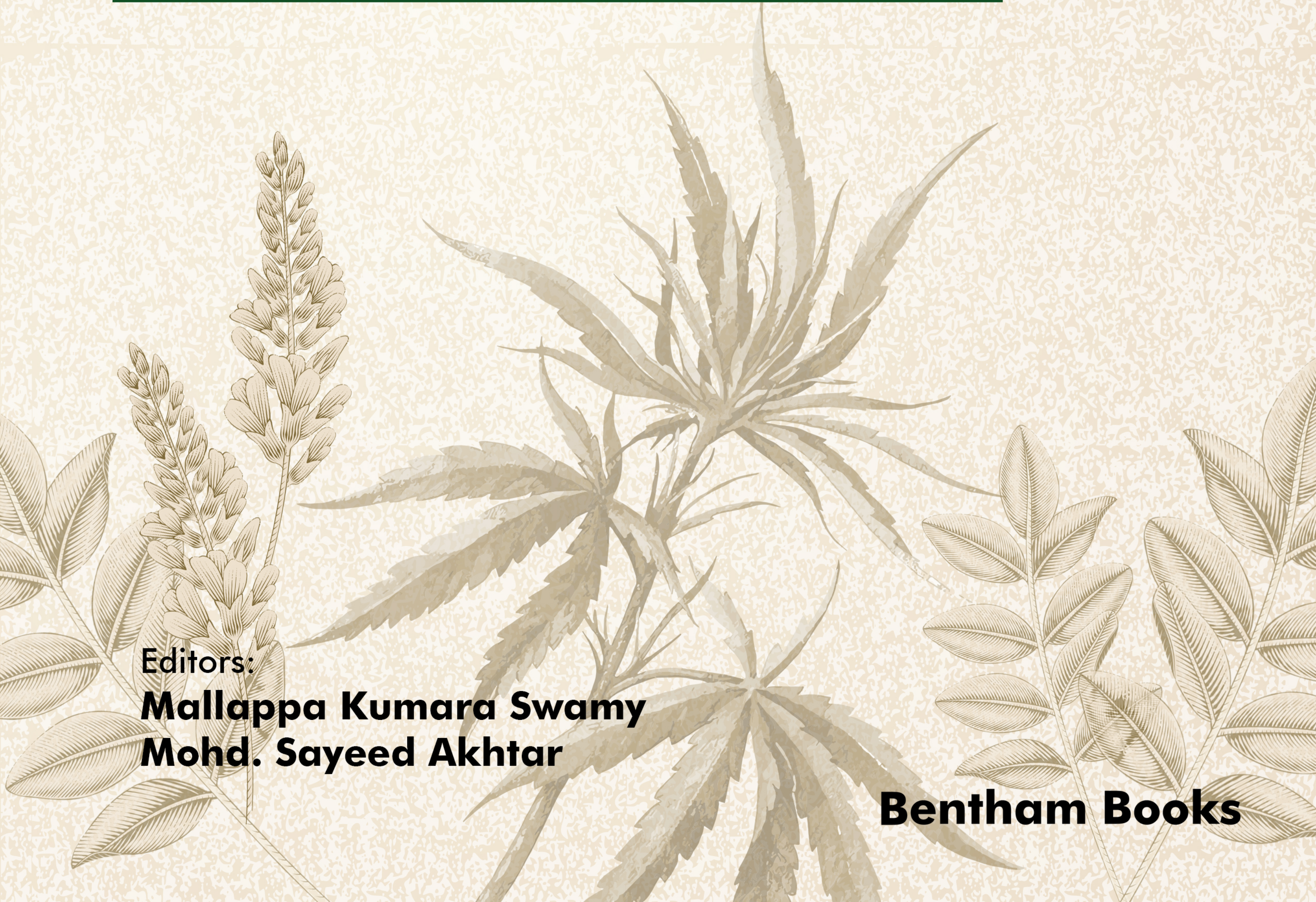
METABOLITES OF MEDICINAL PLANTS: INSIGHTFUL APPROACHES



Editors:
Mallappa Kumara Swamy
Mohd. Sayeed Akhtar

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Edited by

Mallappa Kumara Swamy
Department of Biotechnology
East West First Grade College of Science
Bengaluru-560091, Karnataka, India

&

Mohd. Sayeed Akhtar
Department of Botany
Gandhi Faiz-E-Aam College
Shahjahanpur-242001, Uttar Pradesh, India

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Editors: Mallappa Kumara Swamy and Mohd. Sayeed Akhtar

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FOREWORD

Plants have been used as the prime source of medicines by humans ever since from the ancient times. Even today, plant products are widely used worldwide to address several health problems. In recent times, human population is seen increasingly affected by several life threatening diseases. Although synthetic medicines are utilized to treat these diseases, they are often inefficient, unsafe, and costly to produce. In contrast, plant-based products and medicines are cost-effective, proven to be highly effective in treating diseases, and safe as alternative medicines. Isolated plant bioactive compounds, including alkaloids, glycosides, tannins, terpenoids, polyphenols, saponins, and resins, are known to promote patient health. Consequently, they are extensively used in managing various human ailments such as cardiovascular diseases, diabetes mellitus, cancer, neurological disorders, and infectious diseases.

Based on their traditional uses and experimental evidences, plant products or compounds are isolated or extracted from the medicinal and aromatic plants. Recent surveys indicate a surge in research on the use of plant metabolites as potential leads for drug discovery. Plant compounds exhibit supreme chemodiversity. The initial steps in discovering plant-derived drugs involve identifying novel chemical entities from specific medicinal plants. Selecting the right candidate medicinal plants is imperative, primarily based on tribal non-documented uses, traditionally documented practices, and a comprehensive literature survey. Biological activity-guided fractionation of acknowledged plants aids in standardizing bioactive metabolites as novel drugs. Therefore, bioprospecting of plants and using innovative analytical methods and instruments for extracting, isolating, and characterizing bioactive metabolites from plants are crucial to expedite the drug discovery process. Proper knowledge and a better understanding of plant biology, agronomy, and chemistry allow the restoration of biodiversity and conservation of endangered species. Understanding sustainable cultivation under different climatic conditions, phytochemical variations, and effective isolation and purification methods for phytocompounds can lead to better utilization of these valuable crops. The chemical profiles of bioactive compounds and their levels in plant extracts could be enhanced through breeding. The use of omics approaches, CRISPR/Cas9, gene editing, etc., has the potential to boost the production of phytochemicals. Furthermore, understanding the chemical nature of phytocompounds and their therapeutic actions at the molecular level simplifies the discovery of new drug leads against various health issues.

The present book entitled “Metabolites of Medicinal Plants: Insightful Approaches”, includes 15 chapters contributed by the renowned academicians and researchers from different parts of the world. The first chapter, authored by Indian and Pakistani authors, discusses the economic burden of cancer, the demand and supply of medicinal and anticancer plants, herbal medicines as complementary cancer therapy, and recent progress in anticancer plant research. Chapters 2, 3, and 4, contributed by Indian researchers, delve into the phytochemistry and pharmacological properties of different parts of *Withania coagulans, Tinospora cordifolia,* and *Butea monosperma*, respectively. The fifth chapter, contributed by Indian authors, summarizes recent advancements in the phytochemical screening, therapeutic significance, and nutritional values of *Ocimum sanctum*. Chapters 6 and 7, written by Indian authors, provide a thorough literature review on the morphology, distribution, traditional usage, biotechnology, phytochemistry, pharmacological effects, and safety evaluations of *Psoralea corylifolia* and *Swertia chirayita*, respectively. Chapter 8, written collaboratively by research fellows from India and Saudi Arabia, discusses the beneficial role of *Emblica officinalis* plant fruits and their phytoconstituents in combating metabolic syndrome, along with detailed risk factor analysis. Notably, mechanistic approaches are well explained. Chapter 9, contributed by Indian authors, offers in-depth information on the chemical compositions and preclinical assessments of *Trigonella, Syzium, Punica, Momordica,* and *Gymnema species*, mainly in combating diabetes. Chapters 10 and 11, cooperatively contributed by authors from Oman and India, focus on the chemistry and pharmacological activities of lesser-known fruiting plants in India and the role of certain dietary agents in preventing pathogenesis by *Helicobacter pylori*, respectively. Chapter 12, contributed by Indian authors, discusses nanotechnology-based drug delivery systems for herbal medicines and their prospects. Chapters 13 and 14, written by Indian authors, comprehensively explain the mechanistic role of CRISPR/Cas9, its application in base editing, and its ability to enhance the production of phytochemicals (Chapter 13), and explore mQTL mapping in medicinal and crop plants, emphasizing its significance in unraveling the intricate interplay between genetics and metabolic pathways (Chapter 14). The last chapter, by Indian researchers, elucidates the biosynthetic pathways of major plant metabolites, with special attention to the key enzymes involved.

Understanding and exploring various medicinally valued plants and their bioactive principles is essential to encourage drug discovery studies and support the modern medical field by innovating novel drugs with superior pharmacological activities. This edited book volume covers a wide range of medicinal plant topics, including ethnobotany, phytopharmacology, and modern biotechnological applications. It presents numerous research topics and encourages further exploration of medicinal plants and their products for future medicine preparation. This book will provide valuable information for students, teachers, and professionals involved in research related to medicinal plant phytochemistry, pharmacology, drug discovery, and healthcare practices. I applaud the diligent efforts of the dedicated editors who have played an instrumental role in bringing this remarkable book volume to completion.

Uma Rani Sinniah
Department of Crop Science, Faculty of Agriculture
Universiti Putra Malaysia, 43400 Serdang
Selangor, Malaysia

PREFACE

Human population is seen increasingly affected by several life threatening diseases. Though, several synthetic medicines are useful in treating these diseases, but still they are inefficient and unsafe. Plants based medicine and their products have proven very effecting in treating diseases, and safe to be used as an alternative medicine. Plants are considered as biochemical factories of numerous specialized metabolites that are known to promote patient's health, and thus widely used in the management of several human ailments, including cardiovascular diseases, diabetes mellitus, cancer, neurological disorders, and various other infectious diseases due to their therapeutically valued compounds. Some of these well-known phytocompounds, such as withanolides, rosmarinic acid, podophyllotoxins, caffeic acid, taxol, etc., are used effectively in the modern medicines to combat many diseases. Based on their traditional uses and experimental evidences, plant products or compounds are isolated or extracted from the medicinal and aromatic plants. The chemical profiles of bioactive compounds and their levels in plant extracts or essential oils could be augmented through breeding. Further, chemical nature of phytocompounds and their therapeutic actions at the molecular level will simplify the discovery research to innovate novel drug leads against many diseases. The nanotechnology based drug delivery system of herbal medicines is proven to be feasible alternatives to deliver the plant-derived drugs, effectively. Lately, more number of researches have been focused on identifying bioactive plant metabolites and their underlying genes. The development omics approaches and advancements in the genome sequencing of a large number of medicinally valued plant species have significantly helped in understanding about genes responsible for secreting a particular metabolite. The genes-t--metabolites linking have been elucidated, explicitly *via* using the collective investigations of transcriptomics and metabolomics. The second-generation CRISPR/Cas technology has proven to be a gateway in enhancing the production of phytochemicals due to its simplicity, efficiency, and target specificity.

This book, titled *Metabolites of Medicinal Plants: Insightful Approaches* involves inclusive themes on medicinally important plants and their bioactive compounds. It comprises 15 chapters written by academicians, scholars, and intellectuals. Various topics like economics of medicinal plants, ethnobotany, extraction and analysis, phytochemistry, pharmacological aspects, bioavailability and nanotechnology and omics approaches are systematically reviewed in this book. This compiled concepts of book will benefit academic scholars, academicians, researchers, and scientists, medical practitioners of herbal research and biomedicine. We sincerely thank all authors of this book volume and the team of Bentham Science Publisher for their support at each and every stage of book publication.

Mallappa Kumara Swamy
Department of Biotechnology
East West First Grade College of Science
Bengaluru-560091, Karnataka, India

&

Mohd. Sayeed Akhtar
Department of Botany
Gandhi Faiz-E-Aam College
Shahjahanpur-242001, Uttar Pradesh, India

DEDICATION

DEDICATED TO OUR
PARENTS, FAMILY MEMBERS
AND TEACHERS
WHO TAUGHT LIFE LESSONS

List of Contributors

Azhar Kamal	Department of Bioengineering, Integral University, Lucknow-226026, Uttar Pradesh, India
Asiya Nisa	DBT-BIF Facility, Department of Biotechnology, Maharani Lakshmi Ammanni College for Women, 560012-Bangalore, Karnataka, India
Arvind Kumar Goyal	Department of Biotechnology, Bodoland University, Kokrajhar, 783370-Assam, India
Akhilesh Kumar	Department of Botany, Centre of Advanced Study in Botany, Institute of Science, Banaras Hindu University, Varanasi, U.P, India
Akanksha Sharma	Department of Botany, Central University of Jammu, Rahya-Suchani (Bagla), Samba-181143, J&K, India
Basavaraju Kavyashree	DBT-BIF Facility, Department of Biotechnology, Maharani Lakshmi Ammanni College for Women, 560012-Bangalore, Karnataka, India
Dhanya Sacheendran	Department of Pharmacology, Amrita Institute of Medical Sciences, Vishwa Vidyapeetham, Kerala-682041, India
Damini Supolia	Department of Botany, Central University of Jammu, Rahya-Suchani (Bagla), Samba-181143, J&K, India
Deepak Kumar	Centre for Advanced Study in Botany, Institute of Science, Banaras Hindu University, Varanasi-221005, Uttar Pradesh, India
Fahmina Rizvi	Department of Biotechnology, Era's Lucknow Medical College and Hospital, Era University, Sarfarazganj, Lucknow-226003, Uttar Pradesh, India
Ghulam Mustafa	Department of Economics, Division of Management and Administrative Science, University of Education, Lahore-54770, Pakistan
Giriyapura S. Pavankumar	Sri Lakshmi Group of Institution, Sunkadakatte, Bengaluru, Karnataka-560091, India
Harish Kumar Bastimal	Department of Pharmacology, Manipal College of Pharmaceutical Sciences, Manipal Academy of Higher Education, Manipal-576104, India
Harshita Sahoo	Department of Botany, Centre of Advanced Study in Botany, Institute of Science, Banaras Hindu University, Varanasi, U.P, India
Irfan Ahmad Ansari	Department of Biosciences, Integral University, Lucknow-226026, Uttar Pradesh, India
Irshad Mahmood	Section of Plant Pathology, Department of Botany, Faculty of Life Sciences, Aligarh Muslim University, Aligarh-202002, Uttar Pradesh, India
Jahanvi Ganotra	Department of Botany, Central University of Jammu, Rahya-Suchani (Bagla), Samba-181143, J&K, India
Kajim Ali	Department of Biotechnology, Era's Lucknow Medical College and Hospital, Era University, Sarfarazganj, Lucknow-226003, Uttar Pradesh, India

Kadabagere Narayanaswamy Hemavathi	DBT-BIF Facility, Department of Biotechnology, Maharani Lakshmi Ammanni College for Women, 560012-Bangalore, Karnataka, India
Karkala Maya Sreedhara Pai	Department of Pharmacology, Manipal College of Pharmaceutical Sciences, Manipal Academy of Higher Education, Manipal-576104, India
Karkala Sreedhara Ranganath Pai	Department of Pharmacology, Manipal College of Pharmaceutical Sciences, Manipal Academy of Higher Education, Manipal-576104, India
Mohd. Sayeed Akhtar	Department of Botany, Gandhi Faiz-e-Aam College, Shahjahanpur-242001, Uttar Pradesh, India
Mohd. Kamil Hussain	Department of Chemistry, Govt. Raza P.G. College, Rampur-244901, Uttar Pradesh, India
Mujahid Ali	Department of Physical Education, Government Degree College, Pachperwa, Balrampur-271206, Uttar Pradesh, India
Mohammad Faheem Khan	Department of Chemistry, Era University, Sarfarazganj, Lucknow-226003, Uttar Pradesh, India Department of Biotechnology, Era's Lucknow Medical College and Hospital, Era University, Sarfarazganj, Lucknow-226003, Uttar Pradesh, India
Mohsin Ali Khan	Department of Biotechnology, Era's Lucknow Medical College and Hospital, Era University, Sarfarazganj, Lucknow-226003, Uttar Pradesh, India
Mohammad Saquib	Department of Chemistry, University of Allahabad, Prayagraj-211002, Uttar Pradesh, India
Mohd. Aamish Khan	Department of Biotechnology, , , , Era's Lucknow Medical College and Hospital, Era University, Sarfarazganj, Lucknow-226003, Uttar Pradesh, India
Mohd. Baqar Ali	Department of Biotechnology, , , , Era's Lucknow Medical College and Hospital, Era University, Sarfarazganj, Lucknow-226003, Uttar Pradesh, India
Mahima Verma	Department of Biosciences, Integral University, Lucknow-226026, Uttar Pradesh, India
Mamatha Jayandran	Department of Pharmacology, Amrita Institute of Medical Sciences, Vishwa Vidyapeetham, Kerala-682041, India
Manjeshwar Shrinath Baliga	Sri Lakshmi Group of Institution, Sunkadakatte, Bengaluru, Karnataka-560091, India
Muskan Parveen	Section of Plant Pathology, Department of Botany, Faculty of Life Sciences, Aligarh Muslim University, Aligarh-202002, Uttar Pradesh, India
Manisha Malhotra	Department of Botany, Centre of Advanced Study in Botany, Institute of Science, Banaras Hindu University, Varanasi, U.P, India
Meenakshi Raina	Department of Biosciences, IMS Ghaziabad (University Courses Campus), Adhyatmik Nagar, Ghaziabad, Uttar Pradesh, India

Nadia Hanif	UE Business School, Division of Management and Administrative Science, University of Education, Lahore-54770, Pakistan
Naveed Hayat	Department of Economics, Division of Management and Administrative Science, University of Education, Lahore-54770, Pakistan
Nidhi Dwivedi	DBT-BIF Facility, Department of Biotechnology, Maharani Lakshmi Ammanni College for Women, 560012-Bangalore, Karnataka, India
Noor Fatima	Section of Plant Pathology, Department of Botany, Faculty of Life Sciences, Aligarh Muslim University, Aligarh-202002, Uttar Pradesh, India
Neelam Prabha Negi	Plant Biotechnology division: CSIR-Central Institute of Medicinal and Aromatic Plants, Lucknow, Uttar Pradesh, India
Prakriti Mishra	Department of Biosciences, Integral University, Lucknow-226026, Uttar Pradesh, India
Pankaj Prabhakar	Department of Pharmacology, Indira Gandhi Institute of Medical Sciences (IGIMS), Sheikhpura, Patna, Bihar, 800014, India
Princy L. Palatty	Department of Pharmacology, Amrita Institute of Medical Sciences, Vishwa Vidyapeetham, Kerala-682041, India
Prakash Hemalatha	DBT-BIF Facility, Department of Biotechnology, Maharani Lakshmi Ammanni College for Women, 560012-Bangalore, Karnataka, India
Pratiksha Verma	Department of Botany, Centre of Advanced Study in Botany, Institute of Science, Banaras Hindu University, Varanasi, U.P., India
Rhea Katherine D'souza	Research Unit, Mangalore Institute of Oncology, Mangalore, Karnataka-575002, India
Rashmi Theresa D'souza	Nitte University, Centre for Science Education and Research (NUCSER), Paneer Campus, Deralakatte, Mangaluru, Karnataka-575018, India
Raksha Nayak	Department of Pharmacology, Manipal College of Pharmaceutical Sciences, Manipal Academy of Higher Education, Manipal-576104, India
Rhea Katherine D'souza	Research Unit, Mangalore Institute of Oncology, Mangalore, Karnataka-575002, India
Rose Rizvi	Section of Plant Pathology, Department of Botany, Faculty of Life Sciences, Aligarh Muslim University, Aligarh-202002, Uttar Pradesh, India
Shireen Fatima	Department of Biosciences, Integral University, Lucknow-226026, Uttar Pradesh, India
Sushil Kumar Middha	DBT-BIF Facility, Department of Biotechnology, Maharani Lakshmi Ammanni College for Women, 560012-Bangalore, Karnataka, India
Sham Prasad Sajankila	Department of Biotechnology Engineering, NMAM Institute of Technology-Affiliated to NITTE, Nitte, Karnataka-574110, India
Shweta	Department of Botany, Centre of Advanced Study in Botany, Institute of Science, Banaras Hindu University, Varanasi, U.P, India

Talambedu Usha	Department of Biochemistry, Maharani Lakshmi Ammanni College for Women, 560012-Bangalore, Karnataka, India
Vijaya Marakala	Department of Biochemistry, College of Medicine and Health Sciences, National University of Science and Technology, Sahar, Oman
Vikash Maurya	Department of Botany, Centre of Advanced Study in Botany, Institute of Science, Banaras Hindu University, Varanasi, U.P, India
Vibhav Gautam	Centre of Experimental Medicine & Surgery, Institute of Medical Sciences, Banaras Hindu University, Varanasi-221005, Uttar Pradesh, India
Waseem Ahmad Ansari	Department of Biotechnology, Era's Lucknow Medical College and Hospital, Era University, Sarfarazganj, Lucknow-226003, Uttar Pradesh, India
Zeba Siddiqui	Department of Biosciences, Integral University, Lucknow-226026, Uttar Pradesh, India

CHAPTER 1

Economics of Medicinal and Anticancer Plants

Ghulam Mustafa[1,*], **Nadia Hanif**[2], **Naveed Hayat**[1] and **Mohd. Sayeed Akhtar**[3]

[1] *Department of Economics, Division of Management and Administrative Science, University of Education, Lahore-54770, Pakistan*

[2] *UE Business School, Division of Management and Administrative Science, University of Education, Lahore-54770, Pakistan*

[3] *Department of Botany, Gandhi Faiz-e-Aam College, Shahjahanpur-242001, Uttar Pradesh, India*

Abstract: Despite millions of deaths every year, cancer has caused huge economic and non-economic costs for every nation in the world. Economic costs are higher in developed countries, while non-economic costs such as loss of jobs, family care time, and out-of-pocket expenses are higher in developing countries. These huge economic burdens on cancer patients and the increasing cost of chemotherapy led to the usage of plant-based medicines. Such medicines are more cost-effective because of their medicinal and treatment effectiveness. Most medicinal plants have anticancer ingredients that make them more sought-after. The demand for anticancer plants is increasing day by day. The main factors that shape the demand for anticancer plants are lower-priced plant-based anticancer plants, higher prices of chemotherapy, an increasing world population, particularly the ageing population, and increasing per capita GDP (income) of nations. The present chapter provides an overview of the economic burden of cancer, the demand and supply of medicinal and anticancer plants, herbal medicines as complementary medicine for cancer therapy, and the recent progress of anticancer plants.

Keywords: Cancer, Chemotherapy, Complementary medicine, Economic cost, Medicinal plants.

INTRODUCTION

Humans have relied on nature for their basic needs, such as the production of food, clothing, shelter, flavours and fragrances, fertilizers, means of transportation, and, medicines. Plants have formed the basis of sophisticated traditional medicine systems that have been in existence for thousands of years and continue to provide mankind with new remedies. Healing with medicinal plants is an old treatment method as old as mankind itself. Medicinal plants have

* **Corresponding author Ghulam Mustafa:** Department of Economics, Division of Management and Administrative Science, University of Education, Lahore-54770, Pakistan; E-mail: mustafamalik2087@gmail.com

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played an essential role in the development of human culture, and their history can be traced back to 4000-5000 BC in Chinese culture, where therapeutics used natural herbal preparations as medicines. The Chinese scripture engraved on roots and grasses is considered to be the first written book in the year 2500 BC, which were used to prepare 365 drugs [1]. In India, its history can be traced back to the Rig-Veda Era (1600-3500 BC) and in the Vedas in which numerous ways of the treatment by plants are mentioned [2]. However, the use of medicinal plants has been found across the globe, in history, and even in various religions and cultures. For instance, the Ebers Papyrus represented a collection of 800 proscriptions referring to 700 plant species and drugs used for therapy in Egypt [3]. Moreover, Indigenous cultures (such as African and Native American) used plant-based medicines in their healing rituals [4]. Similarly, according to data from the Bible and the holy Jewish book, the Talmud, during various rituals accompanying a treatment, aromatic plants such as myrtle and incense, were utilized [5]. About two centuries ago, medicinal uses of herbs largely dominated all kinds of treatments. The use of herbal medicines and other botanicals in the West is lower as compared to many developing countries because predictable synthetic drugs are readily available in developed nations. However, the consumption of plant-based medicines has decreased in developed countries in recent years. In contrast, developing countries are still benefiting from the rich knowledge of medical herbalism. For instance, traditional Chinese medicines, Unani medicines in South Asia and the Middle East, Kampo medicine in Japan, and Sidha and Ayurveda medicines in India are still being used on a large scale to date [6].

ECONOMIC BURDEN OF CANCER

Over the past two decades, the economic burden of cancer has rapidly increased despite an overall decline in age-adjusted cancer incidence [7]. Cancer is one such disease in which the financial burden of treatment is a major source of stress for patients and their families. The major reasons for high financial burdens on patients include long-term follow-up patients, readmissions, post-acute care, high cost of drugs, long duration of treatment, sophisticated diagnostic procedures and techniques, chemotherapy and radiotherapy, as well as multimodality treatment protocols incorporating surgery [8, 9]. The cost of cancer estimates depends on the cancer site, study methodology, study period, study population, and types of data. This cost varies from region to region and even within the same region. The cost also depends on gender, age, household size, and family status. For instance, Khushalani *et al.* [10] find that there are relatively higher per-person costs among young adults in the United States and that these burdens are projected to increase. Quantifying the comprehensive economic burden of cancer is crucial to making effective cancer-control policies for both present and future generations [11]. The economic cost is usually a direct cost, such as the cost of chemotherapy and medicinal cost, and an indirect cost, such as out-of-pocket expenses.

Direct Cost of Cancer Treatment

The direct economic burden of cancer is the cost resulting from the use of analgesic medications, physician office visits, emergency department visits, and pain-related hospitalizations. Research conducted by Fortner *et al.* [12] highlighted that the direct expenses associated with cancer treatment were reported to be US $891 monthly per patient, in addition to an extra US $825 monthly per patient specifically attributed to medical costs related to pain. These expenditures encompass the financial outlay for hospitalization and the duration of hospital stays.

The direct costs consist of direct medical and non-medical costs. Medical costs include major medication costs, medical visits and doctors' fees, laboratory test fees, diagnostic services expenditures, and any other costs incurred by health institutions. On the other hand, nonmedical costs include nonmedical personnel, such as patients and their families (*e.g.*, home care costs). In the USA, the direct medical cost associated with lung cancer was US $20.10 billion in 2015 [13]. This cost is substantial and is expected to increase significantly in the future because of improvements in healthcare, trends in treatment patterns, and the expected growth and ageing of the population. The economic burden of cancer has become heavier than that of other health sectors due to direct and indirect costs that further lead to serious economic problems for families [14]. For instance, about one-quarter of families who suffered the loss of someone in their family due to cancer within the last year reported that the cost of care was a major financial burden; a third quarter used all or most of their savings [15].

Direct costs vary from country to country. For instance, in European (EU) countries, it was estimated that about 44% (approximately €553 billion) of the total costs for the economic burden were due to prostate, colorectal, breast, and lung cancer [16]. Similarly, Leal *et al.* [17] estimated that bladder cancer accounted for approximately €143 billion (3% of total cancer costs) in the EU and represented an annual healthcare cost of €57 per 10 EU citizens, with costs varying >10 times between the countries with the highest cost, Luxembourg (€93 for every 10 citizens), and the lowest cost, Bulgaria (€8). In Spain, the economic burden of cancer was estimated at approximately €9,016 million [18]. In China, it was estimated that the total economic burden of lung cancer was US $25,069 million (about 0.121% of GDP). The estimated direct expenditure was approximately US $11,098 million, including US $10,303 million and US $795 million for medical and non-medical expenditures, respectively. Moreover, it was

CHAPTER 2

Withania coagulans: Bioactive Compounds and Pharmacological Significance

Kajim Ali[1], **Mohd. Kamil Hussain**[2], **Mujahid Ali**[3], **Mohammad Faheem Khan**[1,4,*] and **Mohd. Sayeed Akhtar**[5]

[1] *Department of Biotechnology, Era's Lucknow Medical College and Hospital, Era University, Sarfarazganj, Lucknow-226003, Uttar Pradesh, India*

[2] *Department of Chemistry, Govt. Raza P.G. College, Rampur-244901, Uttar Pradesh, India*

[3] *Department of Physical Education, Government Degree College, Pachperwa, Balrampur-271206, Uttar Pradesh, India*

[4] *Department of Chemistry, Era University, Sarfarazganj, Lucknow-226003, Uttar Pradesh, India*

[5] *Department of Botany, Gandhi Faiz-e-Aam Collge, Shahjahanpur-242001, Uttar Pradesh, India*

Abstract: *Withania coagulans* has long been used as a health-beneficial medicinal herb in the Ayurveda system of Indian traditional medicine. It is a rich source of steroidal lactone-type compounds known as withanolides. Among the various withanolides, withaferin A, withacoagin, and coagulin A-R are the key compounds that have been isolated from various parts of this medicinal plant for their pharmacological uses. Traditionally, the consumption of whole plants is strongly associated with diabetes. As per the literature survey, the ethanol or aqueous extracts of fruits have been used for their antidiabetic, free radical scavenging, anti-inflammatory, antibacterial, antifungal, cardiovascular protection, immunomodulatory, and hepatoprotective effects as well as anti-Alzheimer activities. Therefore, the aim of this chapter is to highlight the chemical structures of isolated withanolides (1-33) and their diverse pharmacological properties exhibited by different plant parts in the prevention and treatment of human diseases.

Keywords: Diabetes, Steroidal lactone, *Withania coagulans*, Withanolides, Withaferin A.

INTRODUCTION

Withania coagulans Dunal., (Ver. Rishyagandha) is a well-known Indian medicinal herb that belongs to the family Solanaceae. It is native to the Indian subcontinent, including Afghanistan, Pakistan, and Nepal regions [1]. It is generally recognized by different names in India, *i.e.*, Puneer dodi (Hindi), Indian

* **Corresponding author Mohammad Faheem Khan:** Department of Biotechnology, Era's Lucknow Medical College and Hospital, Era University, Sarfarazganj, Lucknow-226003, Uttar Pradesh, India & Department of Chemistry, Era University, Sarfarazganj, Lucknow-226003, Uttar Pradesh, India, India; E-mail: faheemkhan35@gmail.com

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rennet (English), Indian cheese maker, Paneer ke phool (Hindi), and Paneer bandh (Hindi). The leaves are lanceolate, whole, and covered in a grey tomentum on both sides [2]. The flowers are dioecious and clustered in the axilla. A long calyx and grey tomentum cover the long body, and the corolla is about 8 mm long, ovate with oblong and sub-acute lobes. Stamens are roughly filamentous, longitudinal, and glabrous and are found at the top of the corolla. The anthers are 3-4 mm long. Female flowers have smaller and filamentous stamens than the corolla tube. The seeds are ear-shaped, 2.5–3.0 mm in diameter, and glabrous [3]. In India, extensive literature surveys based on traditional studies have revealed the milk coagulation properties of *W. coagulans,* and hence used in making Indian cheese for different ethnomedicinal uses in the traditional Indian system of medicine. This is because *W. coagulans* possesses bioactive compounds that are effective against numerous ailments [4]. Therefore, the aim of this chapter is to highlight the chemical structures of isolated withanolides (1-33) and the diverse pharmacological properties exhibited by different plant parts in the prevention and treatment of human diseases.

Traditional Uses

Numerous traditional uses of various parts of *W. coagulans* have been reported for decades. The fruits have gained popularity for their anti-diabetic action due to the presence of rennet-like protease enzyme, and berries can be used for milk clotting at the time of cheese production. Besides, berries may be used as a blood purifier. Fruits are carminative and depurative in nature. Therefore, these are used in the treatment of asthma, biliousness, dyspepsia, flatulence, colic, and intestinal and liver disorders. Flower buds show anthelmintic activity [5]. Seeds are emetic, diuretic, and emmenagogue, and hence used for reducing inflammation and curing an ophthalmic infection. The twigs are chewable in nature, suggesting beneficial effects for cleaning teeth and relief from toothache. Moreover, the whole plant shows miscellaneous properties, such as removing nervous exhaustion, disability, insomnia, children, impotence, *etc*.

Bioactive Compounds

W. coagulans is a rich source of bioactive steroidal lactones that are referred to as withanolides, a class of secondary metabolites. Withanolides are naturally occurring polyhydroxy C28 steroidal lactones that have a six or five-membered lactone ring attached to an intact or rearranged ergostane skeleton, as shown in Fig. (**1**).

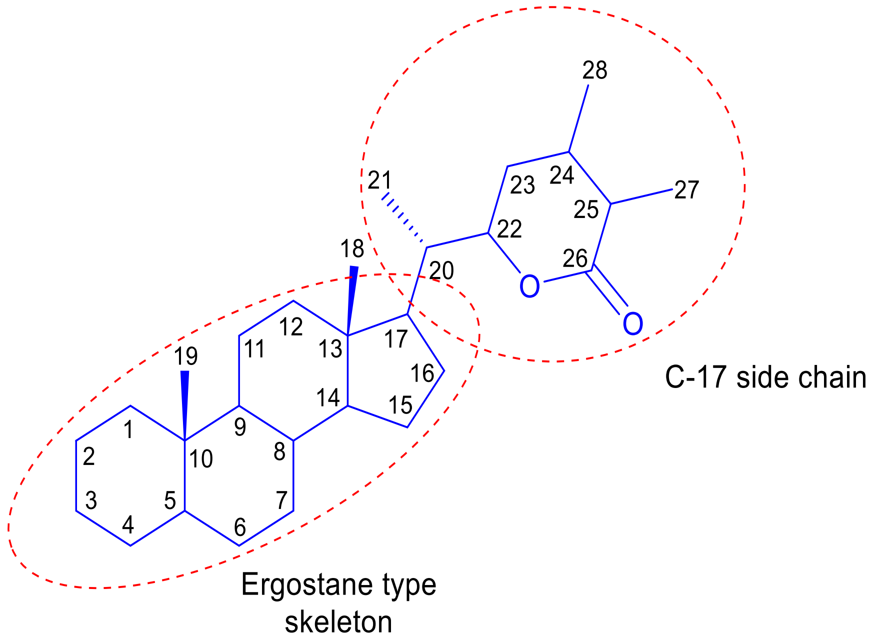

Fig. (1). Basic structure of a withanolide (steroidal lactone), a C28 ergostane skeleton.

Phytochemical investigations revealed that a number of bioactive compounds (withanolides) are found in the whole plant or its parts (fruits, leaves, stems, bark and roots). To date, nearly 33 withanolides have been isolated from *W. coagulans*. The bond line structures of most bioactive compounds are depicted in the figures (Figs. **2** and **3**). Most of the withanolides (1-21) have been purified from the whole plant such as coagulin (1), 14,15b-epoxywithanolide I (2), coagulin B (3), coagulin D (4), coagulin E (5), coagulin F (6), coagulin G (7), coagulin H (8), coagulin I (9), coagulin J (10), coagulin K (11), coagulin M (12), coagulin N (13), coagulin O (14), coagulin P (15), coagulin Q (16), coagulin R (17), 20β-hydrox- -1-oxo-(22R)-witha-2, 5, 24-trienolide (18), withacoagulin (19), 17β-hydrox- -14α,20α-epoxy-1-oxo-(22R)-witha-3,5,24-trienolide (20), coagulin S (21). Most importantly, fruit parts yielded few withanolides (22-29) namely 17β-hydroxywithanolide K (22), coagulin C (23), coagulin L (24), 3β-hydroxy-2-3-dihydrowithanolide F (25), ergosta-5,25-diene-3β,24ζ-diol (26), 3β,14α, 20αf,27-tetrahydroxy-1-oxo-20S,22R-witha-5,24-dienolide (27), sitosterol-β-D-glucoside (28), withanolide F (29). Several withanolides (30-33), such as withaferin A (30), withacoagin (31), (20R, 22R)-6α,7α-epoxy-5α-20-hydoxy-1-oxowitha-2, 24-dienolide (32), and (20S, 22R)-6α, 7α-epoxy-5α-20-dihydroxy-1-oxowitha-2, 24-dienolide (33) have also been isolated and elucidated from its root [3].

CHAPTER 3

Tinospora cordifolia: Medicinal and Therapeutic Potential

Waseem Ahmad Ansari[1], **Mohsin Ali Khan**[1], **Mohd. Kamil Hussain**[2], **Mujahid Ali**[3] and **Mohammad Faheem Khan**[1,4,*]

[1] *Department of Biotechnology, Era's Lucknow Medical College and Hospital, Era University, Sarfarazganj, Lucknow-226003, Uttar Pradesh, India*

[2] *Department of Chemistry, Govt. Raza P.G. College, Rampur-244901, Uttar Pradesh, India*

[3] *Department of Physical Education, Government Degree College, Pachperwa, Balrampur-271206, Uttar Pradesh, India*

[4] *Department of Chemistry, Era University, Sarfarazganj, Lucknow-226003, Uttar Pradesh, India*

Abstract: *Tinospora cordifolia* (TC), a renowned medicinal herb, is widely employed in Ayurveda and other folk medicines under the name "Giloy" in India and neighboring countries for curing diverse human ailments. It encompasses a vast array of bioactive compounds, such as alkaloids, diterpenoids, and steroids. Conventionally, TC is utilized for boosting memory, regulation of the immune system, as well as enhancing mental clarity. The paste of its stem is ingested to treat fever, while the entire plant is utilized for treating jaundice and chronic diarrhea. Furthermore, the extracts of TC have been extensively used in the treatment of various diseases due to their anti-inflammatory, anti-spasmodic, anti-microbial, anti-osteoporotic, anti-asthmatic, anti-allergic, and antidiabetic activities. Therefore, the intention of this chapter is to accentuate the bioactive components of TC and their pharmacological properties of TC.

Keywords: Anti-arthritis, Antidiabetic, Diterpenoids, Giloy, Steroids, *Tinospora cordifolia*.

INTRODUCTION

Tinospora cordifolia (TC) belonging to the Menispermaceae family, is a perennial, glabrous, and its climbing shrub grows on other trees and plants Fig. (1). It is widely distributed throughout the tropical and subtropical regions of India as well as its neighbouring countries like Pakistan, Nepal, Burma, Bangladesh, and Sri Lanka. In India, it is commonly known as Giloya (Hindi),

* **Corresponding author Mohammad Faheem Khan:** Department of Biotechnology, Era's Lucknow Medical College and Hospital, Era University, Sarfarazganj, Lucknow-226003, Uttar Pradesh, India & Department of Chemistry, Era University, Sarfarazganj, Lucknow-226003, Uttar Pradesh, India; E-mail: faheemkhan35@gmail.com

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Amritha (Sanskrit), Guduchi (Marathi), Gulancha (Bengali), Galo (Gujarati), Amrutavalli (Kannada), Amarlata (Assamese). The meaning of 'Amrita' is nectar or pious liquid, which is attributed to the ability to rejuvenate youthfulness and longevity [1]. The leaves are broadly ovate to roundish, simple, pulvinate, and have long (15 cm long) petioles, whereas the flowers are small, leafless, and yellow-greenish in colours [2, 3]; (Fig. **1**). The seeds are curved like half-moon-shaped endospermic and are easily found in Indian forests, particularly on neem and mango trees [4]. TC is generally recognized as a source of isoquinoline alkaloids which are one of the biggest classes of natural compounds with intriguing pharmacological actions [5]. Besides, it contains a variety of bioactive compounds that range from terpenoids, terpenoids, lactone, alkaloids, and steroidal glycosides. Among them, some of the compounds are key components, which are referred to as phenyl propanoid glycosides like cordifoliosides, and have remarkable biological activity [6]. The known pharmacological properties of this plant are antispasmodic, antimalarial, antifilariasis, analgesic, antipyretic, anti-inflammatory, and antioxidant activities. For decades, TC has been widely used as an expectorant, cardiotonic, and aphrodisiac [7]. Therefore, the aim of this chapter is to highlight the bioactive compounds of TC and their pharmacological activities.

A B

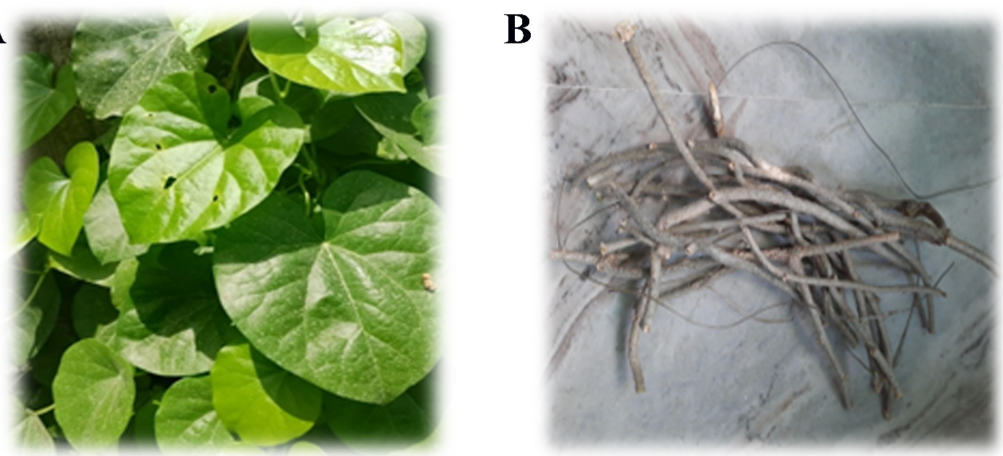

Fig. (1). Overview of *Tinospora cordifolia*; (**A**) leaves and (**B**) stem.

TRADITIONAL USES

Since ancient times, various parts of TC have been used as a home remedy for the management of numerous human ailments. The juice of TC leaves with honey has been taken orally to overcome fever. The aqueous extract of the stem consists of arabinogalactan, which has immunological properties. Alkaloids, sesquiterpenoids, and steroids are abundantly present in the stem of giloy and are used as antipyretic, antiviral, and against urinary disorders. Alkaloids reduce the glucose levels in the blood,control diabetes, and protect from eye infections. The TC stem has been used to prevent respiratory tract infections, skin diseases, poisoning from snakebites, and scorpion stings [8, 9]. The whole plant is a folk remedy in the Ayurvedic and Unani systems of Indian medicine for the treatment of diabetes, malaria, allergic reactions, anxiety, stress, leprosy disease, fever, and jaundice. The prevention of cholesterol increment, stomach disorders, joint pains, peptic ulcers, gonorrhea, and syphilis by the implementing TC has also been reported [10]; (Fig. **2**). The use of TC decoction is highly recommended for rejuvenation or longevity of life [6].

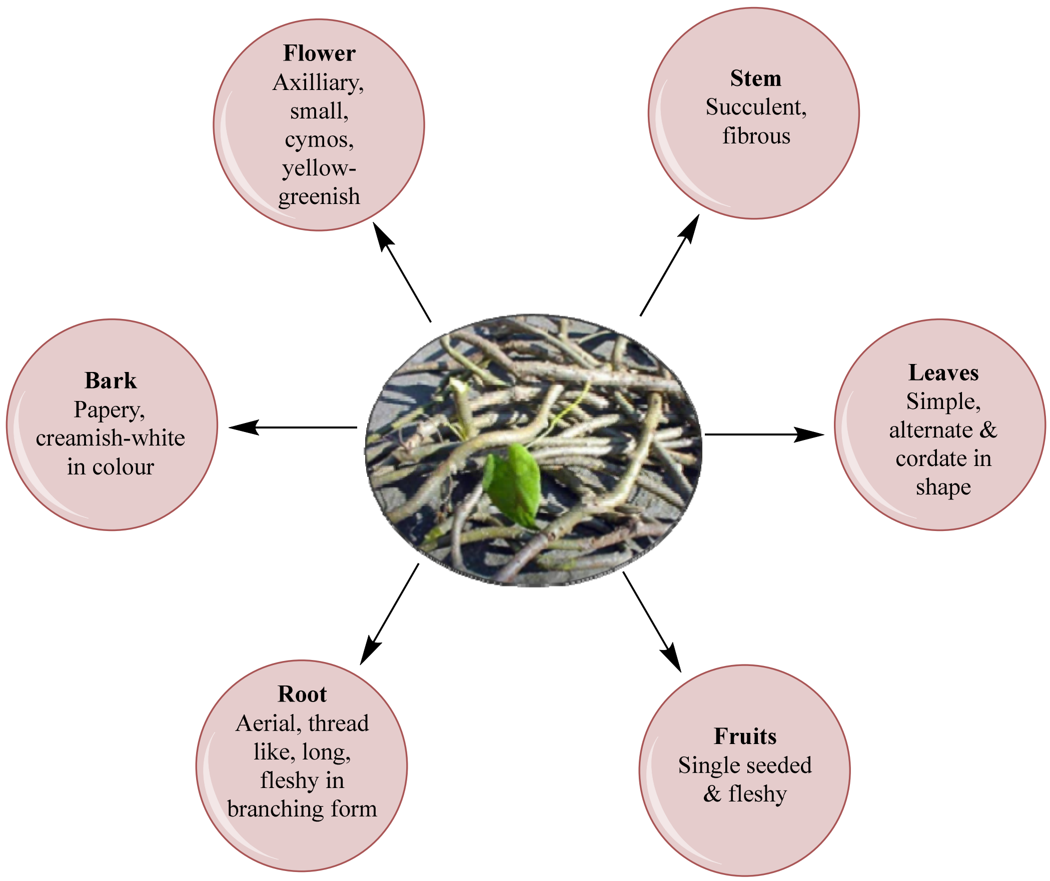

Fig. (2). Schematic representation of different parts of the *Tinospora cordifolia* plant.

BIOACTIVE COMPOUNDS

A versatile medicinal plant, TC is a vast resource of numerous bioactive chemical constituents that are present in various parts, including stems, leaves, or the whole

CHAPTER 4

Butea monosperma: Phytochemistry and Pharmacological Applications

Fahmina Rizvi[1], **Mohsin Ali Khan**[1], **Mohammad Saquib**[2] and **Mohammad Faheem Khan**[1,3,*]

[1] *Department of Biotechnology, Era's Lucknow Medical College and Hospital, Era University, Sarfarazganj, Lucknow-226003, Uttar Pradesh, India*

[2] *Department of Chemistry, University of Allahabad, Prayagraj-211002, Uttar Pradesh, India*

[3] *Department of Chemistry, Era University, Sarfarazganj, Lucknow-226003, Uttar Pradesh, India*

Abstract: *Butea monosperma*, also known as the 'Flame of the forest' or 'Palas' in Hindi, belongs to the important medicinal plant family "Fabaceae." Its endemic presence in Southeast Asia and India has made it a valuable natural resource. This plant has a variety of medicinal applications, such as being an aphrodisiac, anti-inflammatory, anthelmintic, antimicrobial, and many more. The presence of flavonoids, triterpenes, steroids, chalcones, and fatty acids in different parts of *B. monosperma*, including the stem, root, leaves, and flowers, makes it a versatile ingredient in various therapeutic exercises. The stem is the source of (-)-medicarpin, an isoflavone that imparts anti-fungal properties to the plant. Two flavanone compounds, namely butrin and butein (flavanones), have been extracted from *B. monosperma* flowers and are used as contraceptives. Butein, in particular, exhibits anti-tumor activity that opens doors to curing ovarian cancer. Additionally, butein is an excellent free radical scavenger. The seed oil of this plant can also be used for its bactericidal and fungicidal properties.

Keywords: *Butea monosperma*, Butein, Chalcone, Isoflavone, Palas, (-)-medicarpin.

INTRODUCTION

Plants generate various industrial and agricultural basic components like food, medicine, pesticides, perfumes, pigments, and resins, for which different sections of the plant are used to develop these goods. The utilization of a plant or a plant derivative in many sectors depends on the plant's chemical composition. These phytoconstituents can be divided into primary or secondary metabolites, with primary metabolites for growth and development, while secondary compounds are

* **Corresponding author Mohammad Faheem Khan:** Department of Biotechnology, Era's Lucknow Medical College and Hospital, Era University, Sarfarazganj, Lucknow-226003, Uttar Pradesh, India & Department of Chemistry, Era University, Sarfarazganj, Lucknow-226003, Uttar Pradesh, India; E-mail: faheemkhan35@gmail.com

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engaged in defensive mechanisms and in attracting pollinators [1]. *Butea* belongs to the family "Fabaceae," and is a pharmacologically significant plant. The plant is native to India and has various common species, viz., *Butea monosperma*, *B. superba*, *B. parviflora*, and *B. minor* [2]. Among these, *B. monosperma,* commonly known as 'Flame of the Forest', 'Palas', 'Bastard teak' or 'Dhak,' is the most abundant species distributed throughout India [3, 4]. The plant propounds an array of therapeutic and economic benefits [5]. Different plant parts (Fig. **1**) exhibit a wide range of bioactivities, *viz*., the flower's extract possesses an anti-diabetic effect, along with the stem and bark extracts exhibiting anti-diarrhoeal activity [6].

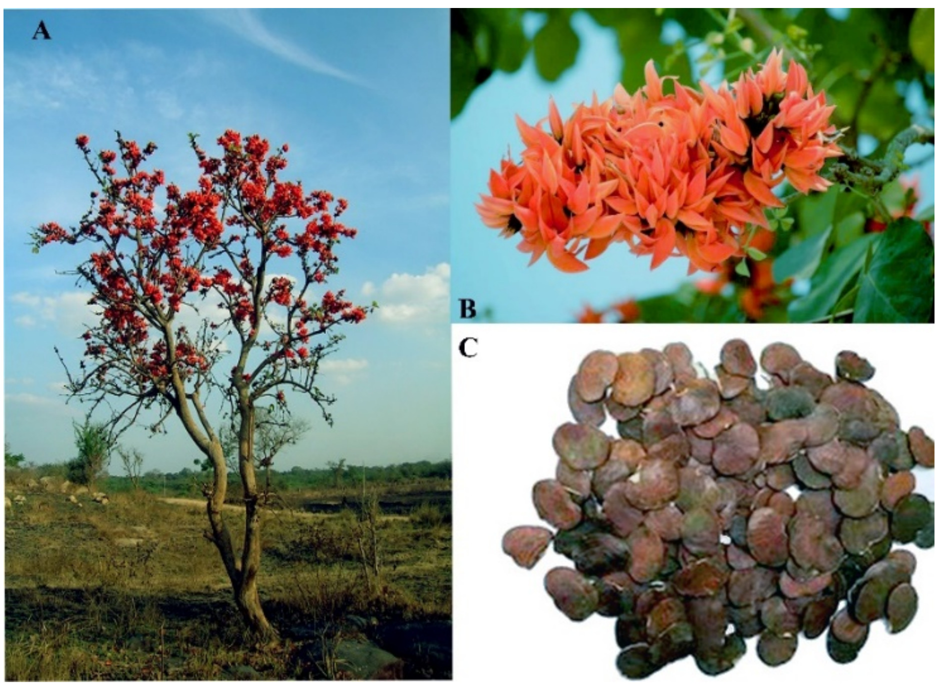

Fig. (1). *Butea monosperma;* (**A**) Whole plant; (**B**) Florets; and (**C**) Seeds.

Native to the Southeast Asia and India, *B. monosperma* is used for its products, such as lumber, resin, animal feed, medicine, and dye. It also serves as a host plant for lac insect, which creates natural lacquer [3, 7]. In terms of host trees for lac insects, this plant is second only to Kusum (*Schleichera trijuga*). *B. monosperma* is a tall (up to 15m in height) and deciduous tree, as well as a somewhat crooked trunk; the bark is grey to greyish brown [3]. Its alternate, long-petioled, trifoliate leaves are glabrous above as well as thick and silky underneath; the leaflets are oblong to rhomboid in form or with a cuneate. The paniculate raceme of the blossoms is densely branched and fascicled, with a silvery tomentose exterior and a glossy inside. The blooms are a vivid orange-yellow hue. *B. monosperma* produces single-seeded samara fruits with reddish-brown, reniform, and flat seeds [8 - 10]. Different sorts of textiles are colored using the plant's flower petals as a source of dye [3, 11]. *Butea* promotes water conservation and aids in recovering the fertility of degraded soil [12]. The medicinal properties of this plant are attributed to flavonoids, triterpenoids, chalcones, glucosides, and other phytocompounds. The major constituent, butein (an anticancer agent), is used against various types of cancers [13, 14].

PHYTOCHEMISTRY

B. monosperma and its products are recognized to have a wide range of biological applications, and they also have benefits for the economy since they include a number of phytocompounds that confer various bioactivities, making the plant significant, both economically and medicinally. Different classes of compounds that have been isolated and purified and their structure elucidated from *B. monosperma* are presented below.

Compounds isolated from Stem and Barks

B. monosperma's stem and stem bark are reported to contain numerous bioactive compounds like (-)-medicarpin (1) [15, 16], 5-methoxy genistein (2) [17] prunetin (3) [16], 3-methoxy 8, 9-methylenedioxypterocarp-6-ene (4) [18]leucocyanidin tetramer (5) [19], Lupenone (6), lupeol (7) [3], and 3α-hydroxyeuph-25-ene (8) [20], β-sitosterol (9) [21], nonacosanoic acid, stigmasterol (10) [20, 22], and 3α-Hydroxyeuph-25-enyl heptacosanoate [23] (Fig. **2**).

Compounds Isolated from Leaves

The leaves of this plant yielded 3,9-Dimethoxy pterocarpan (11) [20]. Similarly, Singh [21] and others also reported the presence of glucosides, stearic, palmitic, oleic, myristic, and linoleic acids (Fig. **2**).

Compounds Isolated from Flowers

Flowers contained butein (12) [19, 21] butin (13) [6, 21], butrin (14), isobutrin (15), coreopsin (16), isocoreopsin (17) [19, 24], monospermoside (18), isomonospermoside (19), palasitrin (20), sulfurein (21), and 3′,4′,7-trihydroxy flavone (22) [6, 24] (Fig. **3**).

CHAPTER 5

Herbal Potentials of *Ocimum sanctum* (Indian Tulsi): A Wonderful Herb

Mohd. Aamish Khan[1], Mohd. Baqar Ali[1], Mohammad Saquib[2] and **Mohammad Faheem Khan[1,3,*]**

[1] *Department of Biotechnology, Era's Lucknow Medical College and Hospital, Era University, Sarfarazganj, Lucknow-226003, Uttar Pradesh, India*

[2] *Department of Chemistry, University of Allahabad, Prayagraj-211002, UP, India, Uttar Pradesh, India*

[3] *Department of Chemistry, Era University, Sarfarazganj, Lucknow-226003, Uttar Pradesh, India*

Abstract: *Ocimum sanctum* has been widely used in many forms of home remedies since the Middle Ages to combat many human diseases. In Indian mythology, it has great significance as a holy or spiritual herb and is recommended in the Ayurvedic system of medicine as a first aid to maintain the health of the heart, eye, liver, and mouth, as well as to cure respiratory, digestive, and skin diseases. It is also used to prevent kidney stones, relieve headaches, fight acne, and reduce fever. Experimental studies have identified it as a highly promising anti-ageing, immunomodulatory, cytoprotective, and anticancer agents. Phytochemical studies have revealed the occurrence of numerous bioactive constituents, such as rosmarinic acid, ursolic acid, oleanolic acid, eugenol, carvacrol, linalool, and β-caryophyllene. Several of these compounds have been used in foods, perfumes, dental or oral items, and other products for many decades. It provides the best nutritional supplements as it has a good amount of vitamins, minerals, and antioxidants. The present chapter evaluates the phytochemical screening, pharmacological significance, and nutritional values of different parts of *O. sanctum,* suggesting it may be a ready source of many therapeutic agents and nutritional elements of biological importance to combat human ailments.

Keywords: β-caryophyllene, Holy basil, Immunomodulatory, Indian tulsi, *Ocimum sanctum*, Rosmarinic acid, Spiritual herb.

INTRODUCTION

Ocimum sanctum L. (OS), "Indian Tulsi" or "Holy Basil," is an aromatic medicinal and perennial herb. It belongs to the *Lamiaceae*, a mint family, which

[*] **Corresponding author Mohammad Faheem Khan:** Department of Biotechnology, Era's Lucknow Medical College and Hospital, Era University, Sarfarazganj, Lucknow-226003, Uttar Pradesh, India & Department of Chemistry, Era University, Sarfarazganj, Lucknow-226003, Uttar Pradesh, India; E-mail: faheemkhan35@gmail.com

emits spicy essence when used as a remedy for cut and wound healing. Hence, OS is also referred to as a wonder herb. The Hindu spiritual and medicinal significance of OS is sculptured in the oldest ancient Ayurvedic book, Charka Samhita (~600 BC), as well as in the Rigveda (Book of Eternal Knowledge 5000 BC). OS is characterised by the scented, hairy, and tall stem, along with simple and opposite green or purple leaves (Fig. **1**). Additionally, the colour of leaves varies with respect todifferent species [1]. The flowers depend upon the varieties, and in most cases, they are elongated and racemes in close whorls. As per the Hindu religious traditions, OS is regarded this plant as a link with the Goddess and thus has religious importance in the Hindu community [2]. OS is cultivated for medicinal purposes in traditional systems of medicine, as well as to obtain essential oil for its essence throughout the Southeast Asian tropics and Indian subcontinent. Three species of OS are widely grown in India. The first green leaf regarded as Rama Tulsi, is the most commonly used in societies; the second leaf known as Krishna Tulsi, has dark green-to-purple leaves; and the third one is a forest variety (Vana Tulsi) as per the classical textbook Bhawaprakash [3]. OS is highly recommended in prophylactic daily doses against respiratory illness, infections, and other diseases. For thousands of years, traditional practitioners like Vaid, Rishi, and Muni have been using OS and are still using it today as an Ayurvedic remedy to cure common colds, headaches, pain, inflammation, stomach upset, heart ailments, as well as various forms of poisoning and malaria [4]. Traditionally, OS is recommended to take in many forms, such as decoction (herbal tea), dried powder, or fresh leaf. Thus, the aim of this chapter is to discuss the herbal potentials of OS or tulsi with an emphasis on bioactive chemical constituents. It also focuses on the different pharmacological activities of OS and its use in cosmetics and foods [5].

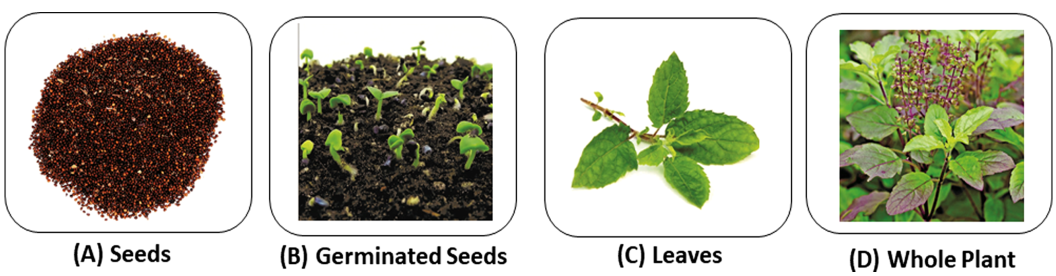

Fig. (1). Different parts of *Ocimum sanctum*.

THERAPEUTIC USES OF *OCIMUM SANCTUM*

The traditional uses of OS have been described in ancient texts of the Indian Ayurveda system of medicine for its rejuvenating, tonic, and vitalizing properties for a healthy life. Ethno pharmacological properties claim that OS is a very beneficial herb having antispasmodic, antipyretic, antidiabetic, antibacterial, antifungal, antioxidant, anti-inflammatory, antitumor, anti-aging activity, anti-atherosclerotic effects [6] as well as immunity enhancement effect. OS is able to treat respiratory illnesses, such as common cold, cough, allergic rhinitis, as well as food poisoning, impotence and arthritis inflammation. Few studies have claimed that OS may act as an antidote for snakebite. The infused leaves are healthier and beneficial for treating gastrointestinal and related disorders in children, and thus can be used in the form of expectorant, carminative, refrigerant, febrifuge, laxative, *etc*. Additionally, because of their mucilaginous and demulcent nature, the seeds are able to treat genitor-urinary disorders. In the form of decoction or herbal tea made from leaves of OS, it can act as an herbal remedy for the prevention of cough, cold, and malarial fever. Besides the traditional uses, OS has been recommended in the Ayurvedic Pharmacopeia of India (1999) for the treatment of pratishyaya, hikka, kasa, aruci, kustha, krimiroga, and parsva sula, which are correspondingly referred to as common cold, respiratory disorders, cough, loss of taste, skin disorders, treatment of just and chest pain. These disorders can be cured if anyone takes 2–3 g leaf powder in a proper therapeutic dose [7].

BIOACTIVE COMPOUNDS

OS contains diversified and complex chemical constituents. Some of them are highly biologically active and found in good quantities, depending on the growing, harvesting, processing, and storage parameters as well as climate conditions where they grow. The leaves contain polyphenols, such as gallic acid, and its derivatives like gallic acid methyl ester, gallic acid ethyl ester, along with caffeic acid, chlorogenic acid, vanillin, vanillic acid, protocatechuic acid, 4-hydroxybenzoic acid, 4-hydroxybezaldehyde, and rosmarinic acid (Fig. **2**) [8]. These compounds were analysed by using high-pressure liquid chromatography (HPLC) and atmospheric pressure chemical ionization mass spectrometry (APCI) techniques. In leaves and aerial parts, research studies have shown the presence of numerous flavonoids, including orientin, luteolin, isothymusin, isovitexin, cirsimartin, isoorientin, and flavonoid glycosides, such as salvigenin, vicenin, eupatorin, apigenin,, crisilineol, and gardenin as depicted in (Fig. **2**). From the whole plant extracts, numerous terpenoids along with steroids have been isolated and identified (Fig. **3**) namely ursolic acid, carnosic acid, oleanolic acid, β-sitosterol, β-sitosterol-D-glucopyranoside, campesterol and stigmasterol by using different column chromatographic as well as spectroscopic techniques [9]. Essential oil, commonly known as basil oil, is the main component of OS aerial parts with a yield of 0.3-4.1% concentration. Its composition includes the presence of a mixture of cyclic or acyclic monoterpenoids, sesquiterpenoids, and some other volatile phenolic compounds, and their occurrence depends upon the

CHAPTER 6

Pharmacological Properties of *Psoralea corylifolia*: An Important Medicinal Plant of Ayurveda and Chinese System of Medicine

Mahima Verma[1], **Shireen Fatima**[1], **Prakriti Mishra**[1], **Zeba Siddiqui**[1], **Irfan Ahmad Ansari**[1,*], **Azhar Kamal**[2] and **Mohd. Sayeed Akhtar**[3]

[1] *Department of Biosciences, Integral University, Lucknow-226026, Uttar Pradesh, India*

[2] *Department of Bioengineering, Integral University, Lucknow-226026, Uttar Pradesh, India*

[3] *Department of Botany, Gandhi Faiz-e-Aam College, Shahjahanpur-242001, Uttar Pradesh, India*

Abstract: *Psoralea corylifolia* L. (*Leguminosae*) is a well-known vital medicinal plant and has been used for treating a variety of diseases since ancient times. It is abundantly available in nature and plays an imperative role in Ayurvedic and Chinese medicines. Studies on the ethnobotanical, ethnopharmacological, clinical, phytochemical, as well as side effects of *P. corylifolia* were found in a variety of scholarly published databases. These plant species have been thoroughly examined both *in vivo* and *in vitro* approaches for diverse phytochemical and biological studies. It is used locally for inflammation, alopecia, leukoderma, eczema, leprosy, and psoriasis and possesses cardiotonic, antibacterial, vasodilator, pigment or cytotoxic, antitumor, and anti-helminthic activities. Approximately more than a hundred bioactive chemicals have been isolated from fruits and seeds so far, with the most important ones belonging to the coumarins, flavonoids, and meroterpenes families. This chapter thoroughly summarises the information on *P. corylifolia's* chemical ingredients and biological activities, providing valuable information for future research and developments on this powerful therapeutic plant.

Keywords: Ayurvedic, Biological activity, Pharmacology, Phytochemical, *Psoralea*.

INTRODUCTION

The family *Leguminosae* is the third-largest terrestrial plant family in terms of biodiversity after *Orchidaceae* and *Asteraceae*, which includes more than 500 genera. *Psoralea* is a broad herbaceous genus with over 130 species found prima-

* **Corresponding author Irfan Ahmad Ansari:** Department of Biosciences, Integral University, Lucknow-226026, Uttar Pradesh, India; E-mail: ahmadirfan.amu@gmail.com

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rily in tropical and subtropical climates. This plant gets its name from the Greek word psoraleos, which means "afflicted by itch or leprosy" [1].

P. corylifolia is an upright herb that grows to a height of 30 to 180 cm every year. It does not propagate in the shade and requires a warm environment to thrive. Clay, sand, and loam types of soil are required for this plant. The plant can thrive in a variety of environments, including acidic, basic, and neutral. March through April is the optimal time to grow this plant. In November, the seeds reach maturity. Several vernacular names of this plant are Chanderlekha, Aindavi, Kushthahantri, Sitavari, Vejani, Krishnaphala, Sugandhakantak, Sasankrekha (Sanskrit), Babchi, Bawachi (Urdu), Bavanchi (Marathi), Babechi (Gujarati), Bavanchalu, Karpokarishi (Tamil), Kala-ginja (Telegu) and Satinwood (English). For a long time, medicinal plants have been one of the significant suppliers of medicines in the world, and they will continue to do so in the future. In Chinese, Buguzhi or Poguzhi refers to the dried fruit of *P. corylifolia*. Buguzhi was used as an aphrodisiac, laxative, anthelmintic, and diuretic both internally and externally and was advised for the treatment of leprosy, leukoderma, psoriasis, and inflammatory skin illnesses. In the United Kingdom and the United States, pharmacopoeias have also listed *P. corylifolia* [2, 3].

Coumarins, flavones, meroterpenes, chalcones, lipids, stigmasteroids, volatile oil, and resins are among the 90 chemicals that have been identified and isolated from *P. corylifolia*. Coumarins, flavonoids, and meroterpenes are the most biologically active elements, with the majority of them present in the plant's seeds or fruit. Antioxidant, antifungal, antibacterial, anticancer, estrogenic, osteoblastic, anti-inflammatory, and immunomodulatory characteristics have been established for these active components.

CHEMICAL CONSTITUENTS

More than 90 chemicals found in *P. corylifolia* can be categorized into five groups based on their chemical structures, viz., coumarins, flavonoids, meroterpenes, benzofuran, and others. Coumarins, flavonoids, and meroterpenes have attracted a lot of attention because of their wide range of bioactivities. The seeds or fruits contain active ingredients, such as bakuchiol, bavachalcone, psoralidin, psoralen, isopsoralen, neobavaisol flavones, and corylifols. Flavonoids (neobavaisoflavone, isobavachalcone, bavachalcone, bavachinin, bavachin, corylin, corylifol, corylifolin, and 6-prenylnaringenin), coumarins (psoralidin, psoralen, isopsoralen, and angelicin), and meroterpenes are found in *P. corylifolia* extracts (bakuchiol and 3-hydroxybakuchiol) [4]. *P. corylifolia* extracts and active components demonstrated a wide range of bioactivities, including antitumor, estrogenic, anti-oxidant, antidepressant, antimicrobial, anti-inflammatory, hepatoprotective, and osteoblastic properties [5] Table **1**. We have summarised the secondary metabolites isolated from *P. corylifolia* using different solvents in tabular form (Table **2**).

Table 1. The major compounds isolated from *P. corylifolia* show a wide range of bioactivities.

Compound Name	Chemical Nature	Pubchem CID Number	Part Used	References
Bakuchiol	Meroterpene	5468522	Seeds/Fruit	[6]
Bavachalcone	Chalcone	6450879	Seeds	[7]
Corylin	Flavonoid	5316097	Whole plant	
Psoralen	Furanocoumarin	6199	Whole plant/root	[8]
Psoralidin	Coumarin	5281806	Whole plant/seed	
Xanthoangelol	Chalcone	643007	Seeds	[9]

Table 2. List of phytochemicals present in *P. corylifolia*.

Type of Extract	Type of Secondary Metabolite						
	Alkaloids	Carbohydrates	Glycosides	Flavonoids	Saponins	Steroids	Triterpenoids
Aqueous	-	+	+	+	+	-	-
Ethanol	+	+	+	+	+	-	-
Chloroform	-	-	-	-	-	-	+
Petroleum ether	-	-	-	-	-	+	+

+ = present; - = absent.

Coumarins

Coumarins are plant-derived polyphenolic chemicals that belong to the benzopyrones class and are the most abundant component in *P. corylifolia*, and they are categorised into three groups: coumestrol, furocoumarins, and other coumarins.

Coumestrols

Natural phytoestrogens are coumestrols with a coumestrol backbone that have biological properties similar to estrogens. One of these chemicals, psoralidin, was extracted from *P. corylifolia,* and its chemical structure was validated in 1961. Another form of coumestrol, isopsoralidin, was discovered in 1974 [10, 11]. Different groups have isolated and discovered further coumestrol, including corylidin, neopsoralen, psoralidin-20, 30-oxide, bavacumestan A, B, and sophora coumestan A in the following years [12, 13]. Dehydroisopsoralidin was isolated

CHAPTER 7

Ethnopharmacological Properties of *Swertia chirayita* and Other Species: A Nature's Treasure

Shireen Fatima[1], **Mahima Verma**[1], **Prakriti Mishra**[1], **Zeba Siddiqui**[1], **Irfan Ahmad Ansari**[1,*] and **Mohd. Sayeed Akhtar**[2]

[1] *Department of Biosciences, Integral University, Lucknow-226026, Uttar Pradesh, India*

[2] *Department of Botany, Gandhi Faiz-e-Aam College, Shahjahanpur-242001, Uttar Pradesh, India*

Abstract: *Swertia chirayita* (Family; *Gentianaceae*) is a well-known medicinal plant from the temperate Himalayas and is used in traditional medicine to treat a number of illnesses, including liver issues, malaria, and diabetes. The medicinal use of *S. chirayita* is extensively documented in the Indian Pharmacy Codex, the British and American Pharmacopoeias, as well as in a number of traditional medical systems, including Ayurveda, Unani, and Siddha. This plant's primary distinguishing feature is its bitter flavor, which arises from the presence of several bioactive compounds that may offer health benefits to people. Growing demand for this important medicinal plant on a national and international scale has prompted unethical wild harvesting and adulteration of the supply. Consequently, there has been a sharp decline in the plant's population, putting it at risk of extinction. Therefore, the objective of this chapter is to give a summary of recent discoveries in the areas of morphology and distribution, traditional usages, biotechnology, phytochemistry, pharmacological effects, and safety evaluations of *S. chirayita*.

Keywords: Ayurveda, Bioactivities, Drug, Medicine, Phytocompounds, Therapy.

INTRODUCTION

The availability and application of pertinent drugs are indicators for the efficacy of the primary healthcare system. Traditional medicine meets about 70% of the local population's medical needs [1]. The majority of people in underdeveloped nations frequently rely on medicinal plants for their availability, accessibility, affordability, and reasonably priced method of therapy in the primary healthcare system. Medicinal plants have long been a source of possible therapies for various

* **Corresponding author Irfan Ahmad Ansari:** Department of Biosciences, Integral University, Lucknow-226026, Uttar Pradesh, India; E-mail: ahmadirfan.amu@gmail.com

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illnesses, whether in the form of traditional formulations or as pure bioactive components, due to their enormous potential to treat a range of health issues. These plants have been found to be effective against diseases caused by microorganisms [2]. According to Wazir *et al.* [3], about 70,000 plant species have been employed to treat a variety of microbiological illnesses. In the assessed indigenous medical systems like Ayurvedic, Unani, and Siddha, different components of medicinal plants have been used to cure a variety of disorders for generations since ancient times.

Swertia chirayita (Family; *Gentianaceae*), belonging to a well-known genus of annual and perennial medicinal plants, is used in traditional medicine to treat a number of illnesses, including liver issues, malaria, and diabetes. In India, there are 40 species of *Swertia*, with *S. chirayita* being the most notable for its therapeutic benefits are included in a variety of herbal treatment formulations (Table **1**). Roxburg initially described *S. chirayita* in 1814 under the name *Gentiana chyrayta*. *S. chirayita*, often known as *"Chiretta,"* is a critically endangered medicinal herb that grows at high altitudes in the sub-tropical Himalayas on the slopes of moist shady locations from Kashmir to Bhutan [4]. However, a full analysis identifying the current knowledge gap and outlining the recorded ethnomedicinal applications, pharmacological properties, and safety evaluation carried out on *S. chirayita* is inadequate. Therefore, the objective of this chapter is to highlight the recent discoveries in the areas of morphology and distribution, traditional usages, biotechnology, phytochemistry, pharmacological effects, and safety evaluations of *S. chirayita*.

Table 1. Traditional applications of *S. chirayita* in ethnobotany.

Plant Parts	Traditional Uses	References
Roots	They are used for asthma, cough, common cold, fever, joint pain, as well as weakness, and they can also be an excellent tonic.	Joshi and Dhawan [5]
Whole plant	It is used as a potent medicine against huge vaginal discharge.	Jadhav and Bhutani [6]
	The fresh leaves and cut stems are kept in water overnight, and the extract is used for headaches and high blood pressure.	de Rus Jacquet *et al.* [7]
	Used to cure malaria by boiling water and drinking 1 cup of the decoction.	Shah *et al.* [8]
	The plant's paste is used to treat skin disorders such as eczema and acne.	Malla *et al.* [9]

MORPHOLOGY AND DISTRIBUTION

The stem of *Swertia* is smooth and measures up to 1m long with thin, easily separated bark of yellowish or purple-brown in color. It is cylindrical at the base and quadrangular with ascending branches. The wood surrounding the internodal sections is porous and yellow. This plant has a large yellowish pith that is readily separated, as well as a simple conical root with short rootlets. The plant spreads rapidly from seed shed throughout the months of October and November. This plant may be grown in the temperate Himalayas, given the proper conditions. The seeds are first planted in a nursery and later transferred to the field conditions [5].

S. chirayita is native to northern India's hilly provinces, the temperate Himalayas at elevations ranging from 1,200 to 3,000 m from Kashmir to Bhutan, and the Khasi highlands of Meghalaya at 1,200-1,500 m [5]. Other important species, such as *S. angustifolia, S. bimaculata, S. calycina, S. ciliata, S. corymbosa, S. decussata, S. densifolia, S. frachetiana, S. hookeri, S. japonica, S. macrosperma, S. paniculata, S. petiolata, S. punctata, S. purpurascens,* and *S. lawii* are also conventional and alternative medicine of *S. chirayita* in India, China, Pakistan, Japan, and other Asian countries to cure the liver, fever, dysentery, diarrhoea, stomach problems and other disorders [10]. Additionally, because of its widespread usage in traditional medicine, its natural habitat has been over-exploited, and it is now on the verge of extinction. It is documented as Qasabuzzarirah in Arabic and Farsi, Chiratitka, Anaryatikta, Kairata and Bhunimba in Sanskrit, Sekhagi in Burma, Chiaravata in Urdu, and Chirratoor Chiraita in Nepalese literatures [11].

BIOACTIVE COMPOUNDS

The extensive usage of *S. chirayita* as a traditional medication in modern medical systems has attracted scientists and researchers to investigate its phytochemistry to identify more bioactive phytochemicals. The presence of a diverse group of bioactive compounds in this plant includes the derivatives of xanthones, terpenoids, lignans, flavonoids, secoiridoids, alkaloids, iridoids, chiratin, palmitic acid, ophelic acid, oleic acid, and stearic acid. All these phytocompounds are ascribed to their wide range of biological activities.

Xanthonoids

Chiratanin, found in several parts of *S. chirayita* was the first dimeric xanthone to be isolated. The occurrence of phytoconstituents, such as amarogentin, swertiamarin, mangiferin, swerchirin, sweroside, amaroswerin, and gentiopicrin imparts pharmacological efficacy to this plant [4]. In *S. chirayita, S. mussotii, S. cordata, S. macrosperma,* and *S. connata*, mangiferin is the most prevalent C-

CHAPTER 8

Emblica officinalis in Preventing Metabolic Syndrome: A First Review Addressing the Benefits and the Mechanism of Action

Pankaj Prabhakar[1], **Vijaya Marakala**[2], **Dhanya Sacheendran**[3], **Rhea Katherine D'souza**[4], **Rashmi Theresa D'souza**[5], **Mamatha Jayandran**[3], **Giriyapura S. Pavankumar**[6], **Princy L. Palatty**[3] and **Manjeshwar Shrinath Baliga**[4,*]

[1] *Department of Pharmacology, Indira Gandhi Institute of Medical Sciences (IGIMS), Sheikhpura, Patna, Bihar, 800014, India*

[2] *Department of Biochemistry, College of Medicine and Health Sciences, National University of Science and Technology, Sahar, Oman*

[3] *Department of Pharmacology, Amrita Institute of Medical Sciences, Vishwa Vidyapeetham, Kerala-682041, India*

[4] *Research Unit, Mangalore Institute of Oncology, Mangalore, Karnataka-575002, India*

[5] *Nitte University, Centre for Science Education and Research (NUCSER), Paneer Campus, Deralakatte, Mangaluru, Karnataka-575018, India*

[6] *Sri Lakshmi Group of Institution, Sunkadakatte, Bengaluru, Karnataka-560091, India*

Abstract: Globally, metabolic syndrome has increased a lot and affecting people of the productive age group. The fruits of *Emblica officinalis* or *Phyllanthus emblica* colloquially known as Amla or Indian gooseberry and their active components have been investigated and observed to be beneficial. Amla possesses beneficial effects against metabolic syndrome in both preclinical, and clinical studies. Amla decreases the components of metabolic syndrome like blood pressure, glucose levels, obesity, and cholesterol levels. Moreover, hepatic triacylglycerol, total cholesterol, and oxidative stress were also attenuated by amla treatment. Amla was found to augment adiponectin levels in adipocytes and hepatic PPAR-α levels as well as decline hepatic regulatory element-binding protein (SREBP-1c) expression caused by high-fat diet in rats. Amla possesses gallic acid, ellagic acid, and polyphenol, which are also beneficial. Amla possesses anti-inflammatory properties by downregulating the expression of pERK, TNF-α, pP38, IL6, COX2, and NOX-4 in metabolic syndrome. Furthermore, amla acts through liver X receptor (LXR), farnesoid X receptor (FXR), PPARγ, cEBPα, FABP4,

* **Corresponding author Manjeshwar Shrinath Baliga:** Research Unit, Mangalore Institute of Oncology, Mangalore, Karnataka-575002, India; E-mails: msbaliga@gmail.com, msbaliga.mio@gmail.com

cyclo-oxygenase-2, SREBP-1c, and NF-κB to improve the components of metabolic syndrome. This chapter analyses the encouraging properties of Amla fruit, and its phytoconstituents in metabolic syndrome.

Keywords: Amla, *Emblica officinalis*, Herb, Indian gooseberry, Metabolic syndrome, Medicine.

INTRODUCTION

Metabolic syndrome (MetS) is known as Reaven's Syndrome, syndrome X, the deadly quartet, and insulin resistance. The term MetS was first coined by Haller and Hanefeld in 1975. In 1923, MetS was first defined by Kylin as "clustering of hypertension, hyperglycemia and gout" [1]. Furthermore, insulin resistance syndrome was first defined by Reaven in 1988 [2]. MetS is a clustering of risk factors, such as insulin resistance, obesity, hypertension, hyperglycemia, and dyslipidemia, coexisting in an individual increases the danger for diseases; 2-fold increase for cardiovascular diseases and up to 5-fold for type-2 diabetes mellitus [3 - 5]. MetS is one of the foremost civic health challenges globally, owing to inactive lifestyles, excess food consumption, and rapid urbanization. The occurrence of MetS may range between approximately 10 to 80% worldwide, subject to the region, environmental conditions, human age, sex, and ethnicity [6]. The key risk factors for an increasing incidence of MetS are attributed to physical inactivity and a Western diet or a diet with high concentrations of fats and carbohydrates, causative to the two central clinical features that are insulin resistance and obesity [7]. Further, the International Diabetes Federation estimated that 25% of the global grown-up people are suffering from MetS [8]. According to the National Heart, Lung, and Blood Institute and the American Heart Association's most recent guidelines, a person can be diagnosed with metabolic syndrome if 3 or more of the following measurements are present [9].

- Central obesity: males > 102cm, females > 88cm waist circumference
- Hypertriglyceridemia: a triglyceride level of less than 150 mg/dL or the use of a specific drug
- Low HDL Cholesterol: 40 mg/dl for men and 50 mg/dl for women, or a particular medicine
- Hypertension: Systolic blood pressure (BP) of 130 mmHg or diastolic BP of 85 mmHg or specified medicine
- A fasting plasma sugar level of less than 100 mg/dl, a specific medicine, or a history of type 2 diabetes.

Currently, MetS and the risk factors associated with MetS are managed by changes in lifestyle and the use of pharmacological interventions which mainly target specific metabolic pathways involved in nutrient metabolism [10]. It has been observed that pharmacological interventions are expensive and may cause many undesired side effects due to continued use. Moreover, there is no single drug available in the market to manage the MetS and associated risk factors. It has been found that they have treated symptomatically using a monotherapeutic approach, usually considering a few health outcomes accompanying MetS. Therefore, there is an urgent need to find some alternative approaches for the management of MetS. These alternative approaches should comprise the use of medicinal plants for the management of MetS [8]. Traditional medicines or medicinal plants are used by a large population of the world now a days. A large segment of the population in developing countries still depends on Ayurvedic practitioners as well as herbal drugs for their primary treatment [11].

According to the World Health Organization (WHO), there are 90% of African and 70% of the Indian population rely on herbal medicine for their basic health care treatment. In addition, traditional medicine covers around 40% of all health care provided, and 90% of general hospitals have traditional medicine units in China [12]. Further, the use of herbal medicines is not restricted to developing countries but has become a multibillion-dollar industry across the world as public interest in natural therapies has also increased greatly in developed countries [8]. Medicinal plants contain many bioactive compounds whose additive and synergistic therapeutic effects are useful in the management of MetS [13]. The WHO acclaims an intake of 400-600 g of fruits and vegetables daily for a healthy life [14]. Nevertheless, there is a common accord that raw fruit and vegetable consumption are more significant in providing health benefits than that of only one of their constituent, and this is because of the additive and synergistic effects of phytochemicals [14]. In the current review, we will discuss the beneficial effects of amla in Mets and the risk factors associated with MetS.

ETIOLOGY OF METABOLIC SYNDROME

Though much research has been performed in recent decades on MetS, the precise underlying etiology is still not completely implicit. The most common issues that are responsible for developing MetS include resistance to insulin, overweight, and obesity [15, 16]. Further, the factors that are responsible for the progress of insulin resistance include obesity, hormones secreted from adipose tissue, excessive accumulation of fat, hypothalamus–hypophysis–adrenal axis disorders, as well as genetic and environmental factors [17].

Pathophysiology of Metabolic Syndrome

The pathogenic mechanisms of MetS are multifaceted and remain to be fully clarified. There exists a significant difference in the topographical distribution of

CHAPTER 9

Selected Medicinal Plants for Combating Diabetes: A Green Anti-Hyperglycemic Approach

Kadabagere Narayanaswamy Hemavathi[1], **Sushil Kumar Middha**[1,*], **Nidhi Dwivedi**[1], **Prakash Hemalatha**[1], **Asiya Nisa**[1], **Basavaraju Kavyashree**[1], **Arvind Kumar Goyal**[2] and **Talambedu Usha**[3,*]

[1] *DBT-BIF Facility, Department of Biotechnology, Maharani Lakshmi Ammanni College for Women, 560012-Bangalore, Karnataka, India*

[2] *Department of Biotechnology, Bodoland University, Kokrajhar, 783370-Assam, India*

[3] *Department of Biochemistry, Maharani Lakshmi Ammanni College for Women, 560012-Bangalore, Karnataka, India*

Abstract: Medicinal plants offer significant therapeutic potential due to the presence of bioactive phytochemicals. This renders them promising candidates for the treatment of a wide range of ailments. Diabetes, a severe metabolic disorder, is conventionally managed using commercial pharmaceutical drugs. Nevertheless, these prescription medications are both economical and linked to various adverse effects. The increasing popularity of herbal remedies is attributed to their cost-effectiveness and their capacity to deliver enhanced therapeutic benefits with fewer associated side effects. This chapter is dedicated to the exploration of well-known medicinal plants, including *Trigonella, Syzium, Punica, Momordica,* and *Gymnema* species, for their efficacy in addressing issues related to diabetes. The principal goal of this chapter is to offer an in-depth examination of the chemical compositions and preclinical assessments that substantiate their anti-diabetic properties.

Keywords: Anar, Diabetes, Gulmar, Jamun, Methi, Preclinical studies.

INTRODUCTION

The prevalence of diabetes mellitus, a common but possibly fatal medical condition, has risen over the past few decades. This trend makes it a significant public health challenge of the 21st century, affecting millions of people [1, 2]. In 2017, 425 million people worldwide had diabetes, and by 2045, that number is

* **Corresponding authors Sushil Kumar Middha and Talambedu Usha:** DBT-BIF Facility, Department of Biotechnology, Maharani Lakshmi Ammanni College for Women, 560012-Bangalore, Karnataka, India and Department of Biochemistry, Maharani Lakshmi Ammanni College for Women, 560012-Bangalore, Karnataka, India; E-mails: ushatalambedu@gmail.com, drsushilmiddha@mlacw.edu.in

expected to rise to 693 million [3]. According to reports, India had the second-largest population with type 2 diabetes mellitus (T2DM) in 2017, with over 72 million people [4]. Diabetes effects the metabolism of carbohydrates, fats, and proteins. This disorder is brought on by problems with insulin secretion, insulin action, or both. Over time, this results in chronic hyperglycemia and a host of complexities, such as neuropathy, nephropathy, retinopathy, cardiomyopathy, vascular damage, and skin-related complications [5, 6]. Type 1 diabetes (T1D) causes a complete lack of insulin and hyperglycemia due to the selective destruction of the pancreatic islets. The aggressive autoimmune process that results in insulitis primarily destroys the cells and is mediated by the infiltration of CD4+ and CD8+ T cells as well as macrophages [7]. The pathophysiology of T2DM is heavily influenced by insulin resistance and deficiencies in insulin secretion. Insulin is secreted by pancreatic cells in response to rising blood glucose levels in the human body. The first-phase insulin release peaks at 2-4 min after the initial rise in arterial levels of glucose and falls sharply by 10-15 min. The second-phase insulin release is more gradual, reaching a steady state at 2-3 h after the initial rise in arterial levels of glucose. Insulin resistance causes insulin secretion to increase more than normal. Insufficient insulin secretion leads to hyperglycemia and, eventually, T2DM, particularly when there is insulin resistance, inflammation, and glucolipotoxicity linked to obesity [8], termed newly as diabesity.

For the treatment and management of diabetes, appropriate diet and lifestyle changes have been shown to be effective. Counselling and recommendations from a dietician or nutritionist are integral components of medical, and nutritional therapy (MNT), which plays a key role in diabetes management. The goal of MNT is to improve metabolic control and improve treatment outcomes [4]. Natural products, especially those with a botanical origin, are the main source for discovering promising lead candidates and are essential to the upcoming drug development programmes. Plant-based preparations dominate all other therapies, particularly in remote regions, because they are simple to access, inexpensive, and have fewer side effects [9]. Additionally, a wide range of plants provide a plentiful source of bioactive chemicals with powerful therapeutic actions and no adverse side effects [2]. Many of the drugs that are currently in use are obtained from plants, which have been an excellent source of drugs historically [10].

For centuries, traditional medicines have treated conditions like DM with plants. A possible resource for new anti-diabetic medicines or phytomedicines/ supplements could be from traditional medical preparations [2]. Galegine, a guanidine isolated from *Galega officinalis* L., belonging to the family Fabaceae, was used to develop metformin, a biguanide. It is the main medication used to treat diabetes at present [11]. The drawbacks of diabetes treatments include low efficacy, low tolerance, more side effects and complications, high cost, and fewer adherences, increasing the need to find new anti-diabetic plant-based drugs [5].

PLANTS AND DIABETES

Over 1200 medicinal plants have been documented to be effective in the management of diabetes [2]. Of these, medicinal plants, *T. foenum-graecum, S. cumini, G. sylvestre, P. granatum,* and *Momordica charantia* are well-studied for their anti-diabetic properties. Fig. (**1**) depicts the foundational schema utilized in the context of these botanical specimens.

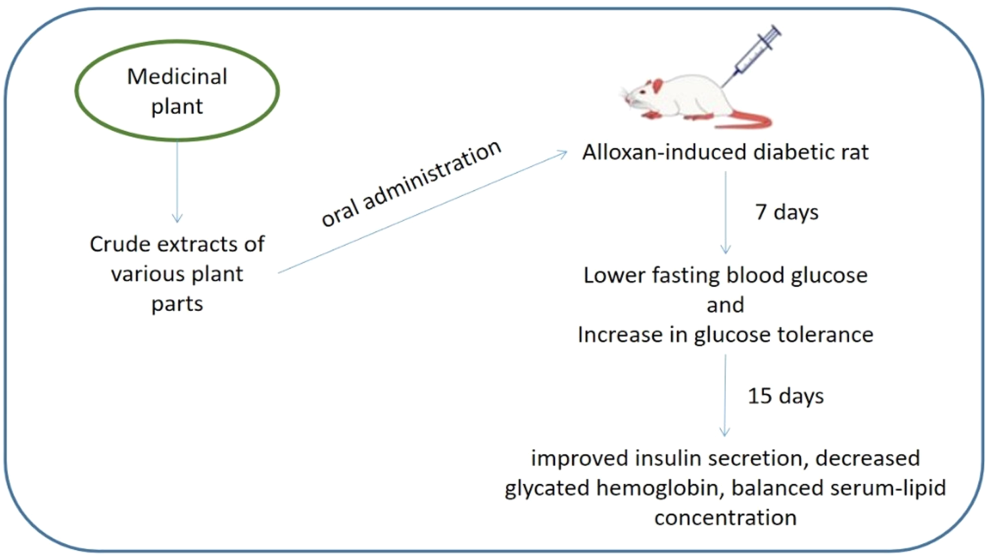

Fig. (1). The fundamental schema applied to antidiabetic plants.

The phytochemistry and anti-diabetic effects of these plants are discussed in the following sections.

T. foenum-graecum (Methi)

Some of the most popular medicinal species of the genus include *Trigonella* are *T. foenum graecum, T. balansae, T. corniculata, T. maritima, T. spicata, T. occulta, T. polycerata, T. calliceras, T. cretica, T. caerulea, T. lilacina, T. radiata,* and *T. spinosa*. The only species of *Trigonella* that is widely farmed is *T. foenum graecum* L., commonly referred to as fenugreek or methi [12].

It is a dicotyl, autogamy, therapeutic plant and belongs to the family of Fabaceae [13]. It is a thin, erect annual crop that reaches a height of 30 cm to 60 cm

CHAPTER 10

Pharmacological Effects of Lesser-known Fruiting Plants Growing in India

Raksha Nayak[1], Karkala Maya Sreedhara Pai[1], Vijaya Marakala[2], Harish Kumar Bastimal[1], Pankaj Prabhakar[3], Rhea Katherine D'souza[4], Sham Prasad Sajankila[5], Karkala Sreedhara Ranganath Pai[1] and **Manjeshwar Shrinath Baliga[4,*]**

[1] *Department of Pharmacology, Manipal College of Pharmaceutical Sciences, Manipal Academy of Higher Education, Manipal-576104, India*

[2] *Department of Biochemistry, College of Medicine and Health Sciences, National University of Science and Technology, Sahar, Oman*

[3] *Department of Pharmacology, Indira Gandhi Institute of Medical Sciences (IGIMS), Sheikhpura, Patna, Bihar-800014, India*

[4] *Research Unit, Mangalore Institute of Oncology, Mangalore, Karnataka-575002, India*

[5] *Department of Biotechnology Engineering, NMAM Institute of Technology-Affiliated to NITTE, Nitte, Karnataka-574110, India*

Abstract: India possesses a diverse array of medicinal plants, some of which have been recorded in different places. Their presence is largely influenced by climate and soil conditions, which are indicative of plant biodiversity. In the recent past, there has been an emphasis on ethnopharmacological research, which focuses on correlating plant utilization for medicinal uses with indigenous communities. The attempts aim to bridge the knowledge gap crucial for future drug development. This chapter overviews the chemistry and pharmacological activities of fruiting plants like *Ziziphus mauritiana, Ixora coccinea, Syzygium jambos, Averrhoa bilimbi, Averrhoa carambola, Carissa carandas, Neolamarckia cadamba, Annona reticulata, Grewia asiatica, Feronia limonia, Syzygium samarangense, and Artocarpus lakoocha.*

Keywords: Ethnomedicine, Minor fruiting plants, Medicine, Pharmacological effects.

INTRODUCTION

India is home to a diverse array of natural resources, principally because of the diverse climates, ecological zones, and geographic locations that support a wide

* **Corresponding author Manjeshwar Shrinath Baliga:** Research Unit, Mangalore Institute of Oncology, Pumpwell, Mangalore, Karnataka-575002, India; E-mails: msbaliga@gmail.com; msbaliga.mio@gmail.com

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diversity of therapeutic plants. The fact is that India is home to 4 of the world's 36 biodiversity "hotspots," including the Western Ghats, the Himalayas, the Indo-Burma region, as well as Sundaland and serveral native species, including fruit-bearing trees and bushes. Climate and soil conditions, which in turn affect plant species richness play a major role in determining where this natural resource is found and flourishes. The area covers a diverse assortment of habitats and is home to numerous places with high levels of biodiversity. Furthermore, because of its varied agro-climatic conditions and regional geography, India is regarded as a rich source of plant genetic resources [1, 2].

Biodiversity refers to the richness and diversity of a region's plant and animal life. The importance of the link between plant use and indigenous populations has been underlined by studies in ethnomedicine. Documents affirm that there is a wide variety of flowering and fruiting plants in the country, and many different species and their morphotypes can be found. Extensive field inquiry in ethno-medicine is necessary to classify plants based on their therapeutic characteristics and chemical composition. Understanding gaps in the hunt for future medication development can be filled by examining ethnopharmacological assessment and documentation of traditional knowledge possessed by local communities regarding medicinal plants [1, 2].

Classical Indian medicine makes use of around 1,800 different species to cure several medical issues, ranging from tuberculosis and cancer to diabetes mellitus, heart irregularities, wound healing, and pharyngitis, and hypertension. The pharmacological effects of plants with several bioactive phytomedicine components have led to their application in many conditions. In addition, the phytochemicals obtained from plants include polyphenols, tannins, alkaloids, and flavonoids are all examples of these. India is renowned for its abundance of medicinal plants, and the herbal therapy practices there are widely recognized as a "living tradition" [1, 2].

The possibility that plants could provide medications has been investigated for nearly a thousand years, and WHO recognizes the therapeutic value of employing traditional medicines, such as herbal treatments, which extend back hundreds of years. The advancement of herbal medicines relies heavily on traditional medicines, which are therapeutic compositions derived from medicinal plants. This study compiles the results of numerous investigations undertaken in India and elsewhere that examine the evidence supporting the various traditional medicinal uses of plants. This study provides a concise overview of some fruiting plants endemic to India, including their geographic range, physical characteristics, chemical components, and therapeutic uses [1, 2]. The article overviews the distribution, chemistry and pharmacological activities of fruiting plants like

Ziziphus mauritiana, Ixora coccinea, Syzygium jambos, Averrhoa bilimbi, Averrhoa carambola, Carissa carandas, Neolamarckia cadamba, Annona reticulata, Grewia asiatica, Feronia limonia, Syzygium samarangense, and Artocarpus lakoocha Fig. (**1**).

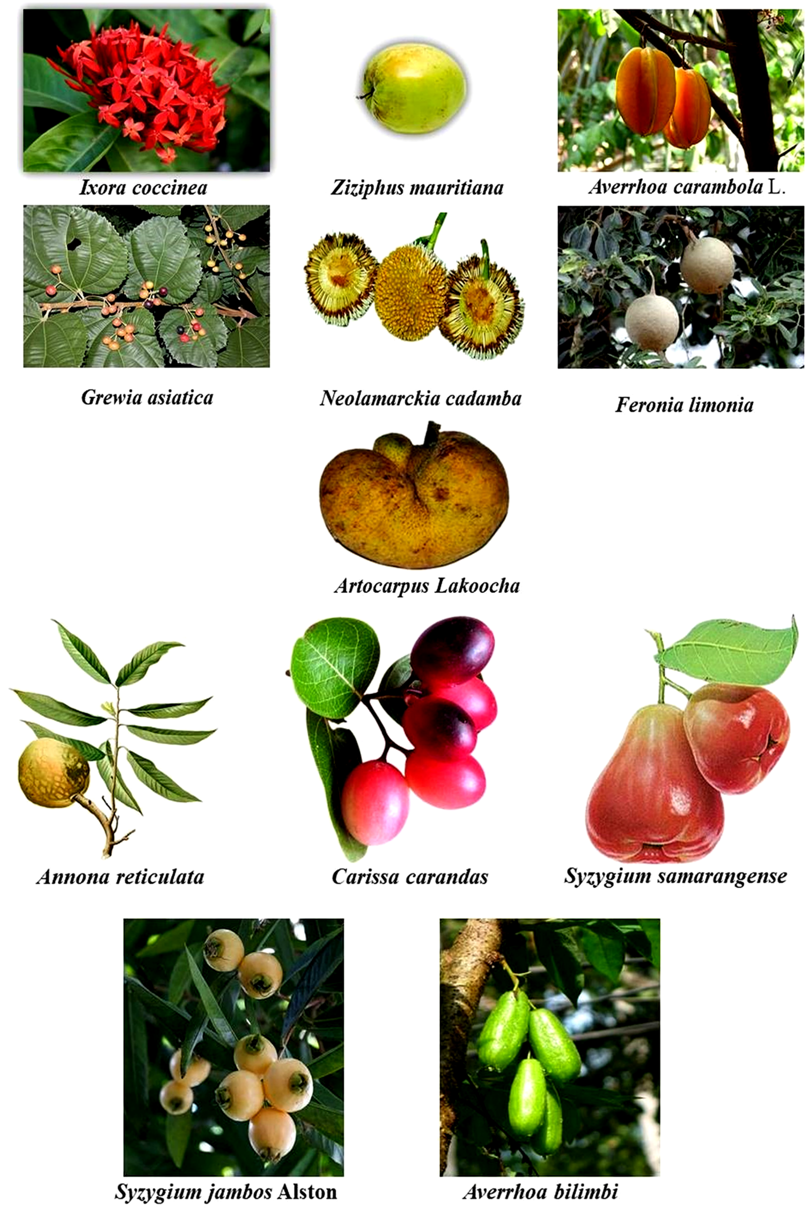

Fig. (1). Photographs of some minor fruits investigated for their medicinal benefits.

CHAPTER 11

The Role of Dietary Agents in Preventing the Pathogenesis by *Helicobacter pylori*

Rashmi T. D'souza[1], Vijaya Marakala[2], Rhea K. D'souza[3], Mamatha Jayandran[4], Pankaj Prabhakar[5], Princy L. Palatty[4] and **Manjeshwar Shrinath Baliga[3,*]**

[1] *Nitte University Centre for Science Education and Research (NUCSER), Paneer Campus, Deralakatte, Mangaluru, Karnataka-575018, India*

[2] *Department of Biochemistry, College of Medicine and Health Sciences, National University of Science and Technology, Sahar, Oman*

[3] *Research Unit, Mangalore Institute of Oncology, Mangalore, Pinto Lane, Karangalpady, Karnataka-575002, India*

[4] *Department of Pharmacology, Amrita Institute of Medical Sciences, Vishwa Vidyapeetham, Kerala-682041, India*

[5] *Department of Pharmacology, Indira Gandhi Institute of Medical Sciences (IGIMS), Sheikhpura, Patna, Bihar-800014, India*

Abstract: Infection with *Helicobacter pylori* poses a threat to public health in numerous regions of the world. This bacterium has been linked to a wide range of stomach disorders, some of which are benign, such as superficial gastritis, while others are rather serious, including chronic atrophic gastritis, stomach cancer, and peptic (gastric or duodenal) ulcers. These conditions can vary in severity and cause significant morbidity in the affected individual. The International Agency for Research on Cancer designated it as a 'Group I carcinogen' in the year 1994 after concluding that it played a significant role in the development of stomach cancer. As a result, there has been a considerable focus on discovering ways to prevent *H. pylori* infections. In this article, we discuss the role that *H. pylori* plays in human gastric disease, with a particular focus on the impact of dietary agents on preventing infection and on the pathogenesis of *H. pylori*.

Keywords: *Campylobacter pyloridis*, Dietary agents, Gastric cancer, *Helicobacter pylori*, Medicine.

* **Corresponding author Manjeshwar Shrinath Baliga:** Research Unit, Mangalore Institute of Oncology, Mangalore, Pinto Lane, Karangalpady, Karnataka-575002, India; E-mails: msbaliga@gmail.com; msbaliga.mio@gmail.com

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INTRODUCTION

Helicobacter pylori, a gram-negative, helical flagellated, and anerobic bacterium previously known as *Campylobacter pylori,* has a worldwide prevalence, with population variation rates varying greatly. Infections with *H. pylori* are also more prevalent in underdeveloped nations than in wealthy nations, and lower socioeconomic status explains this phenomenon [1]. Several studies have linked *H. pylori* infection rates to lower socioeconomic status, but the reason is unclear. In better-income countries, poorer socioeconomic status does not correlate with greater infection rates. Additionally, *H. pylori* infection and other factors vary greatly by geography [2]. Low fruit and vegetable intake was linked to higher *H. pylori* prevalence in several studies, and socioeconomic status is a major factor associated with gastric cancer. On the contrary, diet and infection rates are not consistently linked [3]. *H. pylori* prevalence increases with poorer socioeconomic status, income, and education [4]. Higher education increases household income, which, in turn, affects diet and lifestyle [5].

In addition, tobacco usage increases gastric cancer risk [6] and reports indicate that smoking cigarettes every day or for a long time increases cancer risks linearly [7]. Tobacco consumption increases gastric cancer risks in conjunction with *H. pylori* and cytotoxin-associated gene A (cagA) status [8]. Over the years, excessive alcohol consumption has also been linked to gastric cancer, along with tobacco and smoking. Smoking, food, education, socioeconomic status, and occupation are all closely linked to alcohol consumption and play a vital role. Heavy alcohol consumers without *H. pylori* were also affected in multiple trials, indicating the role of alcohol alone in gastric cancer. In addition, studies showed that drinking alcohol for decades or every day increases the risk of gastric cancer. Heavy drinkers also have higher risks of gastric cancer [9, 10].

MICROBIOLOGY OF *H. PYLORI*

It has been known for years that many microbes live in the stomach. *H. pylori* is a helix-shaped Gram-negative bacteria. Being micro-aerophilic, it requires less oxygen than the atmosphere to flourish. It can produce biofilms and transition between a spiral and a more viable coccoid shape. This coccoid form adheres to stomach epithelial cells *in vitro*, ensuring its survival and epidemiology. Marshall and Warren discovered it, and *Campylobacter pyloridis* which was subsequently known as *H. pylori*, was further cultured [1, 2, 4]. It produces oxidase, catalase, and urease to survive the stomach's hostile environment [3, 5]. *H. pylori* can colonize the gastric epithelium by deactivating stomach acid, as well as moving and adhering through the mucus layer [11, 12]. Inflammation causes peptic ulcer disease (PUD) [13 - 16] and gastric mucosa-associated lymphoid-tissue (MALT) lymphoma [17, 18].

It has two to six enclosed unipolar flagella. These three-meter flagella often feature a bulb at the end [19]. The bacteria's flagella allows it to move fast through viscous fluids like the stomach epithelial cells' mucus [19]. Unlike many gastrointestinal infections, it lacks fimbrial adhesins [20]. *H. pylori* is a neutralophile. Thus, the bacterium can survive brief exposure to pH 4, but growth occurs only at pH 5.5 to 8.0, with optimal growth at neutral pH [21, 22]. The bacteria can survivean exposure of pH 4 breifly but only thrive within that range.*H. pylori* still accounts for a significant amount of poor nations' medical costs despite its declining global prevalence. These nations have higher infection rates. As antimicrobial resistance rises, it becomes increasingly important to develop preventative measures, such as vaccination and improved hygienic conditions [23].

PATHOGENESIS OF *H. PYLORI*

Recent reports suggest that *H. pylori* influences oncogenesis by direct epigenetic effects on gastric epithelial cells and by triggering indirect inflammatory effects on the gastric mucosa [24]. *H. pylori* causing gastric cancer by these mechanisms are supported by various existing scientific evidences. Physiologically, chronic active gastritis is the most frequent *H. pylori*-related illness, and *H. pylori* carriers have these symptoms. These chronic inflammatory processes, intragastric distribution, and severity depend on the strain colonizing the host, the host's genetics and immune response, diet, and acid production. Chronic inflammation causes ulcer illness, gastric cancer, and lymphoma, especially in those with the most severe inflammation [25].

Studies show that *H. pylori*-positive rates vary by age, region, living environment, and socioeconomic status, however, oral transmission predominates [26]. This shows that relatives are more likely to contract the virus, and sharing utensils seems to cause infections [27]. The disease can also spread oro-fecally when people drink contaminated water due to poor sanitation [28]. Thus, from a socio-epidemiological viewpoint, improving living conditions and socioeconomic status are key factors in reducing *H. pylori* infection [29].

Pathogenic bacteria have virulence factors such as CagA, VacA, DupA, OipA, and GGT [30 - 34]. Stomach colonization requires particular systems, and *H. pylori* transverses using flagellar motility to infiltrate the stomach mucous [35]. Bacteria and hosts interact *via* adhesion molecules and stomach cell receptors [36, 37], and the protein CagA causes the “hummingbird” phenotype for pathogenic sequelae. The CagA alters cell polarity and epithelial cell morphology, creating

CHAPTER 12

Nanotechnology-Based Drug Delivery System for Herbal Medicines

Noor Fatima[1], **Muskan Parveen**[1], **Irshad Mahmood**[1] and **Rose Rizvi**[1,*]

[1] *Section of Plant Pathology, Department of Botany, Faculty of Life Sciences, Aligarh Muslim University, Aligarh-202002, Uttar Pradesh, India*

Abstract: Herbal medicines have been used since antiquity to treat diseases and have proven to be feasible alternatives. Numerous therapeutic plant species depend on a supply of active ingredients to function effectively. Since they cannot cross the lipid membrane, have an excessively large molecular size, or are least absorbed, most plant extracts containing biologically active components such as tannins, flavonoids, and terpenes have a lower absorption rate and are therefore less effective and bioavailable. Additionally, because of these restrictions, certain extracts are not used. It has been proposed that incorporating plant extract with nanoparticles enhances the solubility and bioavailability of herbal medicines, allowing for increased uptake. Moreover, using nanosystems, the active component may be delivered to the intended site of action over the course of the treatment period at an appropriate concentration. Conventional therapies do not satisfy them. This chapter discusses herbal medicine's medication delivery method based on nanotechnology and its future prospects.

Keywords: Drug delivery systems, Medicinal plants, Nanotechnology, Natural products.

INTRODUCTION

The understanding and application of plants as herbal remedies have developed in various civilizations throughout the course of human evolution, starting when man first discovered how to choose plants for sustenance and to treat illnesses. However, in the latter half of the 20th century, herbal medicine was gradually replaced by allopathic medicine, especially in the Western world. Allopathic medicine is now used extensively as compared to conventional drugs, particularly in developing nations. In spite of this, the majority of developing nations still rely

* **Corresponding author Rose Rizvi:** Section of Plant Pathology, Department of Botany, Faculty of Life Sciences, Aligarh Muslim University, Aligarh-202002, Uttar Pradesh, India; E-mail: rose.amu@gmail.com

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on these natural remedies, probably due to the high cost of obtaining synthetic drugs. According to the World Health Organization (WHO), in underdeveloped countries, 80% of people rely on cultural practices to meet or complement their health needs. Moreover, due to stability problems and limited lipid solubility, some herbs have significant drawbacks. Most of the normal drugs can reach the target with only a limited amount of control, and most of the drugs will diffuse through the body, reducing the physicochemical and biochemical treatment depending on the product. The supply of active constituents of the majority of the plant species having therapeutic value has great significance in terms of efficacy. The biologically active components found in herbal medicinal extracts, such as tannins, flavonoids, and terpenoids, are incredibly miscible in water but cannot cross cell membranes due to their large molecular size, which results in reduced absorption and reduced bioavailability [1]. Some extracts are not used in practice as a result of these restrictions. Innovative phytomedicine medication delivery systems have been created to solve these issues. These novel drug delivery methods include particle delivery methods including micropellets, microspheres, nanoparticles, and micro- and nanoemulsions, as well as vesicular transport systems like liposomes, ethosomes, phytosomes, and transferosomes [2]. In order to increase stability and bioavailability and reduce toxicity, several natural drugs have been added to these drug-delivery systems. Herbal medications are typically sold in conventional dosage forms, but numerous new techniques, including nanoparticles, are being explored to improve their therapeutic effects and efficient delivery [3].

The usage of herbal remedies has considerably increased in recent years due to nanotechnology. Nanoparticles are regarded as one of the most effective drug-delivery technologies available. An important solution to the problems with herbal remedies that are now being raised is nanotechnology. The development of nano dosage forms for herbal medications has brought about a variety of advantages, according to studies on herbal drugs [4]. These benefits include improved bioavailability, stability, solubility, reduced toxicity, increased biological activity, improved tissue macrophage distribution, regulated delivery, and inhibition of physical and chemical changes and disintegration [5]. Furthermore, due to their distinct size and enhanced carrying capacities, nanodosage form delivery systems are the finest option since they have the greatest ability to administer highly concentrated medication doses to the desired areas. Nanoparticles range in size from 1 to 100 nanometers and are composed of colloidal structures built of alternately synthetic and natural polymers. Depending on the synthesis methods used, nanoparticles can be created in either sphere or capsule form. In nanocapsules, the drug is restricted to a hollow that is surrounded by a specific polymer membrane. In contrast, the drug is evenly and conspicuously distributed in nanospheres [6]. The synthetic biodegradable polymers, polysaccharides, and lipids used to make the nanocarriers are safe to use. Nano-sized substances are known as "nanocarriers" and are primarily used as a component of the transportation system for other materials. The most common types of nanocarriers are polymers, micelles, biological components, liposomes, and other substances. Currently, nanocarriers are used to carry drugs, and they may also be used in chemotherapy due to their outstanding qualities. The body can distribute both hydrophobic and hydrophilic preparations thanks to the use of various nanomaterials in nanocarriers [7]. Since water makes up the majority of a person's body, the main therapeutic impact of nanoparticles is to deliver medications that are not water-soluble to humans effectively. Both water-soluble and insoluble medicines can be held in micelles, depending on the arrangement of the phospholipid particles [4].

DRUG DELIVERY SYSTEMS

The drug delivery system (DDS) is defined by the National Institute of Health, USA, as a formulation of a device that enables the introduction of therapeutic substances into the body and improves efficiency and safety by controlling the rate, time, and place of release of drugs in the body [8, 9]. Drug delivery systems are used in the treatment of various diseases. In conventional DDS, various oral, nasal, mucosal, inhaled, or shot methods are used. There are various drawbacks to conventional DDS, such as their non-selective nature, that may lead to several side effects. Therefore, nanotechnology-based DDS, which uses nanoparticles to deliver drugs, is preferred nowadays. These nanoparticles aim at targeted delivery to reach specific areas of the body with a controlled release. Targeted delivery protects other normal cells of the body and focuses only on the affected areas. Moreover, due to their nano size, these particles can easily penetrate the tissues. The use of nanodrug delivery systems is based on the physicochemical properties of targeted drugs that are selected for treatment [10]. Drugs can be delivered by the following types of nanocarriers:

- **Organic nanocarriers:** These types of nanocarriers include solid lipid nanoparticles, liposomes, dendrimers, virus-based nanoparticles, polymeric micelles, and polymeric nanoparticles.
- **Inorganic nanocarriers:** These types of nanocarriers include mesoporous silica nanoparticles and carbon nanotubes.

Some medicinally important drugs and their respective plant sources are tabulated in Table **1**. The various drugs mentioned above have been used in modern drug delivery systems for achieving targeted delivery using various nanocarriers (Fig. **1**), as mentioned below.

CHAPTER 13

Application of CRISPR-Cas Technique in Enhancing the Phytochemicals Production

Harshita Sahoo[1,#], **Manisha Malhotra**[1,#], **Vikas Kumar Yadav**[1], **Vikash Maurya**[1], **Shweta**[1] and **Akhilesh Kumar**[1,*]

[1] *Department of Botany, Centre of Advanced Study in Botany, Institute of Science, Banaras Hindu University, Varanasi, U.P, India*

Abstract: Plants possess a remarkable skill in the generation of secondary metabolites, which are commonly referred to as phytochemicals. These bioactive molecules are non-nutritive and essential for the growth and expansion of plants. However, these phytochemicals play a critical role in plant resistance against both biotic and abiotic stress. Furthermore, they possess a vast array of pharmaceutical and nutraceutical properties, making them commercially and economically significant. Unfortunately, the synthesis of these compounds is not abundant and can be challenging to extract through a cumbersome chemically synthetic process that is both inefficient and expensive. Fortunately, second-generation CRISPR/Cas technology has proven to be a gateway to enhancing the production of phytochemicals due to its simplicity, efficiency, and target specificity. Therefore, the purpose of this chapter is to discuss the mechanistic role of CRISPR/Cas9, its application in base editing, and its ability to enhance the production of phytochemicals.

Keywords: CRISPR-Cas, Phytochemicals, TALENs, ZFNs.

INTRODUCTION

Plants engage extensively in the production of specialized organic substances, commonly known as secondary metabolites or phytochemicals. These are non-essential and non-nutritive bioactive molecules and hold immense significance to plants as they provide defence against pathogens, regulate signaling pathways, and aid plants in adapting to various biotic and abiotic stressors. In earlier times, these phytochemicals were considered biologically insignificant due to their complex chemical structure and less-known biosynthetic pathways, thus receiving minimal attention from researchers [1]. Nevertheless, organic chemists made effo-

* **Corresponding author Akhilesh Kumar:** Department of Botany, Centre of advanced study in Botany, Institute of Science, Banaras Hindu University, Varanasi, U.P., India; Email: akhilalld@gmail.com

# Contributed equally

rts to explore the chemical characteristics and biosynthesis of these phytochemicals and discovered their capability as therapeutic agents against acute, chronic, and neurodegenerative diseases [2 - 4]. Subsequently, it was also discovered that these bioactive molecules play an influential role in human health and metabolism [5]. Further studies on these phytochemicals have shown their potential pharmaceutical, cosmeceutical, and nutraceutical value [1]. Table **1** specifies some of the biologically significant phytochemicals.

Table 1. Biologically significant phytochemicals.

Biological activity	Phytochemical	References
Anti-carcinogenic	Anthocyanins	[6]
Antioxidant	Lycopene, Rosmarinic acid	[7, 8]
Anti-microbial	Glucosinolates	[9]
Anti-fungicidal	Glucosinolates, Coumarin	
Anti-bacterial, Anti-viral	Glucosinolates, Anabasine, Coumarin	[10, 11]
Anticancer	Lycopene, Resveratrol, Paclitaxel, Sanguinarine, Artemisine, Berberine	[12 - 15]
Anticoagulant	Coumarin	[16]
Anti-inflammatory, Diabetes alleviation	Coumarin, Anthocyanins,	[6, 11]
Cardiovascular diseases	Crocetin, Ginsenoside	[17, 18]
Obesity control	Anthocyanins	[6]
Mitotic inhibitor	Vincristine	[19]

These specialized metabolites are often classified into different types depending on their chemical makeup or biosynthesis or can be classified based on dietary values. Nielsen *et al.* classified phytochemicals into three primary groups based on their biosynthesis: terpenes or terpenoids, nitrogen-containing compounds or alkaloids, and phenolic compounds [5, 20]. Almeida *et al.* classified these phytochemicals into eight classes based on their chemical nature [21]. Phenolic compounds, terpenes, betalains, organosulfur compounds, organic acids, quinones, methylxanthines, and alkaloids [22 - 29], whereas, Liu has classified the dietary phytochemicals [30]. An elaborated combined classification is shown in Fig. (**1**).

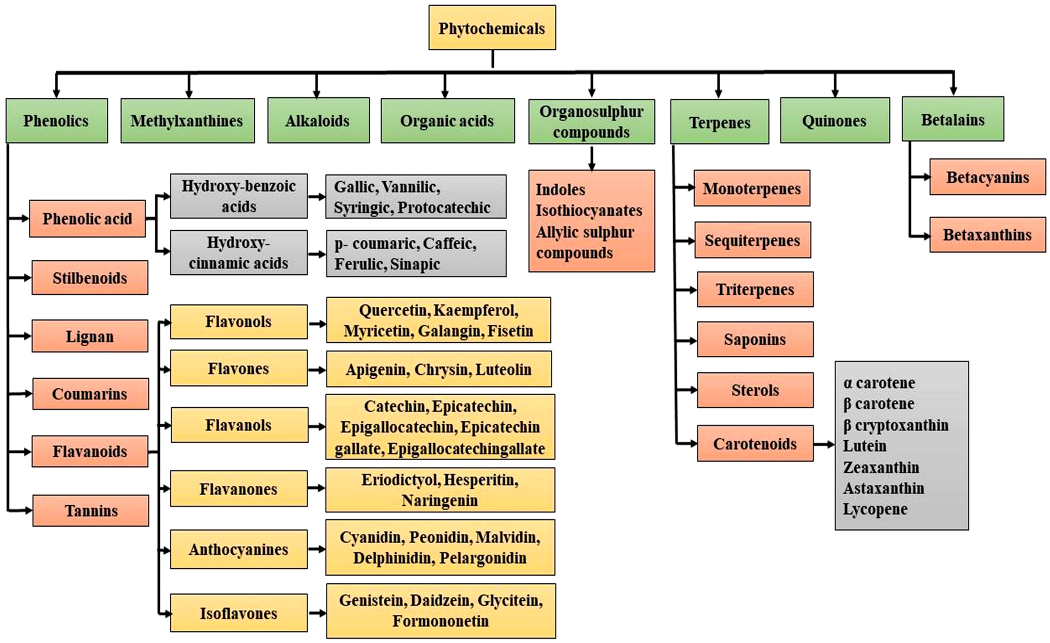

Fig. (1). Schematic representation of the primary classes of phytochemicals [31, 32].

Terpenoids, since derived from isoprene units, are also termed isoprenoids and are potentially involved in providing plants with defence against phytophagous organisms. Furthermore, various terpenoid-based compounds, for instance artemisinin, obtained from *Artemisia annua*, taxol from *Taxus brevifolia,* and cardenolides from *Digitalis purpurea* are involved in the treatment of malaria, cancer [12, 20], heart failure and arrhythmia [33] respectively, hence they are pharmacologically valuable. Other compounds, such as lutein and lycopene, have nutraceutical importance [12]. Another category involves Alkaloids, which are nitrogen-containing compounds derived from amino acids [34]. Various pharmacologically important alkaloids function as anticholinergics, such as scopolamine, obtained from the Solanaceae family, analgesics such as codeine and morphine, obtained from Papaveraceae; anti-cancer drugs, such as vincristine and vinblastine, obtained from Acanthaceae, camptothecin from *Camptotheca acuminata.* The third category includes phenolics, which are aromatic compounds with broad range applications such as in defence, as antioxidants, in pharmacology, and in nutraceuticals. Anthocyanin, for instance, functions as ananti-infammatory and anti-carcinogenic compound [2], some compounds, for instance, Etoposide and teniposide, derived from podophyllotoxin, a lignan from *Podophyllum peltatum,* function as chemotherapeutic agents [20].

CHAPTER 14

Metabolomics Quantitative Trait Loci Mapping of Medicinal Plants and Crops

Pratiksha Verma[1,#], **Vikash Maurya**[1,#], **Vikas Kumar Yadav**[1], **Manisha Malhotra**[1], **Shweta**[1] and **Akhilesh Kumar**[1,*]

[1] *Department of Botany, Centre of Advanced Study in Botany, Institute of Science, Banaras Hindu University, Varanasi, U.P., India*

Abstract: Genetic association studies and quantitative trait loci (QTL) analysis serve as indispensable tools for identifying genes and genomic regions associated with various traits. The rapid development of genomics and its application in plant breeding has profoundly impacted the field, fostering discoveries and revolutionizing breeding strategies. For a better understanding of plant physiology, complete information on biochemical pathways is imperative across different organizational levels, encompassing simple to intricate networks that regulate trait expression. Over the past decades, the emergence of metabolomics as a vital branch of "omics" has played a pivotal role in determining and quantifying metabolites governing cellular processes. The combination of metabolomics and post-genomic approaches has recently allowed proficient examination of genetic and phenotypic associations in cultivated crops. A novel and powerful methodology, Metabolomic Quantitative Trait Locus (mQTL) mapping, has emerged as an approach to unravel the genetic components and loci contributing to the variability in metabolic profiles. This chapter provides an in-depth exploration of mQTL mapping in both medicinal and crop plants, elucidating its significance in unraveling the intricate interplay between genetics and metabolic pathways.

Keywords: GC-MS, Metabolomics, Metabolites, mQTL, NGS.

INTRODUCTION

Since ancient times, the rich diversity of flora has been harnessed for various purposes, ranging from sustenance and energy to traditional medicine. In many parts of African and Asian countries, the majority of people rely on old herb-based medications for disease management [1]. Beyond their utilitarian roles, plants provide a wide range of specialized metabolites, serving as fragrances, flavours, pigments, and insecticides. It is assumed that the plant kingdom contains

[*] **Corresponding author Akhilesh Kumar:** Department of Botany, Centre of Advanced Study in Botany, Institute of Science, Banaras Hindu University, Varanasi, U.P., India; E-mail: akhilalld@gmail.com

[#] Contributed equally

about 200,000 -100,0000 specialized metabolites; however, the majority of them remain unexplored and unidentified [2 - 4].

Over time, the rapid growth of the world population has led to the depletion and shrinkage of arable land, which has ultimately increased the demand for crop production. Environmental changes, such as unseasonal rain, floods, and heat, are affecting natural systems, human health, and agriculture, and these are seen very commonly in recent times [5]. Furthermore, the challenge is to develop fast and effective drugs for treating complex diseases, as the world is already confronting issues of a widespread increase in various diseases.

Conventional methods for discovering plant-based medications are very costly and time-consuming [6, 7]. Therefore, multidimensional strategies must be used to overcome food and medicine crises. Genetic engineering has enhanced the crop yield and allowed further modification by adding desirable traits and removing unwanted ones, thereby improving quality and providing more excellent resistance to stress. Before the advent of genomics, scientists utilized a one-gene-at-a-time approach to comprehend the roles of individual genes in the way plants respond to stress and other factors [8]. The rapid progress in genomics and its integration into plant breeding in recent decades has greatly facilitated discoveries and transformed the field of plant breeding.

Genetic association studies and quantitative trait loci (QTL) mapping are widely used for identifying genes and genomic regions linked to traits [9 - 11]. Strategies that rely on linking DNA markers with advantageous characteristics, like Marker-assisted selection (MAS), have become a standard technique in the field of plant breeding [12 - 15]. In spite of these advancements, creating novel crop varieties does not consistently lead to fruitful outcomes [16, 17]. To enhance our comprehension of plant physiology, complete information on biochemical pathways is essential at various organizational levels, spanning from basic to intricate networks that control trait expression.

Currently, the progress in “omics,” including genomics, transcriptomics, proteomics, metabolomics, and epigenomics, offers valuable insights into the role of certain uncharacterized genes and their associated molecular working in specific plant activities. Several investigations have been performed on metabolomics in the last 2-3 decades, as it represents a vital branch of “omics” that determines and measures the metabolites responsible for controlling cellular processes. Moreover, it is used to uncover environment-gene interactions, characterize mutants, characterize phenotypes, identify biomarkers, and discover new drugs [9]. Consequently, a plant's metabolome is closely related to its phenotype, as it provides an insight into its physiological and biochemical status under stress conditions [8]. Furthermore, the use of advanced analytical instruments such as high-performance liquid chromatography (HPLC), nuclear magnetic resonance spectroscopy (NMR), and mass spectrometry techniques are integral in accelerating metabolite profiling and understanding the relationship between agronomic traits and genomic diversity [18 - 20].

The combination of metabolomics and post-genomic approaches has recently allowed proficient examination of genetic and phenotypic associations in cultivated crops. Metabolic quantitative trait loci (mQTL) are genetic loci that are associated with variations in metabolic traits [21]. mQTL mapping decodes the impact of genetic loci on diverse metabolite levels and traits, potentially unveiling novel genes crucial for governing essential metabolic pathways [21, 22]. The growing emphasis of plant breeding scientists on linking mQTLs to genetic variants is motivated by multiple factors. Additionally, the utilization of mQTL mapping enables the identification of the biological functions of metabolites, allowing plant breeders to pinpoint specific metabolites that could serve as biomarkers for resisting both biotic and abiotic stresses [21]. Utilizing mQTL data could help the creation of climate-smart crop varieties fortified with essential nutrients, thereby promoting specific and sustainable food production and security [23]. Ultimately, mQTL mapping has the potential to reduce the gap between phenotype and genotype, a challenge observed in various complex traits, offering significant potential to address future advanced research questions [21].

METABOLOMICS

Metabolomics refers to a complete quantitative examination of metabolites, providing insights into the composition of metabolites in a given biological system [24]. In the omics field, metabolomics has emerged as a significant scientific advancement in recent years, enabling precise metabolite profiling in plants [25]. This development has received considerable attention in crop science, particularly in the areas of trait mapping and the selection of crop plants.

Metabolomics primarily focuses on examining alterations in low molecular weight metabolites within a specific sample, influenced by either endogenous or environmental factors [26]. It involves identifying and quantifying metabolites and studying metabolite profiles dependent on the locations and genotypes [26]. Research studies have witnessed a vast growth in understanding how plants handle abiotic stresses, resist pathogens, and improve their genetics through metabolomics. Metabolomics tools have proven to be extremely useful in enhancing crop performance in terms of robust ecotypes, pathogen resistance, stress tolerance, and metabolic-assisted breeding [27]. It is an encouraging method for deciphering numerous metabolic networks linked with tolerance to

CHAPTER 15

Pathways of Important Metabolites and Enzymes Involved

Jahanvi Ganotra[1], **Damini Supolia**[1], **Akanksha Sharma**[1], **Meenakshi Raina**[2], **Neelam Prabha Negi**[3], **Vibhav Gautam**[4] and **Deepak Kumar**[5,*]

[1] *Department of Botany, Central University of Jammu, Rahya-Suchani (Bagla), Samba-181143, J&K, India*

[2] *Department of Biosciences, IMS Ghaziabad (University Courses Campus), Adhyatmik Nagar, Ghaziabad, Uttar Pradesh, India*

[3] *Plant Biotechnology division: CSIR-Central Institute of Medicinal and Aromatic Plants, Lucknow, Uttar Pradesh, India*

[4] *Centre of Experimental Medicine & Surgery, Institute of Medical Sciences, Banaras Hindu University, Varanasi-221005, Uttar Pradesh, India*

[5] *Centre for Advanced Study in Botany, Institute of Science, Banaras Hindu University, Varanasi-221005, Uttar Pradesh, India*

Abstract: Plants produce diverse chemical compounds that play a crucial role not only in plant growth and development but also hold great economic and ecological importance for mankind. Plants synthesize these compounds to cope with various abiotic and biotic stresses and also in response to the incessantly changing surrounding environment. Broadly, these compounds are categorized as primary and secondary metabolites. While the former play direct roles in plant growth, development, functioning, defense, and stress tolerance, the latter do not hold any direct importance in the growth and development of plants. Primary metabolites include carbohydrates, organic acids, flavonoids, vitamins, amino acids, glucosinolates, hormones, and phenolics. These are also widely used by humans as dietary compounds. Secondary metabolites, on the other hand, can be broadly sub-divided into four major groups, *i.e.*, terpenoids, phenols, alkaloids, and sulphur-containing compounds. These compounds perform various other physiological roles like protecting plants against microbes and herbivory, insect repellents, allelopathic agents, attractants for pollinators and seed dispersal agents, regulating symbiosis, providing structural support to plants, and alleviating biotic stresses. Additionally, they are also extensively used in cosmetics and pharmaceutical industries, as well as the production of fragrances, drugs, dietary supplements, dyes, and flavours. Although, a myriad of these metabolites are synthesized by plants, and are basically derived by modifying the basic chemical structure of compounds already present in plants. This chapter, therefore, elucidates the

* **Corresponding author Deepak Kumar:** Centre for Advanced Study in Botany, Institute of Science, Banaras Hindu University, Varanasi-221005, Uttar Pradesh, India; E-mail: deepakkumar@bhu.ac.in

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biosynthetic pathways of some of the major plant metabolites, giving special attention to the key enzymes involved.

Keywords: Nitrogen compounds, Methyl jasmonate, Phenolic compounds, Secondary metabolites, Terpenes.

INTRODUCTION

Numerous organic compounds produced by plants showcase no direct association with growth and development. These diverse compounds, termed secondary metabolites, originate from the primary metabolic pathways. Unlike primary metabolites, plants do not require secondary metabolites for their vital biological processes (*e.g.*, photosynthesis, respiration, protein synthesis, and nutrient assimilation). However, plant secondary metabolites act as an important subject of research interest and are endowed with enormous potential, making them suitable for utilisation in cosmetics, perfumery, agriculture, food, and pharmaceutical sectors worldwide. Additionally, secondary metabolites in plants are species-specific and organ-specific [1 - 3]. Furthermore, owing to the sessile lifestyle, plants are usually subjected to a plethora of potential rivals under natural conditions. The prerequisite for the perpetuation of plants throughout evolution has been the development of multiple defense strategies to deter phytopathogens. These defense mechanisms, in turn, show an association with the formation of secondary metabolites. Furthermore, biosynthesis, as well as the accumulation of secondary metabolites in plants, is highly inducible in response to a range of abiotic and biotic environmental cues [2]. The present chapter embodies an overview of various plant secondary metabolites, their classification, and bioactivities, in addition to the elucidation of respective biosynthetic pathways and enzymes involved. The biosynthetic pathways for plant secondary metabolites are performed by employing various building blocks, such as mevalonic acid (terpenes, steroids), shikimic acid (phenols, aromatic alkaloids, tannins), acetate-malonate (alkaloids and phenols), and pentose (glycosides, polysaccharides) [4].

SECONDARY METABOLITES

Plants produce a repertoire of compounds referred to as secondary metabolites. While these compounds do not exhibit paramount significance in primary vital processes, their absence can curtail varied survival functions. These include defense against pathogens and contributing features, namely color, taste, and odor for pollinators and seed dispersers, in addition to mediating plant-plant competition and plant-microorganism symbioses [3, 5, 6]. Plants encounter a variety of abiotic and biotic stress conditions, including CO_2 levels, drought, solar radiation, and attack by pathogens and herbivores can further result in the synthesis and accumulation of secondary metabolites (Table **1** & **2**) [2, 3]. Depending on the biosynthetic pathways, plant secondary metabolites are grouped into three distinct categories: terpenes, phenols, and nitrogen compounds.

Table 1. A list of the type of secondary metabolites produced in plants during various abiotic stresses.

Plant Name	Common Name	Plant Family	Type of Abiotic Stress	Type of Secondary Metabolite Production	References
Salvia miltiorrhiza	Red sage, Chinese sage, Tan shen, or Danshen	Lamiaceae	Hyperosmotic stress	Diterpenes (Tanshinone)	[7]
Panax quinquefolius	American ginseng	Araliaceae	Light stress	Triterpenes (Ginsenosides)	[8]
Solanum lycopersicum	Tomato	Solanaceae	Light stress/ Temperature stress	Diterpenes (Phytol)	[9]
Catharanthus roseus	Cape periwinkle, rose periwinkle, bright eyes, graveyard plant	Apocynaceae	UV-B stress	Alkaloid (Vincristine/ Vinblastine)	[10]
Artemisia annua	Sweet wormwood, sweet annie, sweet sagewort	Asteraceae	UV-B stress	Artemisinin	[11]
Brassica oleracea	Cabbage	Brassicaceae	UV-B stress	Glucosinolates (Neoglucobrassicin and Glucoraphanin)	[12]
Papaver somniferum	Opium poppy	Papaveraceae	Drought	Alkaloids (Morphine)	[13]
Scrophularia ningpoensis	Ningpofigfort/ Chinese figwort	Scrophulariaceae	Drought	Glycosides (Irdoid)	[14]
Eucomis autumnalis	Pineapple flower	Asparagaceae	Drought	Monoterpenes (Iridoids)	[15]
Pisum sativum	Garden pea	Fabaceae	Drought	Flavonoids	[16]
Thymus vulgaris	Spearmint/Thyme	Lamiaceae	Drought	Monoterpenes (Cineole)	[17]
Sesamum indicum L.	Sesame	Pedaliaceae	Salinity	GABA	[18]
Olea europaea	Olive	Oleaceae	Salinity	Polyphenolic (Oleuropein)	[19]
Brassica oleracea	Cabbage	Brassicaceae	Salinity	Glucosinolates (Sinigrin)	[20]
Gossipium	Cotton	Malvaceae	Salinity	Gossypol	[21]

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Mallappa Kumara Swamy

Prof. Mallappa Kumara Swamy is a professor and the head of the Department of Biotechnology at East West First Grade College, Bengaluru, India. He completed his post-doctoral research at the Department of Crop Science, Faculty of Agriculture, University Putra Malaysia (UPM), Serdang, Malaysia. Before that, he had worked as an associate professor and the head of the Department of Biotechnology, Padmashree Institute of Management and Sciences, Bangalore University, Bengaluru, India. He received Ph.D. in biotechnology from Acharya Nagarjuna University, Guntur, India, in 2013. He has more than 20 years of teaching and research experience in the fields of plant biotechnology, secondary metabolite production, phytochemistry, and bioactive studies. He has authored 74 research publications in peer-reviewed journals and 68 book chapters. Recently, he has edited 13 books published by Springer Nature Singapore Pvt. Ltd., Singapore. He is serving as an editorial board member and reviewer for several high-impact factor international journals. His current research is focused on cell and tissue culture technology, phytochemistry, phytocompounds isolation, production and their biological evaluation, and nanotechnology for medical applications.

Mohd. Sayeed Akhtar

Prof. Mohd. Sayeed Akhtar works as senior assistant professor in Gandhi Faiz-e-Aam College, Shahjahanpur, U.P., India. He received Ph.D. from Aligarh Muslim University (AMU), Aligarh, India in 2008, prior to conducting post-doctoral research at the Botanical Institute, University of Basel (BIB), Switzerland (2008–2010), and Chonbuk National University (CBNU), Republic of Korea in 2011. He worked as an assistant professor at Jimma University in Ethiopia from 2011 to 2014 and as a fellow researcher at Universiti Putra Malaysia's (UPM) Institute of Tropical Agriculture from 2014 to 2015. He is author and co-author of more than 150 articles in peer-reviewed journals, conference proceedings, and book chapters, and has edited 30 books with International publishers. He received numerous honors and awards. His current work focuses on the molecular biotechnology, bioremediation, biomineralization, nano-fertilizers, and nanobiotechnology of rhizospheric plant-microbe interactions.