

Spirostane, 316, 318, 324, 325

Sprouts, 311

Stabilization, 360, 364

Stainless-steel knife, 312

Stamens, 9, 136, 168, 248, 272, 308

*Staphylococcus*

*albus*, 190

*aureus*, 31, 32, 59, 70, 96, 149, 333, 361,  
362, 368

Starch grains, 383, 384

*Stegomyia aegypti*, 187

Stem

bark, 81, 225

rot, 15, 17, 92

Sterilization, 79

Steroidal, 108, 187, 299, 311, 318, 323, 324,  
328, 360

analysis, 359

furostane, 318  
 hormones, 311  
 saponins, 299, 323, 324, 328  
 spirostanol saponins, 324  
 Steroids, 23, 30, 31, 34, 55, 96, 170, 300,  
 302, 382, 386, 395  
 Stigma, 308  
 Stilbenes, 243, 254, 255  
 Stilbenoids, 241, 245, 257  
 Stimulant, 39, 43, 68, 107, 241  
 Stolon, 12, 16  
   rot, 17  
 Stomach ache, 1  
 Stomatal index, 81  
 Strawberry latent ring spot (SLRS), 281  
 Streptozotocin, 316, 328, 333  
 Strychnine, 362  
 Stump plantings, 83  
 Stylopodium, 357  
 Substituents, 389  
 Subtropical, 5, 82, 241, 242, 300, 301, 308,  
 310  
   agro-climate region, 5, 10  
 Sucking insects, 91  
 Sucrose, 302, 316  
 Sugar moieties, 324  
 Sulforhodamine blue (SRB), 34, 331  
 Supercritical fluid (SCF), 95  
 Superoxide dismutase (SOD), 99, 149, 331,  
 332, 360, 364, 368  
 Susceptible, 3, 13, 14, 44, 147, 190  
 Swiss  
   albino mice model, 100, 103  
   mice model, 98  
 Symptoms, 15–20, 37, 91, 93, 104, 228,  
 279–281, 306, 358  
 Synergistic effect, 58, 70  
 Synonyms, 4  
 Syrup, 224, 225, 237, 271, 291, 369

## T

Tannins, 23, 29, 30, 34, 36, 44, 68, 76, 95,  
 106, 107, 237, 254, 270, 285, 316, 355,  
 412, 414, 416  
 Taxonomical characterization, 404  
 Taxonomy, 80, 221, 247  
 Tebuconazole, 15

Technology, 56, 63, 111, 113, 149, 238, 239,  
 292, 315  
   transfer, 238, 257, 291, 292, 344  
 Tepals, 312  
 Terpene biosynthesis pathway, 358  
 Terpenoid, 23, 29, 30, 55, 59, 67, 94, 170,  
 270, 358, 359, 395  
 Testisidal cells, 79  
 Testosterone, 311, 318, 327  
 Tetra sulfide, 68  
*Theilavia basicola*, 17  
 Therapeutic, 2, 45, 55–58, 70, 96, 102, 104,  
 116, 117, 132, 133, 155, 164, 224, 241,  
 246, 254, 264, 271, 288, 291, 299–302,  
 305, 368, 370, 381, 382, 395, 412–414,  
 416  
   applications, 133, 164, 254, 291, 382  
   behavioral on-site (TBOS), 56  
   oil, 56  
   potential, 45, 155, 368  
   properties, 57, 224, 241, 246, 264  
   uses, 70, 288  
   value, 57, 58, 254  
 Thin layer chromatography (TLC), 94, 138,  
 254, 316, 318  
 Throat diseases, 1  
 Thymol, 355, 357–363, 365, 364, 368–370  
 Tignic acid, 67  
 Timberlands, 300, 301, 307  
 Time-consuming, 311, 405  
*Tinospora cordifolia*, 381, 382, 384–386,  
 389, 394, 395  
 Tissue culture, 87, 88, 277, 404, 413  
 Tobacco  
   ring spot virus (TRSV), 281  
   streak virus (TSM), 281  
 Tolerant application, 12  
 Tomato ring spot virus (TomRSV), 281  
 Topical application, 59, 78  
 Toxicological risk factors, 104  
 Tracheal chains, 264, 288  
 Tracheids, 383  
*Trachyspermum ammi*, 355, 356, 363–365,  
 367, 369, 372  
 Traditional  
   chinese medicine (TCM), 271  
   evidence, 210  
 Trauma, 33, 39, 146

Triatomine vectors, 79  
*Trichophyton mentagrophytes*, 32, 107  
 Tridemorph, 313  
 Triggering factors, 413  
 Triglyceride, 332, 333  
 Trilobed capsule, 308  
 Triterpenoids, 34, 95, 106, 109, 316  
 Tropical
 

- annual herb, 135
- forest, 113, 117
- weathers, 301, 308

 Tuber developments, 310  
 Tuberculosis, 59, 165  
 Tuberos roots, 300, 302, 305, 311, 314  
 Tubular, 9, 308  
 Tumor
 

- cell growth, 100, 103
- necrosis factor (TNF), 100, 146, 364
  - alpha (TNF- $\alpha$ ), 100, 368

 Turmeric powder, 385

## U

Ulcer index, 332, 359  
 Ulcerogens, 360  
 Ultrasound-assisted extraction (UAE), 29  
 Ultraviolet (UV), 94, 148, 149  
 Unani
 

- medicines, 356
- texts, 58

 Unique products, 291  
 Universal distribution, 222  
 Urea coating agent, 75  
 Urinary disorder, 68, 109  
 Urticaria, 105  
 Usance, 324  
 Utilization, 44, 132, 191, 300, 357, 360, 366, 369, 370, 381

## V

Vaginal, 59, 109  
 Vascular, 81, 383, 395
 

- bundles, 383

 Vector-borne pathogens, 79  
 Vegetative
 

- growth, 11
- propagation, 87, 169, 230

 Ventral, 81  
 Vermicompost, 314

Vernacular names, 4, 60, 134, 166, 382  
 Versatility, 57, 67  
 Verticillasters, 9  
*Verticillium*

- albo-otrum*, 16
- dahlia*, 20

 Vesicular stomatitis (VSV), 33  
 Vessels, 35, 383  
 Veterinary medicine, 58  
 Viral disease, 18, 96, 281  
 Viruses, 18  
 Visceral pain, 147  
 Visual observation, 327  
 Vitamin supplement, 287  
 Vitiligo, 104  
 Volatile
 

- chemical constituents, 137
- constituents, 23, 140
- oil, 20, 23, 31, 44, 133, 137, 138, 149, 170, 285, 407, 412, 416

## W

Wavy margins, 308  
 Weed, 13, 20, 74, 83, 312, 356
 

- infestation, 13

 White
 

- pH (WPH), 231
- tea, 399–412

 Whiter pedicel, 308  
 Whitish, 307–309, 405  
 Widespread, 16, 210, 221, 270, 272  
 Wide-spreading stolons, 9  
 Width, 80, 277, 308, 309  
 Wild-craft neem oil, 65  
 Wilt disease, 16, 17, 357  
 World Health Organization (WHO), 2, 55, 115, 244, 300  
 Worldwide, 3, 18, 60, 74, 132, 133, 150, 155, 164, 230, 238, 268, 269, 271, 274, 290–292, 301, 356  
 Wrapped, 235, 283, 312, 315

## X

*Xanthomonas azadirachtii*, 92  
 Xenobiotic metabolizing, 98  
 Xylem, 383, 395  
 Xylose, 246, 302, 316, 324

**Y**

Yield, 11–13, 18–20, 25, 40, 62–65, 67, 69,  
70, 81, 88, 89, 102, 103, 115, 224, 232,  
252, 270, 276–279, 282, 283, 285, 312,  
314, 318, 358, 404, 407, 412  
Young teal leaf buds, 413

**Z**

Zenith nutrition curcumin, 207  
*Zika virus*, 69  
Zinc (Zn), 65, 356, 412  
Zone, 31, 32, 95–97, 149, 383, 404, 412, 414  
Zoonotic food, 69  
Zygomorphic bilaterally symmetrical, 9  
Zygomorphical, 308  
*C. borivilianum* flowers, 309