AUTOIMMUNE DISORDERS AND SECONDARY PLANT METABOLITES

PART 1

Editors:
M.S. Ashawat
Aditi Kaushik
Akash Jain
Jasmine Chaudhary
Manish Kaushik

Bentham Books

Autoimmune Disorders and Secondary Plant Metabolites

(Part 1)

Edited by

M.S. Ashawat
Department of Pharmaceutics
Laureate Institute of Pharmacy
Kangra, Himachal Pradesh, India

Aditi Kaushik
Department of Pharmaceutical Chemistry
Laureate Institute of Pharmacy
Kangra, Himachal Pradesh, India

Akash Jain
Department of Pharmacology
M.M. College of Pharmacy, M.M. (Deemed to be University)
Mullana, Ambala, Haryana, India

Jasmine Chaudhary
Department of Pharmaceutical Chemistry
M.M. College of Pharmacy, M.M. (Deemed to be University)
Mullana, Ambala, Haryana, India

&

Manish Kaushik
Department of Pharmacology
SBS College of Pharmacy
Kangra, Himachal Pradesh, India

Autoimmune Disorders and Secondary Plant Metabolites *(Part 1)*

Editors: M.S. Ashawat, Aditi Kaushik, Akash Jain, Jasmine Chaudhary and Manish Kaushik

ISBN (Online): 979-8-89881-234-8

ISBN (Print): 979-8-89881-235-5

ISBN (Paperback): 979-8-89881-236-2

Published by Bentham Science Publishers Pte. Ltd. Singapore, in collaboration with Eureka Conferences, USA.

First published in 2025.

need for a court order if at any point you breach any terms of this License Agreement. In no event will any delay or failure by Bentham Science Publishers in enforcing your compliance with this License Agreement constitute a waiver of any of its rights.

3. You acknowledge that you have read this License Agreement, and agree to be bound by its terms and conditions. To the extent that any other terms and conditions presented on any website of Bentham Science Publishers conflict with, or are inconsistent with, the terms and conditions set out in this License Agreement, you acknowledge that the terms and conditions set out in this License Agreement shall prevail.

Bentham Science Publishers Pte. Ltd.
No. 9 Raffles Place
Office No. 26-01
Singapore 048619
Singapore
Email: subscriptions@benthamscience.net

CONTENTS

FOREWORD

The contents of the book "Autoimmune disorders and Secondary Plant Metabolites" have been read in detail by me and it contains highly useful information on the important functions of the secondary plant metabolites in the management of various autoimmune disorders. The editors of this book are the experts who have been working in the field of Pharmaceuticals for years and are known in the subjects of their specializations. Their focused and multidisciplinary approach aims to introduce the basic insights of the book and emphasizes the comprehensive use of the secondary plant metabolites.

All the chapters have been authored by a group of dedicated academicians and scientists who actively engaged in the field of the design and development of novel pharmaceuticals in the management of different autoimmune disorders. As a medical expert for more than 20 years, I foresee that this book will be of great value not only to postgraduates, teachers and research scholars in the field of Pharmaceuticals, but also to the industrial and scientific communities. This work contains substantial data for emphasizing herbal therapeutics as one the newer approach for the design and development of novel pharmacophore and their derivatives in the management of various autoimmune disorders.

In this post-COVID era, phytotherapy would be effectively utilized for the treatment of various diseases more effectively. The overall detail of the subject by the various authors in the different chapters of this book would go a long way in throwing new light on the area of autoimmune disorders.

I sincerely hope this venture is a great success, as it reflects the devotion, dedication and hard work of the team of editors. I am confident that this book will be very useful and gain enough attention from research scholars and academicians working in the field of medical and pharmaceuticals.

May the spirit of discovering better future remedies and optimizing phytopharmaceuticals provide superior medication to the benefit of humanity.

Nor Farid Bin Mohd Noor
Faculty of Medicine
Universiti Sultan Zainal Abidin (UniSZA)
Medical Campus, Jalan Sultan Mahmud
Kuala Terengganu 20400, Terengganu
Malaysia

PREFACE

The human immune system is a multi-faceted network of functionally diverse cells expressing a broad array of receptors that collectively function to respond to infection, eliminate precancerous cells, and maintain metabolic health. The breakdown of this delicately poised immune response is typically life-limiting; however, even subtle changes in its ability to distinguish an invading pathogen from the host can give rise to a spectrum of autoimmune diseases. Indeed, autoimmune diseases affect approximately 5%–8% of the world population and cause tremendous suffering to patients while also representing a major global socioeconomic issue. Although detailed molecular, immunological, genetic, and clinical studies have provided an increasingly sophisticated understanding of the mechanisms that underpin some autoimmune diseases, the drivers of human autoimmune diseases, including environmental triggers and the ensuing pathogenesis, remain poorly understood. In general, current immune-modulatory drugs used in the treatment of autoimmune diseases are broadly acting, non-disease specific, and, consequently, associated with side effects such as infection and malignant disease. Furthermore, it is clear that the majority of patients are not responding optimally to these therapies. Thus, there is a pressing need for the development of new drugs or repositioning of drugs based on a molecular and clinical understanding of the specific autoimmune diseases in individual patients in combination with high-throughput analysis of integrated datasets. Such personalized medicines may go hand in hand with the inclusion of new diagnostics, leading to a better disease understanding and more patient-centric clinical trials that also consider ethnic diversity and patient-reported outcome measures. Prevention should also be part of future early intervention. This book's perspective will highlight the different types of current therapies and showcase how future basic studies, new technologies, and clinical trials could dynamically and reciprocally inform each other, leading to a better understanding of disease mechanisms and, hence, more refined treatments.

Treatment of autoimmune diseases has drastically changed over the last 20 years with development and routine clinical use of synthetic or biologic drugs that block various pathways and components of the immune system, such as cytokines, cell adhesion molecules, and co-stimulatory molecules, or delete entire immune cell populations.

The novelty intensifies in this book's content, reflecting growing interest in exploring herbal alternatives as complementary or alternative therapies for autoimmune diseases. While these herbal options show promise, it is essential to consult with a healthcare professional before incorporating them into your treatment plan. Individual responses may vary, and personalized approaches are crucial for managing autoimmune disorders effectively. Always prioritize safety and work closely with your healthcare provider to find the best combination of therapies for your specific condition. The different plant’s secondary metabolites play a significant role in modern therapy, including the treatment of autoimmune disorders. Insides of book where the attempt is made to focus on the Plants secondary metabolites, have gained prominence due to their relative safety and multifunctionality. Phytoconstituents offer better pharmacokinetic profiles and reduced adverse effects compared to synthetic drugs. Hundreds of phytoconstitutents have shown promising results in biochemical and cell line studies. Certain phytoconstitutents have been studied for their potential in managing autoimmune disorders. In summary, plant secondary metabolites offer a diverse array of therapeutic possibilities, making them valuable allies in the quest for better health. Thus, the research in the field of autoimmune disorders and secondary metabolites increased the hope of the scientific community. This book is focused on the role of various secondary plant metabolites in the management of different autoimmune disorders. The contents are divided into two sections wherein the first section focuses on the basics of autoimmunity as well as the

interrelationship between autoimmune disorders, medicinal plants and drug discovery. The second section of this book strikes, therefore, a great balance at the described role of the secondary plant metabolites in different autoimmune disorders.

M.S. Ashawat
Department of Pharmaceutics
Laureate Institute of Pharmacy
Kangra, Himachal Pradesh, India

Aditi Kaushik
Department of Pharmaceutical Chemistry
Laureate Institute of Pharmacy
Kangra, Himachal Pradesh, India

Akash Jain
Department of Pharmacology
M.M. College of Pharmacy, M.M. (Deemed to be University)
Mullana, Ambala, Haryana, India

Jasmine Chaudhary
Department of Pharmaceutical Chemistry
M.M. College of Pharmacy, M.M. (Deemed to be University)
Mullana, Ambala, Haryana, India

&

Manish Kaushik
Department of Pharmacology
SBS College of Pharmacy
Kangra, Himachal Pradesh, India

List of Contributors

Ashwani K. Dhingra	Department of Pharmaceutical Chemistry, Global Research Institute of Pharmacy, Radaur, Yamuna Nagar 135133, Haryana, India
Ashna Gupta	Department of Pharmaceutics, Guru Gobind Singh College of Pharmacy, Yamunanagar, India
Asbar Banu Bazeer	Department of Medical Biotechnology, Aarupadai Veedu Medical College & Hospital, Vinayaka Mission's Research Foundation (Deemed to be University), Kirumampakkam, Puducherry 607403, India
Bipindra Pandey	Department of Pharmacy, Madan Bhandari Academy of Health Sciences, Hetauda, Nepal
Balaji Govindaswamy	Department of Biotechnology, Bhupat and Jyoti Mehta School of Biosciences, Indian Institute of Technology Madras, Chennai 600042, Tamil Nadu, India
Chandrasekar Ponnusamy	Department of Biotechnology, Rathinam College of Arts and Science, Coimbatore 641021, Tamil Nadu, India
Divya Dhawal Bhandari	Department of Pharmaceutical Chemistry, University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh, Punjab, India
Ekambaram Gayathiri	Department of Plant Biology and Plant Biotechnology, Guru Nanak College (Autonomous), Chennai 600042, India
Jasmeen Kaur	Department of Pharmaceutics, Global Research Institute of Pharmacy, Radaur, Yamuna Nagar 135133, Haryana, India
Kulvinder Kaur	Department of Pharmacy, Global Research Institute of Pharmacy, Radaur, Yamuna Nagar 135133, Haryana, India
Kirtik Ramadoss	Department of Medical Biotechnology, Aarupadai Veedu Medical College & Hospital, Vinayaka Mission's Research Foundation (Deemed to be University), Kirumampakkam, Puducherry 607403, India
Megha Ashawat	Department of Pharmaceutics, Bansthali Vidyapith University, Newai Jaipur, India
Mahalakshmi Suresha Biradar	Department of Pharmaceutical Chemistry, Al-Ameen College of Pharmacy, Bengaluru, India
Manisha Bhatia	Department of Pharmacognosy, MM College of Pharmacy, Maharishi Markandeshwar (Deemed to be University), Mullana, Ambala, India
Murugappan Kumarappan	Department of Biotechnology, School of Biotechnology and Genetic Engineering, Bharathidasan University, Tiruchirappalli 620024, Tamil Nadu, India
Pratima Rao	Department of Applied Sciences, Laureate Institute of Pharmacy, Kangra, India
Prerna Sarup	Department of Pharmacognosy, University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh, Punjab, India
Parul Gupta	Department of Pharmaceutics, Guru Gobind Singh College of Pharmacy, Yamunanagar, India

Palanisamy Prakash	Department of Botany, Periyar University, Periyar Palkalai Nagar, Salem 636011, Tamil Nadu, India
Poorna Chandrika Sabapathy	Directorate of Medical Research, Research and Innovation Lab, Aarupadai Veedu Medical College & Hospital, Vinayaka Mission, India
Prithiviraj Nagarajan	Department of Medical Biotechnology, Aarupadai Veedu Medical College & Hospital, Vinayaka Mission's Research Foundation (Deemed to be University), Kirumampakkam, Puducherry 607403, India
Ravindra Khadka	School of Health and Allied Sciences, Pokhara University, Kaski, Pokhara, Nepal
Rashmi Bhamra	Department of Pharmacy, Global Research Institute of Pharmacy, Radaur, Yamuna Nagar 135133, Haryana, India
Rupa Devi	Department of Pharmaceutics, Global Research Institute of Pharmacy, Radaur, Yamuna Nagar 135133, Haryana, India
Rohit Kamboj	Department of Pharmaceutics, Guru Gobind Singh College of Pharmacy, Yamunanagar, India
Ramachandran Kaliaperumal	Department of Biochemistry, Sri Manakula Vinayagar Medical College and Hospital, Madagadipet, Kalitheerthalkuppam, Puducherry 605107, India
Shankar Thapa	Department of Pharmacy, Madan Bhandari Academy of Health Sciences, Hetauda, Nepal
Sarath Perumal	Department of Biotechnology, School of Bio-science and Technology, Vellore Institute of Technology, Vellore 632014, Tamil Nadu, India
Sweta Kamboj	Department of Pharmaceutics, Guru Gobind Singh College of Pharmacy, Yamunanagar, India
Shikha Kamboj	Department of Pharmaceutics, Guru Gobind Singh College of Pharmacy, Yamunanagar, India
Suganya Kannan	Central Research Laboratory for Biomedical Research and Molecular Biology, Vinayaka Mission's Medical College and Hospital, Vinayaka Mission's Research Foundation, Karaikal, Puducherry 609609, India
Sharangouda J. Patil	Department of Zoology, NMKRV College for Women, Bengaluru 560011, Karnataka, India
Vishakha Saini	Department of Pharmaceutics, Global Research Institute of Pharmacy, Radaur, Yamuna Nagar 135133, Haryana, India
Varinder Kaur	Department of Pharmacy, Global Research Institute of Pharmacy, Radaur, Yamuna Nagar 135133, Haryana, India

CHAPTER 1

Introduction to Immunology and Autoimmune Disorders

Megha Ashawat[1] and **Pratima Rao**[2,*]

[1] *Department of Pharmaceutics, Bansthali Vidyapith University, Newai Jaipur 304021, Rajasthan, India*

[2] *Department of Applied Sciences, Laureate Institute of Pharmacy, Kangra 176031, Himachal Pradesh, India*

Abstract: From the very moment our heart starts to beat, and we take our first breath, there is an army of cells and tissues that make up organs and a system that stands in our defense called the **'Immune system.'** The immune system responds to foreign molecules like viruses, bacteria, or any other organic molecule that is not familiar to the body and the extrinsic particles that, however, can cause us damage whilst not attacking its cells with specific identifiers. This remarkable and intricate network is called the immune system, and as complex as it is, it is fascinating. To study this system, we have a very delicate and integral part of the medical field called **'Immunology.'** Several physiological processes are intertwined with the elaborate defensive system, like clotting, wound healing, maintenance of body temperature, and much more. This chapter will walk you through the fundamentals of immunology, like diverse types of immunities, and what can happen if the body attacks its own cells, such as accidental betrayal. The accident is medically called **the 'Autoimmune disorder,'** which occurs as a result of neglected self-tolerance, leading to attacking the body's own tissues and network systems. Factors like genetics, environment, and lifestyle are generally taken into consideration to diagnose and further treat an autoimmune disorder. Though this is not an event that is often experienced in the body, it might occur sometimes, which leads us to study it and prevent it. Additionally, we will be talking about why and how this accidental betrayal usually happens.

Keywords: Antibodies, Autoimmune disorder, Bacteria, Body defense, Cells, Clotting process, Defense system, Diagnostics, Environment factors, Foreign molecules, Genetics, Immune response, Immune system, Immunology, Lifestyle factors, Pathogens, Physiological processes, Self-tolerance, Tissue network, Wound healing.

[*] **Corresponding author Pratima Rao:** Laureate Institute of Pharmacy, Kathog, Kangra, Himachal Pradesh, India; E-mail: pratimalgs@gmail.com

WONDERFUL WORLD OF IMMUNITY

Ever wondered what it looks like on the inside of our body? Let us open that door today. Imagine a highly trained bodyguard, never resting and protecting you 24/7 from when you are surrounded by germs and harmful foreign substances. That is what our immune system is…

The word immunity comes from the Greek word *"Immunis,"* which, if laid down into basic terms, means protection. Immunity is one's bodily ability to protect oneself from diseases by becoming resistant to them. It is an in-built system for our body, just like the respiratory or cardiovascular system [1 - 5]. The system is extensively evolving to shield human bodies from harmful microorganisms and those invading foreign substances that can potentially cause harm to the delicate system. The cells and molecules in the immune system work together as a network and relay between two major activities called recognition and response. The ability of the immune system to recognize and differentiate between self and non-self makes it so prolifically specific. After recognizing whether the substance is self or non-self, the next major activity is response. Once the system recognizes the foreign substance as harmful, it sends an army of cells and molecules to produce an appropriate response without affecting the body's own cells [6, 7]. But, like every other thing in the world, this system can also go wrong sometimes, which can diverge into two cases, namely, immunodeficiency and hypersensitivity. Immunodeficiency can result in extreme weakness of the system, which is generally caused by Human Immunodeficiency Virus (HIV), which therefore turns the body into a fragile system that can be fatal even after a common cold. On the other hand, if the system gets hyperactive, it turns into an allergy that is deadly if not treated in time [8] [9].

HISTORY OF IMMUNIZATION

Immunization dates back centuries, when, in the late fifth century BC, a plague struck Athens. The Europeans mentioned the concept for the first time. Thucydides, in his writings, observed that- "only those who have recovered from the illness can nurse the sick as the disease cannot attack the same person twice, at least not fatally". This was an astute and significant observation that made people recognize the concept of immunization [10].

Similarly, the Chinese used to powder the skin lesions of people recovering from smallpox and then make children inhale that to make them immune to the disease. As the technique began to expand its way to Asia, Europe, and Africa, progress was only made in the late seventeenth century. Cotton Mather, with his friend Dr. Zabdiel Boylston, in 1721 decided to inoculate his patients with smallpox pustules. People adopted the technique enthusiastically to immunize their children

when the Prince of Wales, U.K., in 1722 had their children immunized with smallpox residues [11].

In 1798, came Edward Jenner famously known as the Father of Vaccination, created the world's first successful vaccine. He analyzed and adopted techniques from previous studies and observed that housekeepers in the era who contracted cowpox once were particularly safe from the smallpox infection too. In the year 1786, Jenner inoculated an eight-year-old boy with cowpox lesions, allowing the system to develop immunity. Later, he infected the same boy with infectious smallpox pus, but the disease did not produce any notable effect on the boy. This experiment finally concluded the theory given by Thucydides in 430 B.C. The technique was called 'vaccination'. The term was derived from a Latin word, '*Vacca*', meaning 'cow', highlighting the significance of cowpox in the discovery process [12].

Although this discovery represented a monumental breakthrough in the field of immunology, the scientists were not able to comprehend how the system brings about protection. In 1879, Louis Pasteur conducted another similar experiment to study the pathogenesis of bacteria *(Pasteurella multocida)* that causes cholera. In the meantime, he contributed to an astute observation as to how vaccines work. It all started when he went on a vacation and told his assistant to inject the chicken in an experiment with the bacterial culture. Somehow, the process got delayed, resulting in an aged bacterial culture to inject. To their astonishment, they found that the inoculated chicken had not died. The immune chickens survived the second dose of bacterial culture, too. This remarkable insight clicked as the phenomenon of vaccination once again. It was then concluded that chickens injected with dead and aged culture bacteria were protected against the disease. The discovery marked the successful invention of the vaccine against rabies and *Bacillus anthracis* [13].

Although the nineteenth century laid the foundation for prolific advancements, the twentieth century witnessed some tremendous developments, including Karl Landsteiner's strong advancements in the field of immunology, as depicted in Table **1**. He discovered the four primary blood groups and received a Nobel Prize for them. In 1943, along with Merrill Chase, he discovered 'delayed hypersensitivity'.

INTRODUCTION

Immunity refers to resistance or exemption from disease. By recognition and response, the system identifies and eliminates harmful substances from the body. The immune system mechanisms are divided into two categories called Innate and Acquired immunity.

CHAPTER 2

Medicinal Plants and Drug Discovery

Bipindra Pandey[1], Shankar Thapa[1,*], Mahalakshmi Suresha Biradar[2] and **Ravindra Khadka[3]**

[1] *Department of Pharmacy, Madan Bhandari Academy of Health Sciences, Hetauda, Nepal*

[2] *Department of Pharmaceutical Chemistry, Al-Ameen College of Pharmacy, Bengaluru, India*

[3] *School of Health and Allied Sciences, Pokhara University, Kaski, Pokhara, Nepal*

Abstract: Plants have been used as a source of medicine for the treatment of different diseases for thousands of years. Bioprospecting of medicinal plants aims at the development of commercially valuable therapeutic goods, which could be used for the treatment of different diseases. The therapeutic values of medicinal plants are due to the presence of different bioactive secondary metabolites. The exploration of phytochemicals from the medicinal plants *via* ethnopharmacological, chemotaxonomical and random selection approach. The phytochemical-based drug discovery was performed by extraction, isolation, identification, bioassay, which further goes for target identification, target validation, lead identification, lead optimization, and clinical trials. The crucial step in drug discovery from the medicinal plant is lead identification and optimization due to their complex structural organization. This problem of drug discovery can be resolved by employing the concept of virtual screening and databases like COCONUT, TCMPG, IMPPAT 2.0, PMDB, PMhub, *etc*. Each of these steps has its specificities, limitations, and advances. In this regard, knowledge about combinatorial biosynthesis, chemical synthesis, and the technique of acquiring drugs from medicinal plants was gathered for this chapter. This chapter concludes by discussing a few significant facets of current case studies in relation to the discovery of novel bioactive compounds from medicinal plants and the creation of affordable, safe, and effective medications to combat the world's expanding list of illnesses.

Keywords: Advantages, Biological activity, Bioprospecting, Challenges, Disadvantages, Drug discovery process, Druggability characters, Ethnopharmacology approach, History, Human disease, Medicinal plant database, Medicinal plants, Modern methods, Natural product, Phytoconstituents, Plant selection approach, Random approach, Traditional medicine, Traditional methods, Zoopharmacognosy approach.

[*] **Corresponding author Shankar Thapa:** Department of Pharmacy, Madan Bhandari Academy of Health Sciences, Hetauda, Nepal; Tel: +977-9860352048; E-mail: tshankar551@gmail.com

M.S. Ashawat, Aditi Kaushik, Akash Jain, Jasmine Chaudhary & Manish Kaushik (Eds.)

INTRODUCTION

Natural products are chemical compounds or substances produced by living organisms, found in nature. Natural products are abundantly available on this planet. Some plants are useful for daily needs, and some have medicinal value. Natural products generated from a variety of natural sources, such as plants, animals, and microorganisms, have played an important role in pharmaceutical and traditional medicine development. Natural products refer to secondary metabolites produced by any living organism; they are small molecules that are not necessary for survival, growth, development, or reproduction. They play a crucial role in plant defence against herbivory and other interspecies threats. These bioactive chemicals frequently feature unique structures and complex chemistries that have been optimized by evolution to interact with biological systems, making them invaluable in drug discovery and development. A remarkable number of contemporary medications have been developed from natural sources, with many of them inspired by traditional medicinal applications.

Medicinal plants have a long history of use in traditional medical systems around the world, including Ayurveda, Traditional Chinese medicine, and Native American healing methods. The medicinal properties of these plants are attributed to a wide range of chemical components, such as terpenes, glycosides, alkaloids, and flavonoids. The therapeutic qualities of these plants are still being investigated and verified by modern science, which is producing novel medications and treatments.

39% out of 520 drugs approved from 1983-1994 were of natural products or derived from natural origin. In that, 60-80% were used as antibacterial and anti-cancer agents. Natural products play a crucial role in drug discovery due to their unique chemical structures and “drug-like” qualities. Natural products help in the introduction of new chemical entities with diverse structures that can serve as templates for semi-synthetic and total synthetic modifications [1].

HISTORY AND ROLE OF MEDICINAL PLANTS IN HUMAN DISEASE

The natural products were used in many ways through prehistoric times. There is archeological evidence that the natural products were used as medicine by Neanderthals around 60,000 years ago. In the recent studies by Hardy *et al.,* yarrow and chamomile were found in the samples of dental calculus of Neanderthals [2]. These two plants are bitter and have less nutritional value. It suggests that these plants were used as a self-medication [3]. In Ancient civilizations, clay tablets bearing medical prescriptions were found in numerous Sumerian and Babylonian sites in 1728 BCE. The oldest medical document Papyrus of Ebers, is dated to the 16th century BCE in Egypt. This document

contains 877 prescriptions and some remedies, including Myrrh, fennel, and other spices. In Southeast Asian countries like India, traditional folk medicine dates to 1500 BCE. The usefulness of medicine was passed on by word of mouth from father to son, for many generations, until it was in the holy writings known as the Vedas. Treating illness using medicinal plants has continued till today, and the system is known as Ayurveda. Ayurveda is derived from the Sanskrit word, where "*Ayu*" means life and "*Veda*" means science or knowledge. Knowledge of medicinal plants is documented in Charaka Samhitha by the father of Ayurveda, Sage Charaka. Chinese, 5000 years ago, used many herbs in the form of tea. One of the teas that they were consuming was made from a leafless creeper known as Ma-Hung (*Ephedra Sinica*) and was used in the treatment of lung disease, to reduce fever, and to relieve coughing. The phytoconstituent, which is extracted from this plant, is known as ephedrine, which is still used to treat asthma.

Hippocrates, who lived in the fourth century BCE and is regarded as the founder of modern medicine, listed 300 remedies. Theophrastus, the 3rd-century BCE father of botany, presented the details of plant appearance and culture in his work Enquiry into Plants. In his book De Materia Medica, the first-century BCE Greek physician Dioscorides listed 800 treatments made from plant, animal, and mineral sources. He has written about the locations, harvesting schedule, preparation steps, and medical categorization.

The intriguing Doctrine of Signature, which was created in herbal medicine throughout the Middle Ages in Europe, is recorded in works by Archimedes. According to the herbalist, plants are meant to benefit humans and have been used for specific organ-related ailments depending on their shape and color. For instance, kidney-related health conditions were treated with kidney-shaped fruits and pulses, and heart-related issues were treated with fruits and leaves that are in heart shape. In addition to being eaten for their nutritional content, plants are also utilized as medicine to treat several illnesses [4]. One thing we can learn from the history of using plants as medicine is that they can treat illnesses. In more recent history, the use of plants as medicines has involved the isolation of active compounds, beginning with the isolation of morphine from opium in the early 19th century.

Throughout history, human civilization has utilized various plants for food, medicine, clothing, and shelter. Vegetarian foods are rich in "super nutrients," including protective antioxidants, phytochemicals, and micronutrients, which promote health and protect against diseases. Plants have several pharmacological roles, such as antioxidant, antiviral, anti-cancer, antimicrobial, antifungal, and antiparasitic activities. They contain free radical scavenging molecules like flavonoids, phenolics, anthocyanins, and vitamins, which exhibit antioxidant

CHAPTER 3

Secondary Metabolites: Nature's Gift for Holistic Health Management

Manisha Bhatia[1], **Divya Dhawal Bhandari**[2] and **Prerna Sarup**[3,*]

[1] *Department of Pharmacognosy, MM College of Pharmacy, Maharishi Markandeshwar (Deemed to be University), Mullana, Ambala 133203, Haryana, India*

[2] *Department of Pharmaceutical Chemistry, University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh, Punjab, India*

[3] *Department of Pharmacognosy, University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh, Punjab, India*

Abstract: Plant Secondary Metabolites (PSM) are compounds vital for plant survival that play a pivotal role in their mechanisms of action, and possess various medicinal properties that can enhance human health. These bioactive substances, generated by plants as defense mechanisms against predators and to attract pollinating insects, are garnering increased attention for their potential pharmacological benefits. PSM encompassing alkaloids, flavonoids, terpenes, saponins, and more, exhibit diverse pharmacological activities such as antihypertensive, anticancer, and antimicrobial effects. Ancient civilizations practiced medicinal plant usage, with secondary metabolites primarily responsible for their therapeutic efficacy. Classified based on structure and biosynthetic derivation into primary and secondary metabolites, the latter category includes terpenoids, phenolics, alkaloids, and glycosides. They serve as crucial sources of bioactive ingredients in both nutraceuticals and modern pharmaceuticals. Secondary metabolites display diverse pharmacological activities, interacting with receptors, cell membranes, and nucleic acids. This comprehensive book chapter delves into their classification, phytochemistry, and pharmacological activities, shedding light on their application in modern medicine for human health enhancement and drug innovation. Understanding these compounds aids in identifying and isolating pharmacologically active lead compounds for drug discovery.

Keywords: Alkaloids, Biological activity, Drug discovery, Flavonoids, Plant secondary metabolites, Polyphenols, Saponins, Terpenes.

* **Corresponding author Prerna Sarup:** Department of Pharmacognosy, University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh, Punjab, India; E-mail: psarup_pu@hotmail.com

M.S. Ashawat, Aditi Kaushik, Akash Jain, Jasmine Chaudhary & Manish Kaushik (Eds.)

INTRODUCTION

Plant chemistry is mainly attributed to the therapeutic potential of herbs. In other words, an in-depth understanding of the chemical composition of plants enriches our comprehension of their potential curative value. Modern chemistry has explained the role of primary plant metabolites in fundamental life functions such as cell division, growth, respiration, storage, and reproduction. These metabolites include small molecules like sugars, amino acids, tricarboxylic acids (Krebs cycle intermediates), proteins, nucleic acids, and polysaccharides, involved in processes like glycolysis, the citric acid cycle, and photosynthesis.

Secondary plant metabolites are organic compounds that are not directly involved in the basic processes of growth, development, or reproduction. Unlike primary metabolites, which include carbohydrates, proteins, and nucleic acids, secondary metabolites often play a role in defense against herbivores and pathogens, as well as in interactions with pollinators and seed dispersers. These compounds can also have significant pharmacological or toxicological effects on other organisms [1]. Secondary plant metabolites are diverse compounds produced by plant cells using precursors from primary metabolism *via* various metabolic pathways such as shikimic acid, acetate, and amino acid pathways. This concept, first introduced by Nobel laureate Albrecht Kossel in 1910, was later expanded by Czapek, who described these compounds as end-products of nitrogen metabolism involving secondary modifications [2].

These secondary metabolites exhibit various biological effects, providing a scientific basis for the use of herbs in traditional medicine across many cultures. They have been identified as antibiotics, antifungals, antivirals, and UV protectants, defending plants from pathogens and environmental damage. Some herbs, like clover or alfalfa, exhibit estrogenic properties, affecting animal fertility.

Secondary plant metabolites are categorized into various classes. The current chapter explores these categories, highlighting their phytochemical structures and pharmacological potential. The main categories, as given in Fig. (**1**), include:

i. Alkaloids
ii. Phenolics
iii. Saponins
iv. Terpenes

Alkaloids

Alkaloids often contain one or more rings of carbon atoms, usually with a nitrogen atom in the heterocyclic ring. The position of the nitrogen atom in the ring varies with different alkaloids and different plant families. These compounds are renowned for their pharmacological properties and have been utilized in traditional systems of medicine and modern pharmaceuticals for centuries. Alkaloids are produced through a complex biosynthesis process regulated by environmental factors, providing plants with adaptive advantages. Many well-known drugs, like quinine and morphine, are derived from natural alkaloids. A particularly fascinating feature of alkaloids is their structural diversity. Alkaloids have a crucial part to play in the development of clinical medicine, along with providing natural defense to organisms. Around 20% of known plant secondary metabolites are alkaloids [3]. These compounds can vary from simple molecules like nicotine to more complex structures such as morphine. This diversity in structure is reflected in their wide range of biological activities. Depending on their specific makeup and the organisms they interact with, alkaloids can function as stimulants, sedatives, analgesics, and even poisons [4, 5]. Alkaloids are categorized based on their chemical structure, biological origin, and biosynthetic pathways. However, the most common classification out of all is based on a chemical structure, which is given below along with a few examples from the particular category [1]:

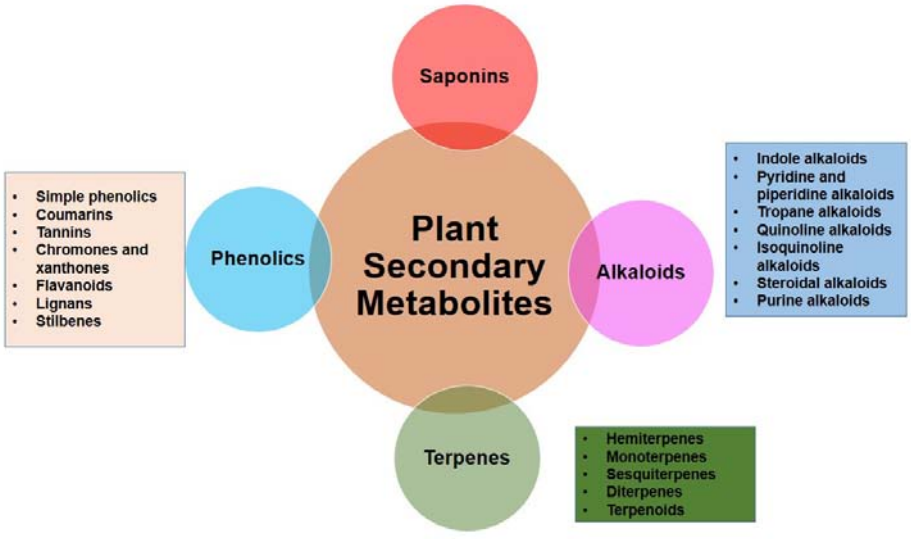

Fig. (1). Types of plant secondary metabolites.

CHAPTER 4

Harnessing The Role of Terpenoids in Type 1 Diabetes Mellitus

Vishakha Saini[1,*], Jasmeen Kaur[1], Rashmi Bhamra[2], Kulvinder Kaur[2], Varinder Kaur[2], Rupa Devi[1] and **Ashwani K. Dhingra[3]**

[1] *Department of Pharmaceutics, Global Research Institute of Pharmacy, Radaur, Yamuna Nagar 135133, Haryana, India*

[2] *Department of Pharmacy, Global Research Institute of Pharmacy, Radaur, Yamuna Nagar 135133, Haryana, India*

[3] *Department of Pharmaceutical Chemistry, Global Research Institute of Pharmacy, Radaur, Yamuna Nagar 135133, Haryana, India*

Abstract: Type-1 Diabetes Mellitus (T1DM) poses major complications due to its autoimmune nature, which is characterized by pancreatic β-cell breakdown, resulting in a lack of insulin as well as dysregulated glucose metabolism. While insulin therapy remains the cornerstone of T1DM management, emerging research investigating adjunctive therapies includes natural compounds, such as terpenoids derived from plants. Regenerative medicine aims to generate new insulin-producing cells derived from various cell kinds to treat T1DM, which is caused by the loss of pancreatic β cells. Terpenoids, also known as isoprenoids, are natural chemicals derived from isoprene that play important functions in all species' metabolisms. Natural terpenoid compounds have been classified into five different categories based on their structure: monoterpenoids (Paeoniflorin, Catalpol, Geniposide), sesquiterpenoids (Curcumol, β-Patchoulene), diterpenoids (Carnosic Acid, Ginkgolide), triterpenoids (Ginsenoside, Ursolic Acid), and tetraterpenoids (Lycopene, Astaxanthin). Terpenoids appear to have a therapeutic impact on non-alcoholic fatty liver disease, largely *via* insulin resistance, regulating lipid metabolism, inflammation, and oxidative stress. Terpenoids can help diagnose diabetic nephropathy by decreasing the production of pro-inflammatory cytokines (α-amylase and α-glucosidase), controlling glycolipid metabolism, and lowering renal inflammation. We look at some of the most beneficial and promising terpenoids that are now being employed in medicine and research, as well as the most recent information on their natural occurrence, biosynthesis, and mechanism of action in the body. Terpenoids promote the proliferation and development of osteoblast cells in high-glucose circumstances. These findings demonstrated that terpenoids stimulated glycogenesis *via* the PI3K/AKT pathway while inhibiting glucosamine-induced gluconeogenesis by downregulating gluconeogenesis enzymes. Despite these encouraging findings, the therapeutic potential of terpenoids in T1DM has to be further investigated through rigorous preclinical and clinical trials.

[*] **Corresponding author Vishakha Saini:** Global research institute of pharmacy, Radaur, Yamuna Nagar 135133, Haryana, India; E-mail: vishakhabanwait@gmail.com

M.S. Ashawat, Aditi Kaushik, Akash Jain, Jasmine Chaudhary & Manish Kaushik (Eds.)

Keywords: Diabetes, Gluconeogenesis, Insulin, Pro-inflammatory cytokines, Terpenoids.

INTRODUCTION

Hyperglycemia, the hallmark of diabetes mellitus, is a chronic metabolic state that has spread like an epidemic over the globe. Diabetes mellitus can lead to limb blindness, kidney amputation, cardiovascular disease, failure, and other problems. Diabetes mellitus patients' lives are affected as a result of these consequences [1]. Diabetes is a vast public health concern around the world. Currently, one in every eleven adults has the illness, and some forecasts suggest that by 2050, more than one-third of humans will have the disorder. Diabetes-related problems claim the lives of over 4 million individuals globally each year. Diabetes healthcare spending was expected to reach $727 billion globally per year in 2017, with medication therapy accounting for 40% of total diabetes spending [2]. Diabetes can be triggered by a lack of insulin production, damage to pancreatic β cells, or insulin resistance from non-use. Sedentary lifestyles may contribute to the increasing proportion of diabetic patients worldwide, projected to spread to 366 million in 2030 among the elderly. Diabetes may lead to consequences such as kidney disease, neuropathy, cardiac and renal problems, retinopathy, and food-related illnesses [3].

T1DM is triggered by the autoimmune destruction of endocrine pancreas cells. TIDM pathophysiology is distinct from that of type 2 diabetes mellitus, where reduced cell production of insulin and insulin resistance coexist [4]. T1DM is a fatal disease that results in insulin insufficiency and diabetes due to the autoimmune destruction of β cells. Ten million individuals worldwide suffer from the illness, and many of its side effects, such as nephropathy, retinopathy, neuropathy, and cardiovascular problems, are fatal [5, 6]. Because T1DM includes several pathways and is controlled by both the immune and endocrine systems, its pathophysiology is complex. Genetic, immunological, or environmental factors are the leading causes of T1DM development [4, 6, 7]. The development and consequences of type 1 diabetes are attributed to immune system dysregulation and β-cell homeostasis. Dendritic cells, macrophages, β cells, and antigen-presenting cells convey auto-antigens, including insulin and glutamic acid decarboxylase, to T-cells during the development of T1DM. Following activation, T-cells divide into several subsets of T cells. Local inflammatory cytokines, such as TNF-α, perforin, and IFN-γ, are generated when cells invade the pancreas, causing insulitis. Furthermore, misdirected autoimmunity Myeloid-Derived Suppressor Cells (MDSC) and other immune cells are influenced by regulatory T cells and natural killer cells [5, 8 - 10]. As a result, β cells undergo apoptosis, leading to dysfunction. The pathogenic situation of diabetes is associated with β-

cell bulk and function decline [11]. The most common endocrine and metabolic disorder affecting children is T1DM. For those with T1DM, insulin treatment may be both life-saving and permanent. A person with T1DM has to follow a thorough self-management plan like blood glucose monitoring, insulin use, exercise, and a balanced diet [12]. Three interconnected processes—genetic susceptibility, autoimmunity, and environmental factors—contribute to the pathophysiology of T1DM. The two main insulin formulations utilized in the pharmacological treatment of T1DM are insulin lispro and insulin aspart, both of which are rapid-acting insulin. Insulin that acts quickly includes regular Humulin, Velosulin BR, and long-acting or intermediate-acting insulin, such as insulin glargine (Lantus), Lente Humulin, and NPH (Neutral Protamine Hagedorn).

The most important and most varied class of complexes derived from plants is called terpenoids, as shown in Table **1**. Food and pharmaceutical companies, among others, have made substantial use of these plant-derived terpenoids [13]. Terpenoids, alkaloids, and phenylpropane chemicals make up the majority of the biologically active components found in therapeutic plants [14]. Terpenoids are one of the most abundant and structurally varied classes of naturally occurring chemicals [15]. There are about 80,000 different types of terpenoids found in almost all living things. Because of their structural variety, terpenoids may be used in flavors, biofuels, and pharmaceutical applications. The Methylerythritol-Phosphate (MEP) pathway in prokaryotes and plant plastids, as well as the Mevalonate (MVA) route in eukaryotes, naturally produce isopentenyl diphosphate and its isomer, dimethylallyl diphosphate. The skeletons of terpenoids are made up of these parts [16]. One of the most structurally diverse classes of natural materials is composed of tens of thousands of naturally occurring hydrocarbons [17]. Terpenoids, of which there have been over 25,000 identified chemical species, are the most prevalent class of secondary metabolites in plants. Based on the quantity of five-carbon units in their structure, terpenes are classified as monoterpenes, sesquiterpenes, diterpenes, triterpenes, tetraterpenes, and high polyterpenes. Terpenes are structurally constituted of one or more five-carbon units. Important volatile plant compounds called monoterpenes and sesquiterpenes support interactions between plants, microorganisms, and animals as well as defensive reactions [18]. These include pain-relieving anti-malarial artemisinins, cannabinoids, anti-cardiovascular tanshinones, anti-tumor paclitaxel, and ginkgolides [13].

CHAPTER 5

Advances in Therapeutic Modulation of Cannabinoids for Effective Treatment and Research in Multiple Sclerosis

Balaji Govindaswamy[1,*], Sarath Perumal[2], Chandrasekar Ponnusamy[3] and **Murugappan Kumarappan[4]**

[1] *Department of Biotechnology, Bhupat and Jyoti Mehta School of Biosciences, Indian Institute of Technology Madras, Chennai 600042 ,Tamil Nadu, India*

[2] *Department of Biotechnology, School of Bio-science and Technology, Vellore Institute of Technology, Vellore 632014, Tamil Nadu, India*

[3] *Department of Biotechnology, Rathinam College of Arts and Science, Coimbatore 641021, Tamil Nadu, India*

[4] *Department of Biotechnology, School of Biotechnology and Genetic Engineering, Bharathidasan University, Tiruchirappalli 620024, Tamil Nadu, India*

Abstract: A complicated and long-lasting neurodegenerative illness, Multiple Sclerosis (MS) is characterized by lesions in the Central Nervous System (CNS). Although the exact etiology of MS and the processes behind this rise are yet unknown, complex gene-environment interactions most likely have a significant impact. Growing research indicates that certain symptoms of multiple sclerosis and spinal cord damage, such as pain and spasticity, are effectively suppressed by Cannabinoids. Natural cannabis products and single Cannabinoids are often smoked or taken orally, with different administration routes. Transdermal, sublingual, ocular, and aerosols have only been employed in a few studies and are not highly relevant in modern practice. This chapter focuses on novel approaches of Cannabinoids drugs with synthetic material, co-drug development, mechanism of action, and demonstrating the use of Cannabinoids receptor agonists in the treatment of multiple sclerosis. Furthermore, the chapter explains the preclinical and clinical approaches, suggesting that Cannabinoids CB1 and/or CB2 receptors may decrease some of the pathological alterations that lead to the signs and symptoms of multiple sclerosis in addition to alleviating them and using synthetically derived Cannabinoids, also explains how it reduces the effects of MS and prolongs 'patient's lifespan. Thus, the chapter delivers the potentiality of using Cannabinoids with advances to overcome the Pharmacokinetic and Pharmacodynamic pathways.

[*] **Corresponding author Balaji Govindaswamy:** Department of Biotechnology, Bhupat and Jyoti Mehta School of Biosciences, Indian Institute of Technology Madras, Chennai 600042, Tamil Nadu, India; E-mail: balajishilou.08@gmail.com

M.S. Ashawat, Aditi Kaushik, Akash Jain, Jasmine Chaudhary & Manish Kaushik (Eds.)

Keywords: Aetiology of MS, Blood Brain Barrier, Cannabinoids, Cannabis, Cellular pathway, Central Nervous System, Endocannabinoid, Genes, Immune cells, Lesions, Lifespan, Multiple Sclerosis, Muscle atrophy, Myelin sheath, Neurodegenerative, Pathology, Receptors, Sativex, Spasticity, Spinal cord.

INTRODUCTION

A common and crippling autoimmune illness, Multiple Sclerosis (MS) primarily affects the Central Nervous System (CNS), which includes the brain and spinal cord. The immune ' 'system's breakdown of myelin, the coating that protects nerve fibres, is a defining feature of multiple sclerosis [1]. The effective conduction of electrical impulses along the nerves is disrupted by this demyelination process, which results in a variety of neurological symptoms and gradual impairment [2]. The abnormal activation of CD4+ T lymphocytes, which identify myelin antigens presented by Major Histocompatibility Complex (MHC) class II molecules, is central to the pathophysiology of multiple sclerosis [3, 4]. These auto-reactive T cells multiply and release pro-inflammatory cytokines, such as aggravating inflammation and drawing more immune cells to the central nervous system [5]. Through the generation of myelin-specific antibodies and the development of ectopic lymphoid follicles inside the meninges [6], B cells also contribute to the pathology associated with multiple sclerosis. Microglia and astrocytes are activated in MS due to the inflammatory milieu, which results in the production of neurotoxic chemicals such as nitric oxide and reactive oxygen species [7]. Demyelination, axonal damage, and the death of oligodendrocytes are the outcomes of this inflammatory cascade [8]. Sclerotic plaques are a hallmark of MS lesions seen on MRI and are linked to chronic demyelination and axonal degeneration [9]. Myelin sheaths are necessary for the quick and accurate transfer of electrical impulses between neurons in a healthy central nervous system [2, 10]. In the CNS, oligodendrocytes create myelin, which insulates nerve fibres and helps action potentials spread by saltatory conduction [11]. Auto-reactive lymphocytes in MS cause demyelination and damage to neuro-axons by piercing the blood-brain barrier and starting anti-inflammatory responses against myelin and oligodendrocytes [12]. Genetic predisposition and environmental stimuli interact intricately during the pathophysiology of multiple sclerosis [13]. Numerous genetic loci, many of which are involved in immune modulation, have been discovered by genome-wide association studies as being related to an elevated risk for multiple sclerosis [14]. The genesis of MS has also been linked to environmental variables, including smoking, vitamin D insufficiency, and viral infections (Epstein-Barr virus) [15].

The development of synthetic Disease-Modifying Therapies (DMTs) such as fingolimod, alemtuzumab, and ocrelizumab has completely changed the way that

MS is managed [16]. Through their targeting of different components of the immune response, these drugs have been shown to be effective in decreasing the number of relapses, slowing the course of the illness, and enhancing the quality of life for patients [17 - 19]. However, a variety of adverse effects are associated with its usage, including flu-like symptoms, bradycardia, gastrointestinal issues, and increased risk of infections and secondary cancers [20]. Beyond immunomodulation, these synthetic drugs can also negatively impact normal inflammations, elevated oxidative stress, impaired cell division, and increased susceptibility to CNS [21, 22]. Additional difficulties with long-term treatment include cumulative toxicity, the possibility of developing secondary autoimmune illness, and the requirement for therapeutic medication because neutralizing antibodies or tolerance develop [23, 24]. These treatments have long-lasting impacts, so ' 'it's critical to have tailored treatment plans and routine monitoring to optimize positive results and reduce negative ones [25]. In order to maximize the therapeutic use of these medications and enhance the quality of life and prognosis for MS patients, ongoing research into the mechanism and long-term effects of these treatments is necessary [26, 27].

Natural drugs may be less likely to cause adverse effects than synthetic medicines and have the potential for neuro-protection, immunomodulation and symptomatic alleviation. Moreover, natural medications are gaining attention in the therapy of multiple sclerosis [28 - 31]. These natural substances, which come from a variety of plants and food sources, have demonstrated potential in MS ' 'patient's treatment of chronic pain, reduction of neuroinflammation, and alleviation of spasticity [32 - 34] using their interaction with the ' 'body's own regulatory systems which are vital to the preservation of Central Nervous System (CNS) homeostasis [35]. They have antioxidant and anti-inflammatory qualities that might prevent neurodegeneration and encourage remyelination [36]. Some are renowned for their neuroprotective and cognitive-enhancing qualities, which may improve cognitive function and tiredness in MS patients [32, 37]. Others have shown promise in lowering the severity of relapses and inflammation in MS due to their immunomodulatory actions [38]. These organic substances provide an alternative method of treating multiple sclerosis, intending to optimize the effectiveness of current treatments while reducing side effects [39, 40]. But in the case of MS, thorough clinical trials are necessary to confirm their safety, effectiveness, and long-term advantages. Natural-based medications are relevant for MS because of their many modes of action that match the ' 'illness's intricate pathophysiology [27, 41]. This allows for a comprehensive approach to disease treatment and enhances ' 'patient's quality of life in general.

Research into cannabis as a potential treatment for multiple sclerosis is a promising and developing area. The key ingredients for *Cannabis sativa* known as

CHAPTER 6

Investigating Botanical Bioactives: Innovative Strategies for Treating Systemic Lupus Erythematosus

Parul Gupta[1], Ashna Gupta[1], Sweta Kamboj[1], Shikha Kamboj[1] and **Rohit Kamboj[1,*]**

Department of Pharmaceutics, Guru Gobind Singh College of Pharmacy, Yamunanagar 135001, Haryana, India

Abstract: Systemic Lupus Erythematosus (SLE) is an inflammatory illness characterised by chronic inflammation and multi-organ dysfunction. Secondary plant metabolites have received attention as potential innovative treatment agents. These metabolites provide a variety of pharmacological actions that are effective in managing SLE. These metabolites include polyphenols, alkaloids, terpenoids, and glycosides. While their immune-modulatory activities can address the immunological dysfunction characteristic of the disease, their anti-inflammatory qualities improve in lowering the chronic inflammation observed in SLE. These substances additionally show strong antioxidant activity, which reduces oxidative stress, a major factor in the pathogenesis of SLE. These natural compounds have been shown in numerous studies to have the capacity to suppress pro-inflammatory cytokines, control lymphocyte proliferation, and alter the function of various immune cells. Compared to traditional manufactured medications, secondary plant metabolites have a lower potential for side effects due to their natural origin. For SLE patients, ongoing research and clinical trials are crucial in determining the therapeutic potential of these natural substances and developing effective treatment strategies.

Keywords: Anti-inflammatory, Immunomodulatory, Natural therapy, Oxidative stress, Polyphenols, Secondary plant metabolites, Systemic lupus erythematosus.

INTRODUCTION

Systemic Lupus Erythematosus (SLE) is an autoimmune, multi-organ disease characterized by a range of clinical signs. Young women are more likely to have SLE. Compared to females, men are more likely to develop SLE (1:5–10) [1, 2]. External factors that commonly raise the risk of SLE include UV radiation, demethylating medications (Azacitidine, Decitabine), as well as viral infections

* **Corresponding author Rohit Kamboj:** Guru Gobind Singh College of Pharmacy, Yamunanagar 135001, Haryana, India; E-mail: rkamboj538@gmail.com

M.S. Ashawat, Aditi Kaushik, Akash Jain, Jasmine Chaudhary & Manish Kaushik (Eds.)

(Epstein-Barr virus). SLE is more frequently linked to women because higher hormone concentrations, such as those found in prolactin and oestrogen, activate autoimmune characteristics. Both hormones boost plasma cell survival rates, which results in a high affinity for autoreactive B cells [3, 4]. Auto-antibodies and antibody-immune complexes are generated in SLE, leading to tissue injury and inflammation [5, 6]. Patients with SLE go through periods of remission and relapse [7]. The skin, kidneys, joints, heart, lungs, liver, *etc*., and blood vessels are among the organs that may be affected by SLE [8, 9]. Numerous indices, including the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), Safety of Oestrogens in Lupus Erythematosus National Assessment (SELENA), and British Isles Lupus Activity Group (BILAG) index, can be used to evaluate the state of the diseases because different organs are involved in SLE [10]. Genetic factors (the presence of genes that activate inflammation, genes that express toll-like receptors, and genes that are involved in the STAT signaling system) are the key etiological factors that cause SLE [11 - 13]. DNA repair genes, including TREX1, KLK1, and KLK3, have also been shown to be absent or to be hidden in the genetic architecture of SLE-responsive people [14 - 16]. The etiology of SLE is demonstrated in Fig. (**1**).

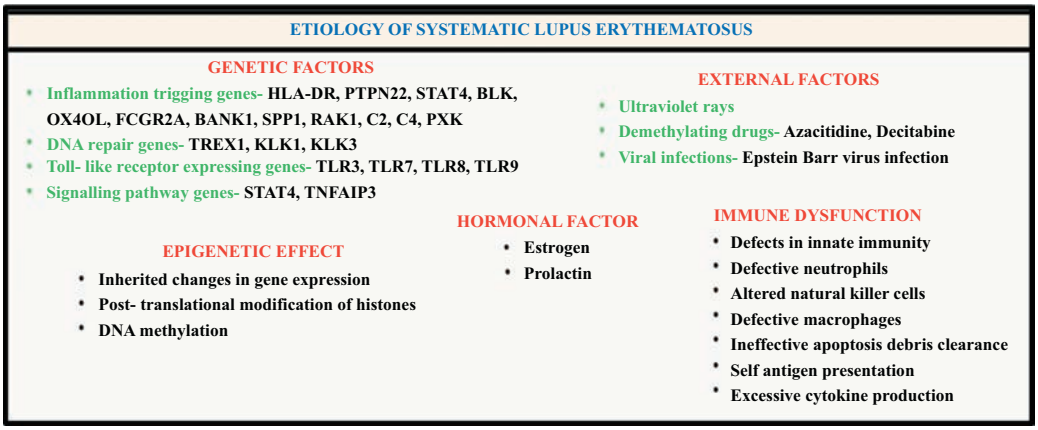

Fig. (1). The etiology of systematic lupus erythematosus.

Anti-double-stranded DNA (anti-dsDNA) antibodies play a crucial role in the pathogenesis of Sickle Cell Disease (SCD) and their levels are linked to disease activity. In other cases, therapy aims to restore normalcy in anti-dsDNA antibody levels [7]. Lupus nephritis causes kidney injury by inflammatory reactions triggered by increased B and T lymphocyte activity, autoantibody misproduction, immune complex accumulation in kidney tissue, and dysregulation of T-regulatory cells [17, 18]. Pharmaceuticals used to treat SLE include systemic lymph node irradiation therapy, nonsteroidal anti-inflammatory medications,

antimalarial drugs, immunosuppressive drugs, glucocorticoids, and plasma treatment. In spite of this, SLE patients continue to have unacceptably high rates of morbidity and mortality [8, 19]. The recommended medications lower patients' quality of life and expose them to side effects [20]. Patients are encouraged to try complementary and alternative treatments, including acupuncture, moxibustion, herbal remedies, medicinal plants, phytochemicals, vitamins, and mineral supplements, as well as spiritual therapies like yoga. Additionally, a lot of work has gone into finding safe and efficient supplements and drugs for the condition that make use of both natural and synthetic derivatives of natural components. Using PubMed, the Cochrane Library, Web of Science, Scopus, the National Library of Medicine (NLM) catalogue, and Google Scholar, a thorough literature search was conducted. The American College of Rheumatology's (ACR) guidelines are now used to diagnose SLE. According to the ACR, a patient has lupus if they exhibit four of the eleven indications or symptoms shown in Fig. (**2**).

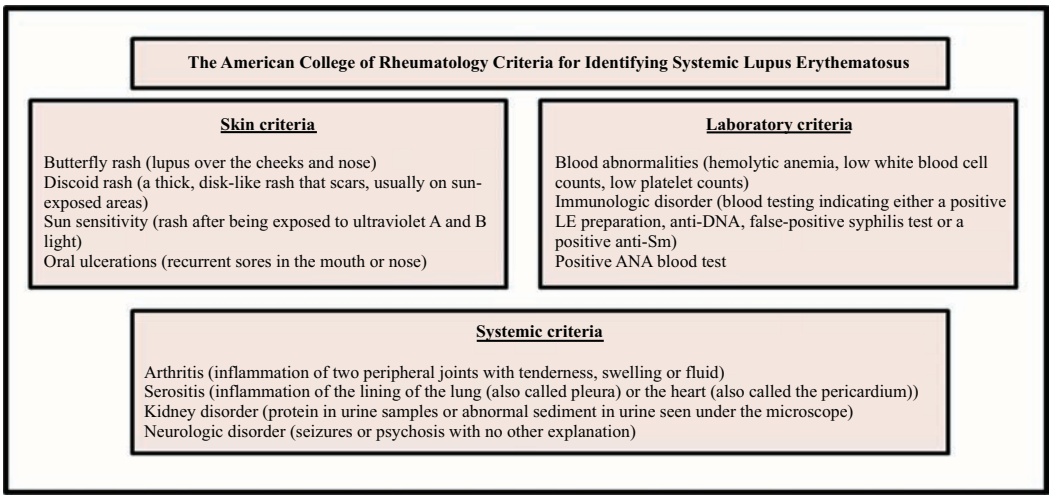

Fig. (2). The criteria for identifying systemic lupus erythematosus by the American College of Rheumatology.

Pathophysiology of SLE

SLE has a complicated pathophysiology, and our knowledge of it is always changing. When genetically vulnerable people are exposed to environmental stressors, their tolerance breaks down, which triggers the development of autoimmunity. The immune system is exposed to self-antigens as a result of cell damage brought on by infections and other environmental causes. This stimulation of T and B cells results in a chronic, self-directed immunological response that is self-sustaining. Organ damage is caused by complement activation, autoantibody synthesis, and cytokine release.

CHAPTER 7

Advancements in Immunology: Comprehensive Insights into Autoimmune Disorders, Diagnostic Innovations, and Emerging Therapeutic Strategies.

Ekambaram Gayathiri[1], Palanisamy Prakash[2], Ramachandran Kaliaperumal[3], Suganya Kannan[4], Poorna Chandrika Sabapathy[5], Asbar Banu Bazeer[6], Kirtik Ramadoss[6], Sharangouda J. Patil[7] and **Prithiviraj Nagarajan[6,*]**

[1] *Department of Plant Biology and Plant Biotechnology, Guru Nanak College (Autonomous), Chennai 600042, India*

[2] *Department of Botany, Periyar University, Periyar Palkalai Nagar, Salem 636011, Tamil Nadu, India*

[3] *Department of Biochemistry, Sri Manakula Vinayagar Medical College and Hospital, Madagadipet, Kalitheerthalkuppam, Puducherry 605107, India*

[4] *Central Research Laboratory for Biomedical Research and Molecular Biology, Vinayaka Mission's Medical College and Hospital, Vinayaka Mission's Research Foundation, Karaikal, Puducherry 609609, India*

[5] *Directorate of Medical Research, Research and Innovation Lab, Aarupadai Veedu Medical College & Hospital, Vinayaka Mission, India*

[6] *Department of Medical Biotechnology, Aarupadai Veedu Medical College & Hospital, Vinayaka Mission's Research Foundation (Deemed to be University), Kirumampakkam, Puducherry 607403, India*

[7] *Department of Zoology, NMKRV College for Women, Bengaluru 560011, Karnataka, India*

Abstract: Autoimmune diseases are among the most challenging conditions to manage in healthcare practice because of the chronic and often multifactorial nature of their pathophysiology. This chapter focuses mainly on autoimmune disorders and begins by establishing the context of the immune system, as well as its components, with a description of its functions, antigen presentation, clonal selection, memory cells, and the key mechanisms of immune responses. Moving on, it discusses autoimmune disorders, outlining their classification and employing the pathophysiology, molecules involved, and genetic factors, including HLA genes and gene mutations. Diagnostic procedures involving hematological examination, radiological imaging, and fine-needle aspiration cytology are employed to portray the modern techniques used in the

[*] **Corresponding author Prithiviraj Nagarajan:** Department of Medical Biotechnology, Aarupadai Veedu Medical College & Hospital, Vinayaka Mission's Research Foundation (Deemed to be University), Kirumampakkam, Puducherry 607403, India; E-mail: prithivinaga@gmail.com

M.S. Ashawat, Aditi Kaushik, Akash Jain, Jasmine Chaudhary & Manish Kaushik (Eds.)

diagnosis of autoimmune disorders. An assessment of pharmacological and non-pharmacological treatment options currently available examines the former in terms of corticosteroids, immunosuppressing agents, biologics, and small-molecule inhibitors, while the latter includes lifestyle interventions and complementary medicine. This chapter also focuses on advanced research and new treatment directions, such as gene therapy, monoclonal antibodies, repurposing drug approaches, malaria transcription intervention factor targeting, immune checkpoint blockage, autophagy regulation, and biodegradable nanoparticles to build up antigen-specific tolerance. New treatment regimens are characterized by pharmacodynamics, evidence-based, side effects or complications, and improved benefits compared with earlier interventions. The chapter concludes with a summary of the key points, emphasizing the importance of advancing our understanding and treatment of autoimmune disorders through ongoing research and innovation.

Keywords: Autoimmune disorders, Biodegradable nanoparticles, Cytology, Gene therapy, Hematology, Immune cells, Immune response, Immunology, Monoclonal antibodies, Small-molecule inhibitors.

INTRODUCTION

The immune system is one of the most intricate and constantly changing systems of the body that helps defend against pathogens, illnesses, and other foreign substances. It is involved in the regulation of homeostasis through the ability to differentiate between self and non-self and their subsequent management to either eliminate or neutralize threats [1]. The immune system is broadly categorized into two major categories, namely the innate immune system and the adaptive immune system. All these systems have individual but closely related functions in protecting the body against pathogens such as bacteria, viruses, fungi, and parasites, as well as identifying and eliminating cancer cells [2]. The main task of the immune system is to protect the integrity of an organism and its health by distinguishing between self and non-self entities and not harming the host's tissues. This is a very fine equilibrium between the innate and adaptive immune systems. The innate immune system is the first defense mechanism that is rapid and provides a general response to pathogens. Some of these are mechanical barriers, such as the skin and mucous membranes, and cellular defenses, such as phagocytes and natural killer cells [3]. In contrast, the adaptive immune system requires a more focused and specific response that involves the activation of lymphocytes, including B and T cells, which enables them to deal with the same pathogen in the future in a more efficient way [4].

Types and Roles of the Immune System

The immune system is the body's defense mechanism against diseases, illnesses, and foreign substances that invade the body.

The two types of immune responses are:

- The Innate immune system
- Adaptive immune system.

Innate Immune System

Innate immunity is considered the first line of defense that helps the body protect itself against pathogens. This system is non-specific, meaning that it operates in response to all pathogens, without the possibility of remembering specific pathogens.

The Innate Immune System Comprises Several Key Mechanisms and Components

Physical Barriers

The first line of defense includes anatomical barriers such as the skin and mucosal surfaces. These barriers function as the first line of defense, preventing pathogens from entering the body. The skin is a protective barrier that is hard and does not allow penetration, whereas mucous membranes trap and eliminate pathogens using mucus and cilia.

Phagocytic Cells

Macrophages and neutrophils are important components of the innate immunity. These cells are known as phagocytes, which engorge and destroy pathogens through a process known as phagocytosis. When a pathogen is consumed, it is engulfed by the cell as a phagosome, which then fuses with a lysosome, thus enzymatically destroying the pathogen [5].

Natural Killer Cells

These cells are very significant in the identification and elimination of infected or cancerous cells. Natural Killer (NK) cells are lymphocytes that eliminate target cells through apoptosis or programmed cell death by using cytotoxic granules containing perforin and granzymes. This mechanism is efficient for the removal of cells affected by infection or neoplastic diseases.

Inflammation is one of the basic mechanisms of innate immunity. Inflammatory mediators such as cytokines and chemokines are produced in damaged or infected tissues. These mediators dilate blood vessels and make the blood vessel walls more permeable, allowing immune cells to travel to the infected or injured area. Immune cells that are attracted to the area include neutrophils and macrophages,

SUBJECT INDEX

A

B

C

D

E

F

G

H

I

L

M

N

O

P

Q

R

S

T

U

V

W

X

M.S. Ashawat

Prof. (Dr.) M.S. Ashawat is the Director and Principal of Laurate Institute of Pharmacy (An Autonomous, NAAC- A Grade- H.P Technical University Off Campus Research Center), Himachal Pradesh, India. with over 25 years of experience in pharmaceutics and academic leadership. He has authored 13 books, published more than 130 research papers, and supervised multiple Ph.D. scholars. His expertise includes herbal cosmetics, intradermal delivery, nanocarriers, and regulatory science. He has served in key roles such as National Coordinator of APTI and is an active member of IPA and AAPS. Recognized with awards like "Principal of the Year," he has chaired national and international conferences and contributes significantly to research, academic governance, and editorial leadership in pharmaceutical sciences.

Aditi Kaushik

Dr. Aditi Kaushik is a Professor at Department of Pharmaceutical Chemistry, Laureate Institute of Pharmacy with over 17 years of academic and research experience. She specializes in molecular modeling, ADMET profiling, network pharmacology, and multi-target drug discovery, particularly for neglected diseases and antimicrobial resistance. She has published over 45 research papers, holds 10 patents, and has guided several undergraduate and postgraduate research scholars. Dr. Kaushik is actively involved in promoting IPR and entrepreneurship education, serves as a reviewer for Scopus-indexed journals, and contributes to analytical method development and regulatory compliance. As an editorial board member, she brings strong interdisciplinary expertise, advancing collaborative research and academic excellence in pharmaceutical sciences.

Akash Jain

Dr. Akash Jain is a Professor of Pharmacology at M.M. College of Pharmacy, Maharishi Markandeshwar (Deemed to be University), Haryana, with an extensive research profile including over 65 international publications. He holds 5 granted patents, 6 patents under process, and 5 copyrights, along with authoring books and book chapters. His key research areas include metabolic syndrome, neuropharmacology, and experimental pharmacology. Dr. Jain has guided students across all levels from B. Pharm to Ph.D. and has actively presented his work at national and international conferences. A member of the Indian Hospital Pharmacists' Association and a reviewer for reputed journals, he also contributes to organizing academic and research-focused events. His work reflects strong leadership, scholarly excellence, and impactful contributions to pharmaceutical education and research.

Jasmine Chaudhary

Dr. Jasmine is a Senior Associate Professor at Department of Pharmaceutical Chemistry, MM College of Pharmacy, MM(DU), Mullana with more than 17 years of academic and research experience. Her expertise includes the synthesis of analgesic and antimicrobial compounds and analytical method development. She has supervised B. Pharm, M. Pharm, and Ph.D. scholars and has published over 50 research papers, 15 book chapters, and holds 4 granted process patents. A reviewer for international journals and an active member of professional organizations, she frequently participates in scientific conferences and academic development programs. As an editorial board member, she contributes strong research insight, scientific rigor, and leadership to the advancement of pharmaceutical sciences.

Manish Kaushik

Manish Kaushik is an Associate Professor of Pharmacology at SBS College of Pharmacy, Palampur, with over 16 years of experience in academic teaching and institutional administration. His leadership roles include contributing to academic governance, regulatory documentation, and student welfare initiatives. His research focuses on metabolic disorders, antimicrobial resistance, and phytopharmacology, with publications in Scopus-indexed journals and contributions to Bentham Science titles. He is also the co-editor of a book on autoimmune disorders and secondary plant metabolites. As an editorial board member, he offers a multidisciplinary perspective that integrates research expertise with academic leadership to support high-quality scholarship and collaboration in pharmaceutical sciences.