Phytomedicine Innovations: The Future of Plant - Based Therapies

First Edition

Dr. Priya Trivedi and Dr. Jeetendra Sainkhediya

Edited Book

PHYTOMEDICINE INNOVATIONS: THE FUTURE OF PLANT - BASED THERAPIES

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Published by

JPS Scientific Publications
India

(ISBN Number, Book Editing and Review – 2024; Book Published 2025)

Published by

JPS Scientific Publications, Tamil Nadu, India.
E.mail: jpsscientificpublications@gmail.com
Website: www.jpsscientificpublications.com

Published in India.

International Standard Book Number (ISBN): 978-81-977907-4-4

Preface

In an era where modern medicine continues to make remarkable advancements, the timeless wisdom of plant-based therapies remains an invaluable resource for health and healing. *Phytomedicine Innovations: The Future of Plant-Based Therapies* delves into the intersection of traditional knowledge and cutting-edge scientific research, offering a comprehensive exploration of the therapeutic potential of medicinal plants. This book brings together diverse perspectives on phytomedicine, showcasing its applications in addressing contemporary health challenges. From the revolutionary CRISPR-Cas9 technology for enhancing medicinal plant properties to the ethnomedicinal uses of Leguminosae families in India, each chapter highlights the versatility and efficacy of plant-derived compounds. The book also examines the metabolic and therapeutic effects of bioactive alkaloids like trigonelline, the coagulant properties of *Moringa oleifera*, and eco-friendly solutions for pest management using invasive plants such as *Lantana camara* and *Eichhornia crassipes*. The integration of biotechnology, nanotechnology, and synthetic biology with traditional phytomedicine opens new avenues for sustainable and effective treatments. These innovations not only enhance the bioavailability and efficacy of plant-based therapies but also pave the way for novel drug discoveries. This work is a testament to the collaborative efforts of researchers, scientists, and traditional healers who are bridging the gap between ancient wisdom and modern science. It is designed for academics, healthcare professionals, and enthusiasts eager to explore the transformative potential of phytomedicine. As we navigate the complexities of global health challenges, the role of plant-based therapies becomes increasingly pivotal. This book serves as a guide and inspiration, encouraging further research and innovation in the field of phytomedicine for a healthier, more sustainable future.

ABOUT THE EDITOR – Dr. Priya Trivedi

Dr. Priya Trivedi is an esteemed academician, researcher, and educator with over 20 years of teaching experience and a decade of research expertise in Botany and Environmental Science. She holds an M.Sc. in Botany, an M.Ed., and a Ph.D. in Botany from Devi Ahilya Vishwavidyalaya (DAVV), Indore, where her doctoral research focused on "Phytochemical Analysis of Bark of Some Trees under Different Ambient Air Pollution Conditions in Indore". As a dedicated researcher, Dr. Trivedi has successfully completed a UGC-funded Minor Research Project (2015-2017) as the Principal Investigator. Her scholarly contributions include 30+ research and review papers in reputed national and international journals, 10+ book chapters, three Indian patents, and multiple conference presentations. She has also authored several environmental awareness articles for magazines. Currently serving as the Principal of Maa Narmada Mahavidyalaya, Dhamnod, Dr. Priya Trivedi is deeply involved in academia and scientific outreach. She is a Ph.D. guide at DAVV, an Executive Editor at ISERS (International Society of Environmental Relationship and Sustainability), and holds key leadership roles in various academic and environmental organizations, including: General Secretary, SHAKTI (State Level), General Secretary, IQAC (Bestow Edutex International), Treasurer, SESD (Society for Environment and Sustainable Development), President & Ambassador, Institution's Innovation Council, Indore International College and International Speaker, RKDx TALKS (Global RK Quotes Speakers Forum). Dr. Priya Trivedi is also a fellow member, session chair, keynote speaker, and resource person at national and international conferences. Her multifaceted contributions extend to editing and reviewing journals, mentoring researchers, and advocating for environmental sustainability and science communication. Through her relentless dedication to education, research, and environmental advocacy, Dr. Priya Trivedi continues to inspire the academic and scientific community.

ABOUT THE EDITOR – Dr. Jeetendra Sainkhediya

Dr. Jeetendra Sainkhediya is a renowned Botanist and Researcher with expertise in Plant Taxonomy, Biodiversity, Ethnobotany, and Environmental science. He holds an M.Sc. in Botany (Specialization: Taxonomy) from Holkar Science College, Indore (DAVV), an M.Phil. in Botany from Vikram University, Ujjain, and a Ph.D. in Botany from Devi Ahilya Vishwavidyalaya (DAVV), Indore, where his pioneering research focused on the *"Flora of Harda District, Madhya Pradesh, India".* A dedicated researcher, Dr. Sainkhediya has successfully completed a three-year Minor Research Project funded by the Madhya Pradesh State Biodiversity Board, Bhopal. His extensive academic contributions include 50+ Research and Review papers in esteemed National and International Journals, Six Book Chapters, and Three Indian patents. He has also presented 15+ Research papers at conferences worldwide, enriching scientific discourse. Beyond his research, Dr. Jeetendra Sainkhediya is an accomplished science communicator, having authored numerous articles on Environmental conservation. He serves as the Editor of the *International Research World Journal of Multidisciplinary Scientific Research (IRWJMSR)* and *Sustainability*, while also contributing as a Reviewer and Editorial Board Member for several Prestigious Journals. A sought-after Resource person, he has delivered Expert Lectures on Ecology, Ethnobotany, Herbal Medicine, and Plant Taxonomy, Bridging Academia and Practical applications. His work continues to influence Biodiversity Documentation, Sustainable Practices, and Botanical Research, making him a respected voice in the Scientific Community. Through his scholarship, editorial leadership, and advocacy for environmental awareness, Dr. Jeetendra Sainkhediya remains a driving force in advancing Botanical and Ecological Sciences.

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BIOTECHNOLOGY AND PHYTOMEDICINE: CRISPR AND BEYOND

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Abstract

Phytomedicine is the practice of using plant-derived compounds for medicinal purposes. It is an ancient practice which has evolved alongside advancements in science and technology. The chapter begins with the historical background of phytomedicine and the role of nutraceuticals, which have gained importance in recent times for their potential health benefits. The focus then shifts to metabolic engineering as an eco-friendly alternative approach for producing valuable compounds through microbial platforms, emphasizing the advantages of CRISPR over traditional genetic engineering methods. This chapter also provides the history of CRISPR and its mechanism to provide a detailed understanding of the CRISPR technology. CRISPR is known for targeted gene editing, enabling the enhancement of medicinal properties in plants and the development of disease-resistant varieties. The chapter outlines various applications of CRISPR in the field of phytomedicine, including the enhancement of medicinal compound production, elimination of unwanted compounds, creation of novel therapeutic agents and improvement of the nutritional content of medicinal plants. The focus of the chapter then shits beyond CRISPR technology and enters the field of Nanotechnology in phytomedicine. The potential role of nanotechnology as a drug delivery system for phytochemical compounds is also discussed in this chapter briefly. On the whole, this chapter provides a detailed understanding of how the integration of biotechnology and CRISPR technology is paving the way for innovative approaches in phytomedicine, offering promising solutions for enhancing the efficacy and sustainability of plant-based therapies.

Keywords: Phytomedicine, Biotechnology, CRISPR-Cas9 and Nanotechnology.

1. Introduction

Hippocrates' famous quote made around 2500 yr ago, "Let food be thy medicine, and medicine be thy food," serves as the basis of modern medicine (Hussain *et al.*, 2023). The development of phytomedicine has often stemmed from traditional or historical use, or from long-term evidence that consumption of phytomedicine is associated with improved health outcomes (Li *et al.*, 2021). Since the beginning of human history, phytochemicals with different therapeutic effects from various parts of plants have been used as food, spice, and medicinal purposes (Ozdal *et al.*, 2021). Nutraceuticals are dietary supplements used to ameliorate health, delay senescence, prevent diseases, and to support the proper functioning of the human body. In the current scenario, nutraceuticals are gaining attention due to their nutritional and therapeutical potentials. Based on their sources, they are categorized as herbal bioactive compounds and dietary supplements (Sachdeva *et al.*, 2020). Many researches have shown that nutraceuticals are potential medicines for treating a wide range of illnesses, cardiovascular diseases, diabetes mellitus, different types of cancer, osteoporosis, obesity and osteoarthritis. These nutrients contain many minerals, antioxidants, water soluble and fat-soluble vitamins which are taken from our diet and are beneficial for many of our health problems (Ghani, U *et al.*, 2019). However, supply limitations and difficulties faced in extraction from natural sources such as plants, animals or fungi, restricts the large-scale use and production of nutraceuticals. Metabolic engineering via microbial production platforms has been evolved as an eco-friendly alternative approach for the production of nutraceuticals by utilising simple carbon sources (Wang *et al.*, 2016). With the advantage of metabolic engineering techniques and process optimization, polyunsaturated fatty acids, carotenoids, and flavonoids, including resveratrol and naringenin, have been manufactured in various microbial cell factories, giving remarkable yields. Different metabolic engineering techniques have been found to optimize microbial cell factories, each with its own advantages and disadvantages. Strategies like promoters and ribosomes-binding sites (RBSs) libraries screening, plasmid-based expression of multicopy genes, have been reported for the regulation of gene expression of metabolic pathways. Apart from these, other gene editing toolkits have been used for gene insertion and disruption in microbial cell factories, including HDR-based Cre-lox or FLP-FRT systems, Transcription Activator Like Effector Nucleases (TALENs), and Zinc Finger Nucleases (ZFNs). However, Clustered Regularly Interspaced Short Palindromic Repeat (CRISPR) toolkit allows for targeted gene editing with much greater precise than other traditional genetic engineering strategies. CRISPR-modified microbial cell factories results in less unpredictable, off-target effects than those observed in conventional genetic engineering techniques and

thus meets safety standards due to more precise and targeted gene editing ability. The potential of CRISPR enables the design and engineering of complex microbial cell factories that possess multiple genes designed to produce the desired end product and also allows for rapid screening and identification of the most suitable strain for a given application, making it a more reliable and effective bioengineering toolkit than other tools (Hussain *et al.,* 2023).

Biotechnology has revolutionized the field of medicine by offering tools that have drastically accelerated the pace of innovation in drug discovery, diagnostics, and therapy. Among the most promising areas of intersection between biotechnology and medicine is Phytomedicine - the use of plant-derived compounds for therapeutic purposes. With advances in genetic engineering, particularly CRISPR-Cas9 and other genome-editing technologies, the potential to enhance and harness the medicinal properties of plants has reached unprecedented heights. This chapter explores how biotechnology, particularly CRISPR and beyond, is transforming the field of phytomedicine.

2. Genetics and Biotechnology for improving Medicinal Plants

Phytomedicine is a practice that began with error and trial by our ancestors and thus it is as ancient as human evolution. This ancient practice involves the use of herbs as medication, founded on customary prudence or with scientific understanding. Today, phytomedicine involves not only the therapeutic application of herbal remedies but also rigorous exploration of their efficacy, quality, and safety. This includes studying the mechanisms of action of specific herbal extracts and their components, as well as examining pharmacological, pharmacokinetic, clinical, and toxicity findings (Nigam, 2021). Plant based natural products have emerged as potential leads in drug discovery to mitigate human mortality and morbidity. Many biotechnological techniques have been used to modulate plant secondary metabolite pathways to increase the production of valuable secondary metabolites for therapeutic, dietary and industrial use. With the advent of Next-Generation Sequencing (NGS) technique, it is now feasible to analyse the genetic diversity and biosynthetic pathways of medicinal plants. Novel biotechnology-based breeding strategies such as targeted genome editing methods have proven to be excellent toolkit for the engineering of customized medicinal plants with optimized secondary metabolite profile conditions (Dey, 2021).

Assessment of the genetic diversity, conservation, proliferation, and overproduction are the major ways by which genetics and biotechnology accelerates the improvement of medicinal plants faster. Plant tissue culture (PTC) serves as a platform to apply other biotechnology-based breeding methods (BBBMs) in

medicinal plants. The main BBBMs that are directly dependent on PTC are the *Agrobacterium*-mediated gene transformation and artificial polyploidy induction. Manageable regulation of endogens and/or transferred genes via engineered zinc-finger proteins or transcription activator-like effectors can help targeted manipulation of secondary metabolite pathways in medicinal plants. Gene editing technologies such as the sequence-specific nucleases of Transcription Activator-Like Effector Nucleases (TALENs), Zinc-Finger Nucleases (ZFN), and Clustered Regularly Interspaced Short Palindromic Repeats-associated (CRISPR) can help produce user-designed medicinal plants. These cutting-edge targeted genome editing techniques are paving way for advances in plant synthetic biology, thereby creating new avenues for introducing medicinal plants into various industries (Niazian, 2019).

3. History of CRISPR-Cas9: A Breakthrough in Genetic Engineering

Clustered regularly interspaced short palindromic repeats (CRISPR) and CRISPR-associated (Cas) system forms a part of the adaptive immunity in prokaryote system to defend against invasive genetic elements, including viruses and plasmids (Han and She, 2017). The CRISPR/Cas system was first discovered in 1987, following the identification of similar DNA sequences in the genome of *Escherichia coli* during research on genes involved in phosphate metabolism. These DNA sequences, termed CRISPR, work in conjunction with Cas proteins, such as Cas9, to provide defense mechanism. A technological breakthrough in the field of genetic engineering came from Emmanuelle Charpentier and Jennifer A. Doudna, who reported that crRNA and tracrRNA can be combined together to form a single synthetic guide RNA (sgRNA), thereby simplifying the CRISPR/Cas9 system as the researchers now need only two elements to program the targeted cutting of DNA: a Cas9 nuclease and a single guide RNA that guides the nuclease Like Šikšnis, Charpentier and Doudna proved that Cas9 could cut purified DNA *in vitro*, guided by specially designed sgRNAs. This work was published in *Science* on June 28, 2012 and Doudna filed a patent application for the CRISPR/Cas9 gene editing system (Shmakova *et al.,* 2022). Emmanuelle Charpentier and Jennifer A. Doudna were awarded with the Nobel Prize in 2020 for developing the CRISPR/Cas9 gene editing tool that has been used for targeting and modifying the human genome (Khan *et al.,* 2022).

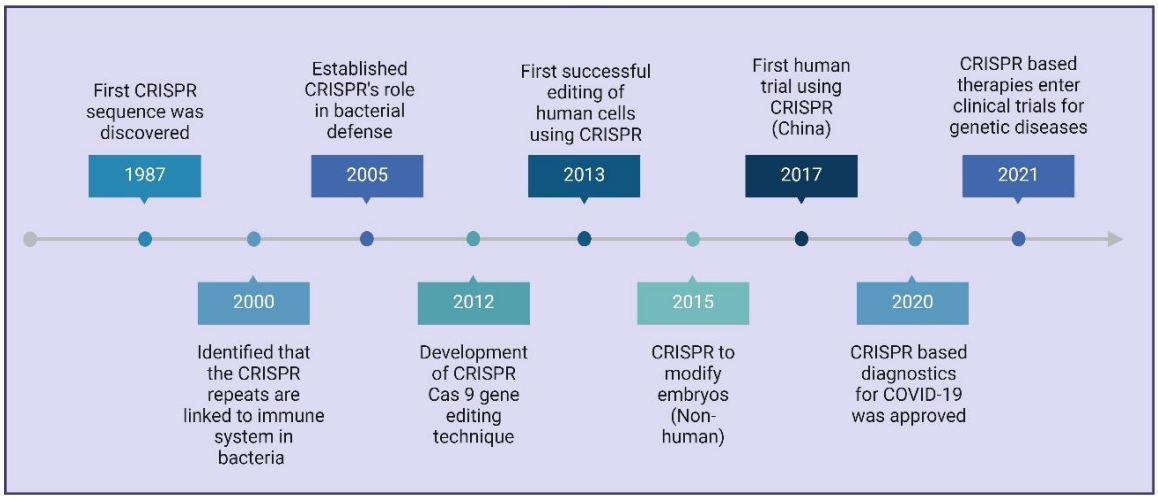

Figure - 1. Time-line chart of the Development of CRISPR-Cas Technology

4. Mechanism of CRISPR CAS9 Technology

Yushizumi Ishino was the first one to report the CRISPR, but its biological application was not understood at the time. Based on effector proteins, this system has been categorized into two main classes with six subtypes (Figure - 2). The type 2 CRISPR-Cas9 system is the most widely used method in the field of genome editing which comprises of three main components: a CRISPR RNA (crRNA), an endonuclease named Cas9, and a transactivating crRNA (tracrRNA). This system consists of two components, first one is the Cas9 protein which can cleave the DNA and second is the guide RNA that identifies the sequence of DNA to be rectified (Tavakoli *et al.,* 2021).

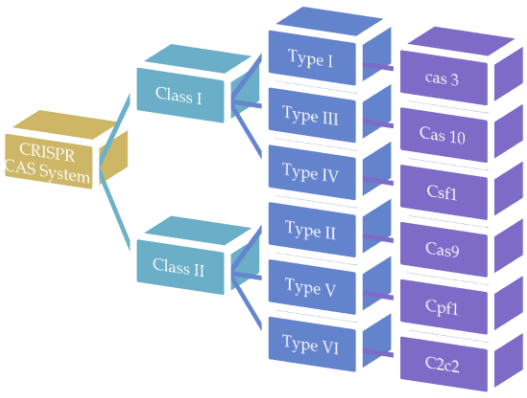

Figure - 2. Classification of CRISPR-CAS system

As previously described, CRISPR/Cas9 cleaves foreign DNA *via* two components, Cas9 and sgRNA. Cas9 is a DNA endonuclease that is obtained from different bacteria, such as *Brevibacillus laterosporus*, *Staphylococcus aureus*, *Streptococcus*

pyogenes, *Streptococcus thermophilus*. However, *Streptococcus pyogenes* is the most widely used one for Cas9 isolation. Cas9 consists of two domains namely, HNH domain and RucV-like domain. The HNH domain cleaves the complementary strand, while the opposite strand of the double-stranded DNA is cleaved by RucV-like domain (Fig.2). The sgRNA is a synthetic RNA which is about 100 nucleotides long. Its 5′-end has a 20 nucleotide sequence that acts as a guide sequence to identify the target sequence accompanied by a Protospacer Adjacent Motif (PAM) sequence, which is often the consensus NGG (N-any nucleotide; G-guanine) (Liu *et al.,* 2017).

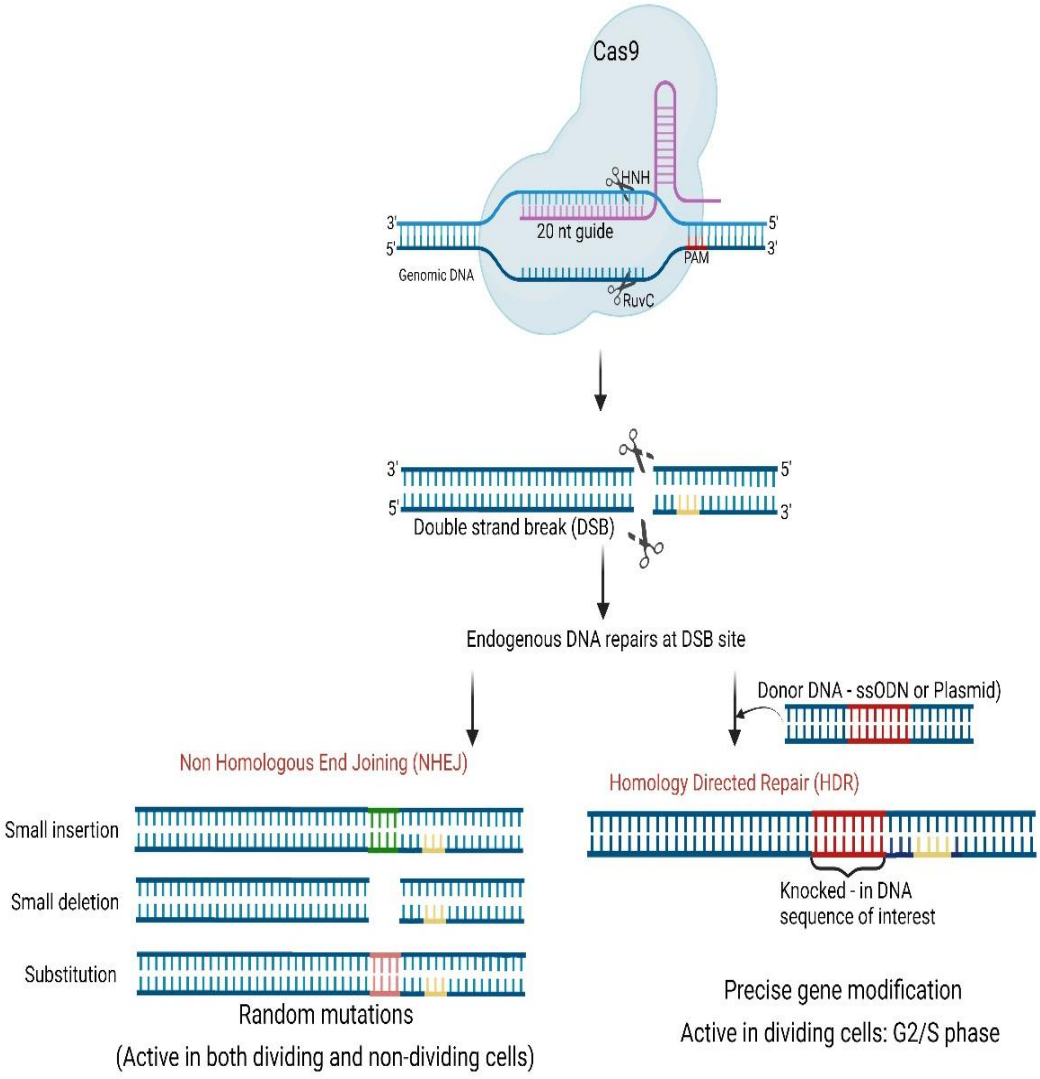

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Figure - 3. The mechanism of CRISPR–Cas9–mediated Genome Engineering

The synthetic sgRNA or crRNA–tracrRNA structure directs the Cas9 to almost arbitrary DNA sequence in the genome through a user-defined 20-nt guide RNA sequence and introduces a double-strand break (DSB) in targeted genomic DNA. Then, host-mediated DNA repair mechanisms take part to repair the DSB generated by two distinct Cas9 nuclease domains. In the absence of a donor template, the prevalent error-prone Non-Homologous End Joining (NHEJ) pathway is activated and causes indels (insertions and deletions) or even substitutions at the DSB site, thus resulting in the loss of gene function. In the presence of a donor template containing the sequence of interest flanked by homology arms, homology directed repair (HDR) which is a error free pathway is initiated through homologous recombination to create desired mutations. This provides the basis for achieving precise gene modification, such as gene knock-in, deletion, correction, or mutagenesis. CRISPR–Cas9 RNA-guided DNA targeting can be detached from cleavage activity by mutating the catalytic residues in the HNH and RuvC domains, making it a versatile platform for a wide range of applications beyond genome editing.

Abbreviations: crRNA, CRISPR RNA; nt, nucleotide; PAM, protospacer adjacent motif; sgRNA, single-guide RNA; tracrRNA, *trans*-activating CRISPR RNA (Jiang and Doudna, 2017).

5. CRISPR/CAS - Editing Oriented to Plants

The development of the CRISPR system has greatly helped in gaining knowledge of a specific enzyme in plant metabolism. This system is known to be effective and convenient in creating multiple gene mutations simultaneously in plants. Thus, the interaction between two or more genes in a specific metabolic pathway can be readily tracked through screening the metabolic profiles in the mutant plants resulted from CRISPR tool. Another advantage of the CRISPR system is its ability to produce '*trans*-gene-free' monocot and dicot plants (Sabzehzari *et al.,* 2020). Researchers are greatly involved in understanding the critical genes involved in metabolic pathways and finding novel synthetic methods for increasing the production of effective compounds. The application of the CRISPR-Cas system to study gene function and regulation of metabolic networks in medicinal plants is essential and meaningful, making it a potential tool for improving quality and breeding ideal germplasms in medicinal plants (Guo *et al.,* 2022). An outline for generating CRISPR-Cas gene edited medicinal plant is given below:

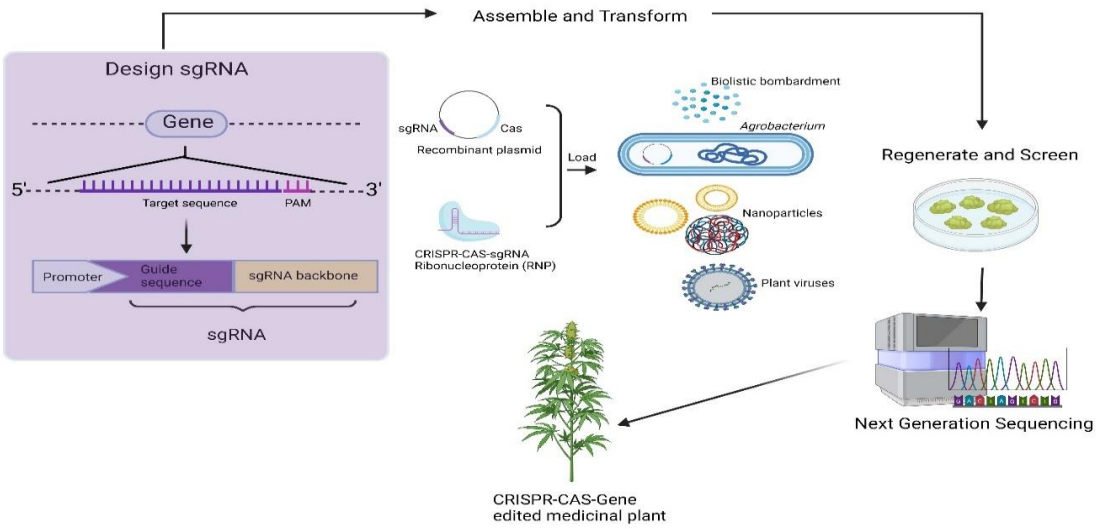

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Figure - 4. Outline of generating CRISPR-CAS Gene Edited Medicinal Plant

Modification in the biosynthetic pathway of plants in the context of CRISPR/Cas9-based editing tool started with the successful implementation of CRISPR/Cas9 in tomatoes which resulted in the production of carotenoid and *γ-aminobutyric acid* (Mitra *et al.,* 2023). *Rehmannia glutinosa* is an important Traditional Chinese medicine (TCM) which possess pharmacological and economic value. In a study conducted by Li *et al.,* (2021) they combined the transcriptome database of *R. glutinosa* and phytoene desaturase (PDS) gene sequences which resulted in the *PDS* gene of *R. glutinosa*. Then, the *PDS* gene was employed as a marker gene to validate the applicability and gene editing efficiency of the CRISPR/Cas9 system in *R. glutinosa*. *Agrobacterium* mediated genetic transformation of the constructed CRISPR/Cas9 system into *R. glutinosa* led to the successful regeneration of both fully albino and chimeric albino plants. The next-generation sequencing (NGS) confirmed that the albino phenotype was indeed caused by *RgPDS* gene target site editing, and it was found that base deletion was more common than insertion or substitution. The outcomes of the study revealed that zCas9 has a high editing efficiency on the *R. glutinosa* genome. Further, this research laid a foundation for further use of gene editing technology to investigate the molecular functions of genes, to create excellent germplasm, to accelerate domestication, and to improve the yield and quality of *R. glutinosa*.

Kui *et al*. (2017) successfully edited five targeted genes, *coumarate 3-hydroxylase (C3H)*, *cinnamate 4-hydroxylase (C4H)*, *4- coumarate: coenzyme A ligase (4CL)*, *cinnamoyl co-enzyme A reductase (CCR)*, and *irregular xylem5 (IRX)* in the lignocellulose biosynthesis pathway using the CRISPR-Cas9 system and analysed the mutation rates of different target sites between 10 and 100 percentage by using PCR amplification and sequencing techniques. This study demonstrated that genome editing in *Dendrobium officinale* can be successfully applied utilising CRISPR-Cas9-mediated genome editing system, suggesting that this technology has great potential as a tool for the genetic investigation and molecular breeding of *D. officinale* (Guo *et al.,* 2022).

Zhou (2018) reported gene editing of phenolic acid metabolic pathway in *Salvia miltiorrhiza* using the CRISPR/Cas9 system by introducing a binary vector with a specific sgRNA. The target gene was selected from a family of eleven *RAS* genes based on bioinformatics analysis, and the target was specifically edited by CRISPR/Cas9 system which resulted in successful editing of the target loci. They also achieved specific mutation mediated by the CRISPR/Cas9 system, and observed variations in phenolic acid levels, indicating the potential of this new technology as a tool for genome modification in medicinal plants and *RAS* as a crucial enzyme regulating the biosynthesis of phenolic acids.

6. Potential applications of CRISPR in Phytomedicine

i) Enhancement of Medicinal Compound Production

As previously mentioned in this chapter, CRISPR is used to modify the biosynthetic pathways in the plants to increase the production of desired medicinal compounds.

Examples:

- **Increased production of Artemisinin in *Artemisia annua*** – It is used as an anti-malarial drug (Koerniati and Simanjuntak, 2020).
- **Efficient production of Vindoline from Tabersonine by Metabolically Engineered *Saccharomyces cerevisiae*** – It is an important alkaloid used in chemotherapy and slo possess anti-diabetic activities (Liu *et al*., 2021)

ii) Development of Disease-Resistant Medicinal Plants

CRISPR can be used to enhance the resistance of medicinal plants to diseases and pests. This ensures a stable and consistent supply of phytomedicines by preventing crop loss due to biotic stress.

Examples:

- **Rice (*Oryza sativa*)** – CRISPR strategy is employed to develop *Oryza sativa* to make them resistant to bacterial blight (Oliva *et al*., 2019)
- **Tomato (*Solanum lycopersicum*)** – Similarly, CRISPR strategy was employed to develop tomatoes resistant to powdery mildew fungus (Pramanik *et al*., 2021).

iii) Elimination of Unwanted Compounds

Examples:

- **Generation of SGA (steroidal glycoalkaloids) - free hairy roots of tetraploid potato (*Solanum tuberosum*)** – CRISPR strategy was used to edit genes responsible for the production of SGA which is a toxic compound found in potatoes (Nakayasu *et al*., 2018).

iv) Improvement of Nutritional and Medicinal Properties

Examples:

- **Increasing beta-carotene levels in rice to improve the nutritional content** (Zafar *et al*., 2020) - This biofortified rice can be used in phytomedicine to combat vitamin A deficiency, which is crucial in developing countries.
- **Significant accumulation of Tartaric acid in Apples** (Kumar *et al*., 2022) – Tartaric acid is known for their antioxidant properties. This can make apples a more potent source of phytomedicine for managing oxidative stress-related diseases.

v) Developing Novel Medicinal Compounds

Examples:

- **Curcumin in Turmeric (*Curcuma longa*)** – CRISPR strategy was used to generate engineered *Saccharomyces cerevisiae* to produce curcumin from glucose (Rainha *et al*., 2024).

vi) Accelerated Breeding of Medicinal Plants

Examples:

- ***Cannabis* (*Cannabis sativa*) -** CRISPR can be used to selectively breed *Cannabis* plants to produce higher levels of therapeutic cannabinoids like CBD while reducing psychoactive THC levels (Guo *et al*., 2022).

vii) CRISPR-Enhanced Bioreactors for Phytomedicine Production

Examples:

- **CRISPR-Edited Yeast for Alkaloid Production -** CRISPR can be used to edit yeast strains to produce plant alkaloids in bioreactors. This enables the production of plant-based medicines like morphine and codeine without the need for large-scale cultivation of plants (Pyne *et al.*, 2020).
- **CRISPR-Engineered Microbes for Terpene Production (**Sun *et al.*, 2024) **-** Microbes can be engineered using CRISPR to produce terpenes, a class of compounds with various medicinal properties. These can be scaled up in bioreactors for pharmaceutical use.

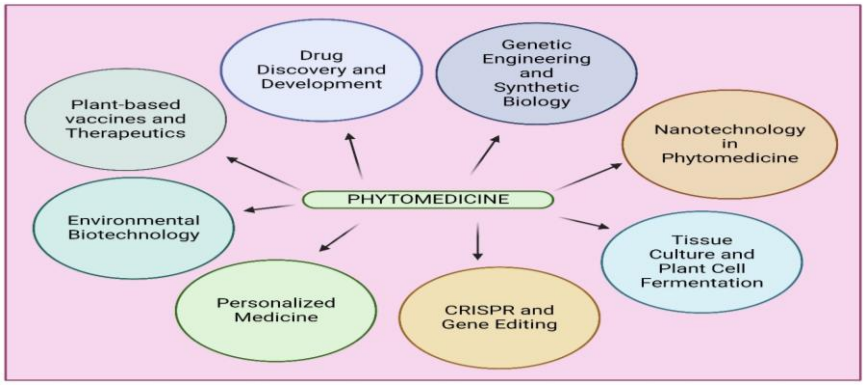

Figure - 5. Application of CRISPR-Cas in different fields

Table – 1: Application of CRISPR-CAS9 technology for Metabolite enhancement in Medicinal plants

Species name	Name of the metabolite	Gene targeted	CRISPR strategy	Transformation method	Improvement achieved	Reference
Dendrobium officinale	Polysaccharides, bibenzyls, essential oils	C3H, C4H, 4CL, CCR, IRX	Frameshift	Hairy roots	10 % - 100 % efficiency	Kui *et al.* (2017)
Comfrey (*Symphytum officinale*)	Homospermidine toxic free	HSS	Knockout	Hairy roots	Reduced level of Homo spermidine	Zakaria *et al.* (2021)
Salvia miltiorhiza	Laccase	SmLAC7 and SmLAC20	Targeting conserved regions to knockout multiple genes of laccase family	Hairy roots	Accumulation of lignin and phenolic acid	Zhou *et al.* (2021)
Atropa belladona	Anticholinergic tropane alkaloids, hyoscyamine, scopolamine, anisodamine	Hyoscyamine 6β-hydroxylase (A bH6H)	Pre-mature stop codon	Tissue culture cotyledon	63.6% mutation rate, 3.68 - 4.21 fold increase in hyoscyamine	Zeng *et al.* (2021)
Dioscorea zingiberensis	Diosgenin	Dzfps	Frameshift	Hairy roots	Decreased squalene level	Feng *et al.* (2018)
Nicotiana tabacum	Nicotine free	*Nt* BBL	Knockout	Tissue culture	99.6 % Nicotine free	Schachtsiek and Stehle (2019)

Table – 2 Application of CRISPR-CAS9 Delivery System in the field of Nutraceuticals

Nutraceuticals	Medicinal property	Microbes used for production	CRISPR strategy	Modification	Production yield	Reference
β-carotene	Antioxidant property, Provitamin A Activity, improves Cognitive Function	*Saccharomyces cerevisiae*	CARM	Laboratory evolution of *S. cerevisiae*	10.5 times increased	Zhao *et al.* (2022)
		Escherichia coli	CRISPR-Cas9 system	Integration of almgs gene	44.2 mg g^{-1} DCW	Wu *et al.* (2017)
Hyaluronic acid	Wound Healing, Joint Health, Hydration and Moisture Retention	*Bacillus subtilis*	CRISPR-Cas9 toolkit	Repression of pfkA and zwf genes	131 % increased	Westbrook *et al.* (2018)
Lycopene	Antioxidant Effects, Cardiovascular Health, Skin Protection	*Escherichia coli*	CRISPR-λ-Red system and CRISPR-Cas9 system	Integration of lycopene synthetic pathway and deletion of redundant sequences	9.1 mg g^{-1} DCW	Su *et al.* (2020)
		Yarrowia lipolytica	CRISPR-Cas9 system	Integration of lycopene biosynthesis pathway genes	3.61 mg g^{-1} DCW	Liu *et al.* (2022)
γ - Aminobutyric acid	Neurotransmitter, Anxiety Reduction, Blood Pressure Regulation	*Escherichia coli*	CRISPR-Cas9 technology	Removal of cryptic plasmids (pMUT1 and pMUT2)	17.9 g L^{-1}	Lan *et al.* (2021)
Resveratrol	Antioxidant Properties, Cardiovascular Benefits, Anti-Aging Effects	*Escherichia coli*	CRISPRi system	Repression of malonyl-CoA pathway relative genes	187.1 mg L^{-1}	Wu *et al.* (2017)
Zeaxanthin	Crucial for Eye Health, Antioxidant Activity, Skin Protection	*Escherichia coli*	CRISPRi	Repression of ftsZ, mreB, pbp, and rodZ genes	45.7 % increased	Shen *et al.* (2016)
		Escherichia coli	dCas9-Lag system	Plasmid localization	0.89 mg g^{-1} DCW	Xie *et al.* (2020)
Astaxanthin	Powerful Antioxidant, Anti-Inflammatory Effects, Skin Health	*Saccharomyces cerevisiae*	CRISPR-mediated recombination	TDA4 gene deletion	1.26 mg g^{-1} DCW	Jin *et al.* (2022)
		Escherichia coli	dCas9-Lag system	Plasmid localization	0.41 mg L^{-1}	Xie *et al.* (2020)

7. Beyond CRISPR: Emerging Biotechnologies in Phytomedicine

7.1. Nanotechnology – A promising approach in Phytomedicine

A major part of the modern pharmacopeia has its origins in phytomedicine. Employing nanotechnology in the field of phytomedicine holds enormous potential to overcome and mitigate numerous shortcomings associated with conventional phyto-therapeutics. Significant progress has been made in enhancing the properties of nano-phytomedicine with high specificity, sensitivity, and efficacy in treating a wide range of diseases. Additionally, it also helps to manage and resolve biopharmaceutical challenges associated with phytomedicine (Barkat *et al.,* 2020). In

the future, novel approaches to the treatment of different diseases may be made possible by a variety of plant-derived bioactive antimicrobial peptides such as cyclotides, knottin peptides, and thionein. Naturally occurring phytochemicals or plant derivatives such as Epigallocatechingallate (EGCG), Curcumin, Quercetin, Resveratrol, Apigenin and Anthocyanidins have been studied extensively for maintaining and promoting health (Gul *et al.,* 2021). But the delivery of phytomedicine is never easy because of its poor aqueous solubility, poor permeation, low systemic availability, instability and extensive first pass metabolism (Gunasekaran *et al.,* 2014).

7.1.1. Green Nanotechnology

The production of nanoparticles through herbal extracts plays a significant role in the field of nanotechnology. It is termed as 'Green technology' because it does not involve the usage of harsh and harmful chemicals (Mishra *et al.,* 2022). Incorporation of phytomedicines into nanotechnology enhances the solubility, absorption rate, and permeation membrane of phytomedicine (Aziz and Setapar, 2020). In phytoformulation research, developing nanotechnology-based dosage forms, such as solid lipid nanoparticles (SLNs), polymeric nanoparticles (nanospheres and nanocapsules), proliposomes, liposomes, nanoemulsions, etc., offers great advantages. These include enhancement of solubility and bioavailability, improvement of stability, suppression of toxicity, improvement of pharmacological activity, sustained delivery, improving tissue macrophage circulation, and defense against physical and chemical degradation. Nano-sized drug delivery systems (NDDS) of herbal drugs help to overcome problems associated with traditional plant medicines. Hence, incorporating nanocarriers as an NDDS in traditional medicine systems can help combat more chronic diseases like diabetes, cancer, asthma, and others with the aid of herbal drugs (Verma *et al.,* 2019).

7.1.2. Nanotechnology-Based Drug Delivery System for Phytochemical Compounds

For effective delivery of herbal drugs, new drug delivery systems based on nanotechnology have been developed (Figure - 6). These delivery systems include, lipid-based carrier systems consisting of vesicular systems (liposomes, phytosomes, transfersomes, ethosomes, and niosomes), lipid particulates (SLN and NLC), and nano-emulsions **(**Dewi *et al.,* 2022).

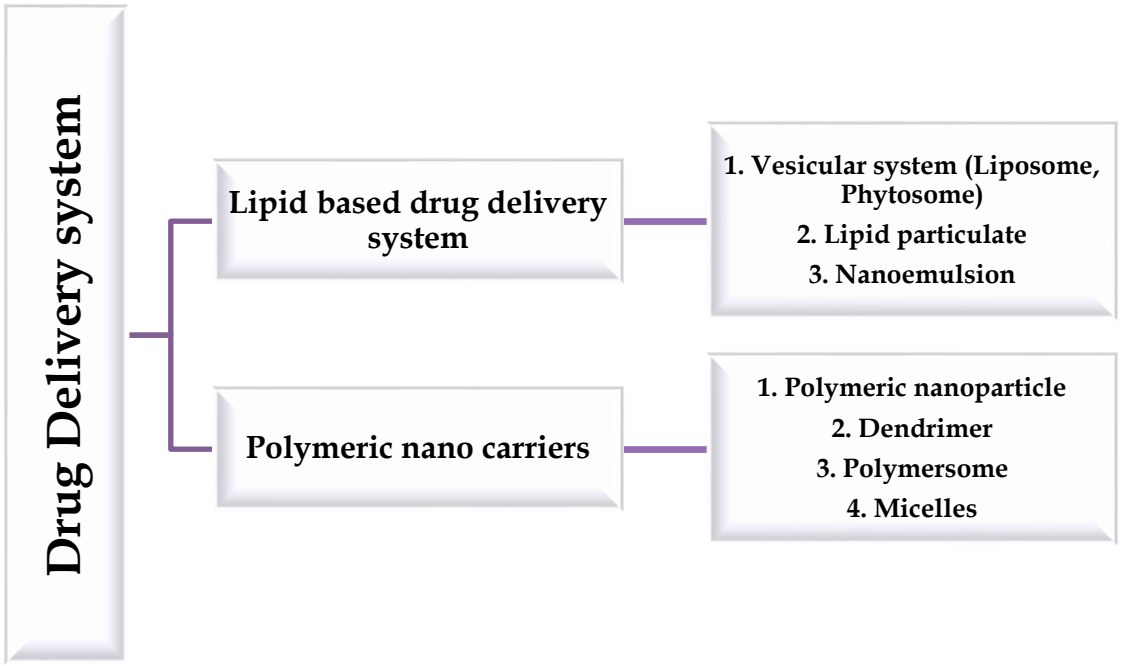

Figure – 6: Classification of drug delivery system

Liposomes and nano-emulsions are also called as bilayer phospholipid vesicles and possess greater potential in nutraceutical industries as they are capable of encapsulating both hydrophilic and lipophilic materials. This ensures a synergistic effect and helps protect bioactive compounds that are highly sensitive, ensuring enhanced bioavailability, sustainable release and storage stability (Puri *et al.*, 2022). Song *et al.*, (2022) encapsulated curcumin and tetrandrine in a liposome carrier system and the results of that study demonstrated high solubility and bioavailability for curcumin and tetrandrine after their encapsulation within the liposome carriers. In addition, *in vivo* studies show no significant toxicity of this system to zebrafish.

Phytosome is novel technology that is shown to address all afore mentioned problems and limitations of traditional systems of herbal drug delivery. Plant extract or its components get anchored to phospholipids (chiefly phosphotidylcholine), forming a lipid responsive complex which are termed as phytosome. Combining the emulsifying property of phospholipids with the herbal extract/phytoactive constituent, the phytosome affords considerably improved bioavailability and deliver faster and enhanced absorption in intestinal tract. Recently, phytosome approach has been employed in several well-known natural drugs such as ginseng, green tea hawthorn, olive oil and grape seed etc (Kumar *et al.*, 2020).

7.2. Base Editing and Prime Editing

Base editing and prime editing are the advanced forms of CRISPR technology that allow for more refined genomic edits without resulting in double-strand breaks. Base editing enables the conversion of one DNA base into another, while prime editing permits more complex edits, including insertions and deletions with high precision. Both techniques are being investigated for their potential to enhance the production of bioactive metabolites in medicinal plants, providing a more controlled approach to genetic modification (Erdoğan *et al.,* 2023). The base editing tools are classified into two: cytosine base editors (CBEs) and adenine base editors (ABEs). These base editing tools either consists of a nicked Cas9 (nCas9) or catalytically inactivated Cas9 (dCas9) coupled with a particular deaminase. The deaminases are known to induce transitory alterations in DNA by converting C•G to T•A or A •T to G •C. Moreover, the prime editing tool contains two main components: a fusion protein that includes Cas9 nickase (H840A) and reverse transcriptase, in addition to a second component called prime editing guide RNA (pegRNA). The Cas9 nickase variant (H840), consisting of a RuvC functioning domain, introduces nick in the non-target DNA strand. Reverse transcriptase then works with a pegRNA template to modify the necessary DNA. The prime editing tool has evolved into a sophisticated platform for facilitating accurate base substitution, DNA deletion, and DNA insertion (Das *et al.,* 2024).

7.3. Synthetic Biology Approaches

Synthetic Biology combines biological research with engineering principles to design and construct new biological parts, devices, and systems. In the context of phytomedicine, synthetic biology is being used to redesign metabolic pathways in plants, enhancing their ability to produce therapeutic compounds and metabolites. This approach allows for the creation of plants that can produce desired phytochemicals with higher yield (Guo *et al.*, 2022).

7.4. Omics Technologies

The integration of genomics, transcriptomics, proteomics, and metabolomics is collectively known as omics technologies. It provides deeper insights into the genetic and biochemical networks of medicinal plants. These technologies facilitate the identification of specific genes and metabolic pathways that can be targeted for modification, leading to enhanced production of therapeutic compounds and improved plant resilience (Mitra *et al.*, 2023).

8. Conclusion and Future Prospects

In conclusion, the intersection of biotechnology and phytomedicine, particularly through the lens of CRISPR and other advanced techniques, presents a transformative potential for the future of medicinal plant research and application. The ability of CRISPR/Cas9 to facilitate precise genetic modifications paves the way for enhancing the production of valuable phytochemicals, optimizing therapeutic properties, and improving the overall efficacy of medicinal plants. However, the journey ahead is not without challenges, including the need for extensive genomic data, the development of more efficient delivery systems, and the establishment of regulatory frameworks that address ethical considerations. As researchers continue to explore the capabilities of CRISPR and nanotechnology, the future prospects for phytomedicine look promising, with the potential for significant advancements in drug development, sustainable practices, and the conservation of biodiversity. The ongoing integration of these technologies will likely lead to innovative solutions that not only enhance the therapeutic potential of medicinal plants but also contribute to global health and well-being.

9. References

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Leguminosae Families Ethnomedicinal Plants Used by Traditional Healers in Alirajpur, Madhya Pradesh, India

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Chapter - 2

Phytomedicine Innovations: The Future of Plant – Based Therapies
ISBN: 978-81-977907-4-4
First Edition
Chapter – 2, Page: 22 - 28

2

LEGUMINOSAE FAMILIES ETHNOMEDICINAL PLANTS USED BY TRADITIONAL HEALERS IN ALIRAJPUR, MADHYA PRADESH, INDIA

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Abstract

Medicinal plants are without issue available and there isn't any facet impact in comparison to fashionable medication. Ethnomedicinal plants are usually acquired through word of mouth and its miles loss of life amongst younger generation with the prevalence of modern-day remedy. So there may be urgency in deciphering and recording such facts. Survey will become accomplished within the 12 months 2020-2021 in precise season. An Ethnomedicinal observe turned into done in 10 precise cities of Alirajpur district with an average to file the data with regard to folkloric employments of indigenous plant species. Records became accumulated thru interview with a hundred and fifty informants across 10 villages of Alirajpur. Secondary records have been received from medical database. Leguminosae is the most important circle of relatives in the region. Announced plant species as one of a kind commonplace arrangements are utilized by the metropolis people for the administration and moreover treatment of various afflictions jogging from wind chomp to fever. Gift have a look at evaluations 41 plant species which is distributed in 26 genera. *Borassus flabellifera* L. is particular species internal within the vicinity. The rate of eroding biodiversity is growing and 10% of the recorded organic wealth is at the verge of extinction because of care and action need to be taken

on priority foundation for the conservation of unusual, species. The natural element dominates on this area and the kind of herbs is 21 and shrubs 2 and trees 13 together with 5 species of climber.

Keywords: Ethnomedicinal Flora, Ethnic plant, Leguminosae, Indigenous people.

1. Introduction

India has historical clinical understanding in human civilization which is about 5000 thousand years old, which changed into based on plants and perhaps preserving the identical importance in thoughts, flowers have been worshiped in Indian civilization so they may be covered and their expansion and propagation befell. This legacy can be passed directly to our future generations additionally. Ayurveda device itself is a complete understanding for the overall fitness and durability of guy. A entire record of the many hundreds of plant species used for human functioning could fill volumes, but historians have often tended "to push aside flora as much less than essential in records" (Yadav *et al.*, 2013). Due to the transition to western civilization, our traditional information is step by step disappearing and with a view to become modern, we are transferring aside this historical past. Especially our medicinal plants and minerals are continuously getting depleted. Discussions have been held to attract attention towards the Ayurvedic scientific gadget that's natural for human civilization and is in harmony with its bodily wishes and nature. The arboreal plant life of Alirajpur is consists of majority of medicinal species which may be very common and exciting. No actual plant life of Alirajpur has been posted till these days. There no any separate proper report at the arboreal flowers of Alirajpur town is available in literature, so gift paintings have been undertaken. The present paintings are very last consequences of two years innovations.

2. Study Area

Alirajpur District becomes carved out of Jhabua District on 17th May additionally 2008. A village called Amkhut is considered as Switzerland of M.P. and another village named "Kathiwada" is referred to as 'Cherapunji' of M.P. In 18th century the ruler of this metropolis called Rajpur had the capital at "Aali ", close by village however alas the capital changed into destroyed by means of hearth and therefore transferred to this metropolis and was renamed as 'Alirajpur'. Alirajpur district mendacity among 22018'N range and 74020'E longitude, covers an area of 3182 rectangular kilometers. Mahee and Narmada rivers make its eastern and Southern border. According to census 2011, Alirajpur population is 728,999. Alirajpur District average Rainfall is 850 mm. Alirajpur District temperatures degrees between 230 - 300C are located. Bhagoriya is a unique cultural public festival of Alirajpur district.

3. Methodology

The plant exploration paintings changed into carried in precise seasons. Region artwork modified into done in Oder to analyze the historically the use of plant life, with floristic have a have a look at of numerous components of hilly region in particular seasons. Subject journeys have been organized in line with first rate seasons of flowering and fruiting seasons of the plants. The sector work protected interviews, observations and plant series. Voucher range is given to every plant and location information and different relevant data is referred to in filed dairy. Information modified into collected through interviews with 100 fifty informants across 10 villages of Alirajpur block. Interviews had been conducted to the local population, the herbalist, Badwa. Questions concerning the application of various flowers, Plant detail used, course of administration, were requested through questionnaire. All habitats of the study region surveyed carefully. The flowers and distribution pattern of the flowers have been studied. Amassed plants specimen turned into systematically tagged, presses dried and hooked up on herbarium sheets. Plant series and herbarium schooling was accomplished by way of using popular method (Jain and Rao, 1976). Plant specimens have been preserved by using dipping the entire specimens in saturated solution of Mercuric chloride and alcohol. Dry and preserved plant life mounted on herbarium sheets (11.5 × 17.5 inch) by means of manner of adhesive glue and fevicols. Statistics stated within the region phrase e book within the direction of field survey become transferred to label and pasted on respective herbarium sheet on proper facet of the lowest of herbarium sheet. identity of flowers is finished with the help of plants (Verma *et al.*, 1993; Mudgal *et al.*, 1997; Khanna *et al.*, 2001; Shah, 1978; Duthi, 1960; Gamble, 1915; Hains,1921 - 1924; Cook, 1903; Hooker, 1872 - 1897; Naik, 1998 and different taxonomic literature and moreover some Taxa identified with in BSI, Allahabad, India. Medicinal plant life species were moreover photographed at collection time and in preserved from after allotment of voucher variety. Secondary records were received from medical database. The medical call of the vegetation changed into matched and organized in consultation with the strolling list of all plants species (http://www.the plant listing.org), monetary, and medicinal charge of indigenous vegetation carried out in the look at location has been enquired within the marketplace of Alirajpur. On this regard, a questionnaire becomes accompanied to interview the close by plant creditors and medicinal vegetation dealers inside the close by markets. Market chain for the economic plants creditors and people interview in medicinal plants alternate grow to be investigated. On the basis of survey primarily based list of medicinal flora have become prepared with emphasis on plant marketplace availability popularity, and charge of plants. The available literature available on the market survey become moreover accrued and made a evaluation from it to observe it with gift findings. All

the species have been indexed in alphabetical order thru their scientific name, circle of relatives, and habitat.

4. Results and Discussion

Ethnomedicinal plants applied normally by specific local tribes and distinct metropolis individuals, regardless of the fact that, comparative takes a shot at restorative plants in connection to their conventional uses had been archived in advance than as distinct above, however the statistics imitated in this about recorded kinds of restoration flora are substantially new and feature no longer been recorded earlier than. Be that as it could, the prevailing research uncovers that introduced flowers anticipate a essential element within the important medicinal services of the provincial population within the examination location. The present exam uncovers the folkloric employments of Leguminosae circle of relatives's 41 Ethnomedicinal plant species having a place with 26 genera and 25 families (Table - 2). The natural element dominates in this area and the sort of herbs is 21 and shrubs 2 and trees 13 together with 5 species of climber. Table-1are indicates category clever distribution of texa. Flora have been applied either internal or remotely to remedy distinct afflictions. A large portion of the plant species are utilized to remedy at the least than two illnesses. the existing research grow to be caused file the ethnomedicinal plant assets of Alirajpur, and to research the common studying or conviction of those plants used by the metropolis people for their crucial human company's wishes. Such Ethnomedicinal facts is required for taking over massive scale development and safety of therapeutic plants that may guide the country monetary device of individuals via the inspiration of home grown remedy ventures and advancement of medicinal services framework in our state. Further, logical exam in moderate of the same old getting to know healing plants can be a technique inside the disclosure and development of novel medication leads.

Table - 1: Category Wise Distribution of Texa

Category	Climbers	Herbs	Shrubs	Trees
Number of taxa	05	21	02	13

Table - 2: Family Leguminosae Medicinal Plants of Alirajpur (M.P.), India

Botanical name	Habitat	Disease
Abrus precatorius L.	Climber	Tetanus and Rabies
Acacia leucophloea (Roxb.) Willd.	Trees	Preventive of Infections and Snake bites
Acacia nilotica (L.) Delile	Trees	Burns, Wounds and Stomachache
Aeschynomene aspera L.	Herb	Wounds and Urinary infection
Aeschynomene indica L.	Herb	Wound, Urinary infection and Hepatitis
Albizia amara (Roxb.) B. Boivin	Trees	Shampoo for Hair and Skin diseases
Albizia lebbeck (L.) Benth.	Trees	Conjunctivitis and Jaundice
Alysicarpus bupleurifolius (L.) DC.	Herb	Stomach ache, Snakebite and Fever
Alysicarpus tetragonolobus Edgew.	Herb	Fever, Skin diseases and Stomach-ache
Bauhinia purpurea L.	Trees	Antidiabetic and Inflammation
Butea monosperma (Lam.) Taub.	Trees	Diarrhea and Dysenteric
Caesalpinia bonduc (L.) Roxb.	Shrub	Fever, Inflammation and Diabetes
Cajanus platycarpus (Benth.) Maesen	Climber	Stomachache
Cajanus scarabaeoides (L.) Thouars	Climber	Dysentery and Swelling inflammatory
Cassia fistula L.	Trees	Joint pain and Chest pain
Clitoria annua J. Graham	Climber	Urinary and Skin disorders
Clitoria ternatea L.	Climber	Memory enhancer
Crotalaria albida Roth.	Herb	Anti-inflammatory
Cullen corylifolium (L.) Medik.	Herb	Impotency and Premature ejaculation
Dalbergia latifolia Roxb.	Trees	Diarrhea, Worms and Indigestion
Dalbergia sissoo DC.	Trees	Inflammations, Hernia and Skin diseases
Desmodium dichotomum (Willd.) DC.	Herb	Dysentery and Wounds
Desmodium scorpiurus (Sw.) Desv.	Herb	Burn and Inflammations
Indigofera linifolia (L.f.) Retz.	Herb	Diuretic and Burn
Indigofera linnaei Ali	Herb	Burn and Inflammations
Indigofera tinctoria L.	Herb	Fever, Stomach pain and Wounds sores
Indigofera trifoliata (Naik) Sanj.	Herb	Leucorrhoea and Nutritive tonic
Lathyrus aphaca L.	Herb	>30 % balanced diet (eaten in diet)
Mimosa rubicaulis Lam.	Herb	Ulcer, Wound and Fever
Pithecellobium dulce (Roxb.) Benth.	Trees	Diarrhea, Dysentery and Constipation
Pongamia pinnata (L.) Pierre	Trees	Tumors, Piles, Skin diseases and Ulcer
Prosopis cineraria (L.) Druce	Trees	Asthma and Leukoderma
Rhynchosia bracteata Baker	Herb	Abortifacient and Healing of wounds
Rhynchosia minima (L.) DC.	Herb	Inflammations
Senna alata (L.) Roxb.	Herb	Typhoid, Malaria and Ringworms
Senna alexandrina Mill.	Shrub	Laxative
Senna occidentalis (L.) Link	Herb	Antibacterial and Anti-inflammatory
Tamarindus indica L.	Trees	Wound healing and Abdominal pain
Tephrosia pumila (Lam.) Pers.	Herb	Ulcers and Asthma
Tephrosia purpurea (L.) Pers.	Herb	Leprosy, Ulcers and Asthma
Zornia gibbosa Span.	Herb	Dysentery

5. Conclusion

The anthropogenic hobby has affected the floristic composition of the area however also pose a terrific danger to a few species that have low abundance and are uncommon on this place. Because of different factors consisting of changing environmental conditions, biotic factors, destruction of habitat and so forth affected flora. Biotic factors, destruction of habitat a few plant species dealing with threats for his or her lifestyles. Conservation of the medicinal flora is one of the crucial segments in the herbal resource control. Earlier than few a long time, it has floristically very rich with various habitats. But due to various factors the flowers of the location have induced rapid destructions of habitats of the plant life. The floristic composition of the location but additionally pose an incredible risk to a few species that have low abundance and are rare on this area so the existing examine can be beneficial for the future researchers in particular to ecologists and taxonomists to examine the flowers of this area and layout studies in such manner for defensive and keep of its biodiversity earlier than these species inhibited to this place emerge as completely vanished.

Acknowledgement

Our sincere way to nearby humans of Alirajpur is notably stated. help and co-operation for the duration of plant survey rendered through Indigenous human beings of the place is quite stated.

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Chapter - 3

Phytomedicine Innovations: The Future of Plant – Based Therapies
ISBN: 978-81-977907-4-4
First Edition
Chapter – 3, Page: 29 - 48

3

TRIGONELLINE METABOLISM AND ITS THERAPEUTIC EFFECTS

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Abstract

Trigonelline, a naturally occurring alkaloid predominantly found in coffee, fenugreek seeds, and certain medicinal plants, has gained exciting attention due to its diverse metabolic and therapeutic properties. Upon ingestion, trigonelline undergoes metabolism in the liver and intestines, where it is converted into various bioactive compounds such as nicotinic acid. These metabolites play a significant role in the regulation of physiological processes, including glucose metabolism, lipid regulation, and neuroprotection. Emerging research has highlighted trigonelline's potential therapeutic effects, particularly its anti-inflammatory, antioxidant, antidiabetic, neuroprotective, and anticancer properties. Trigonelline's ability to modulate oxidative stress, inhibit pro-inflammatory pathways, and improve insulin sensitivity makes it a promising candidate for treating metabolic disorders such as type 2 diabetes and neurodegenerative diseases. Additionally, its anticancer effects have been observed in various in vitro and in vivo models, where it influences apoptosis, cell proliferation, and tumor suppression. This book chapter aims to provide a comprehensive understanding of trigonelline metabolism and its wide-ranging therapeutic applications, offering insights into its potential as a novel therapeutic agent for chronic diseases.

Keywords: Alkaloid, pharmaceutical benefits, metabolism, trigonelline

1. Introduction

For centuries, traditional medicine has relied on plant-based remedies to treat a wide range of illnesses, a practice deeply rooted in ancient healing systems. Ayurveda, Traditional Chinese Medicine (TCM), and indigenous herbal practices have long been pillars of health management in various cultures, where the therapeutic properties of plants have been harnessed to manage diseases and maintain overall well-being. These traditional systems of medicine are built on the premise that natural compounds, particularly those derived from plants, have the power to restore balance within the body and address the root causes of illness. Their continued use and popularity across generations can be attributed to the perceived effectiveness of plant-based therapies, which are often seen as gentler and more holistic compared to modern pharmaceutical approaches (Rizvi *et al.*, 2022). Ayurveda, a system of medicine originating in India over 5,000 years ago, emphasizes the use of herbs and plant-based compounds to maintain health and treat ailments by balancing the body's energies (doshas). Similarly, TCM, which dates back at least 2,000 years, incorporates plant-based formulations, including herbs and roots, as integral components of its approach to healing, targeting the underlying imbalances believed to cause disease. Indigenous healing practices worldwide, from the Americas to Africa, have also extensively utilized local flora to develop remedies for a multitude of ailments, ranging from infectious diseases to chronic conditions (Jaiswal and Williams, 2016).

In contrast, modern medicine, which has evolved primarily over the past few centuries, has focused on synthetic drugs and chemically derived treatments, revolutionizing healthcare with significant advancements, particularly in combating infectious diseases, managing chronic conditions, and performing life-saving surgeries. The development of antibiotics, vaccines, and synthetic drugs has undeniably saved millions of lives and continues to be indispensable in addressing acute medical issues. However, despite these advancements, modern medicine has its limitations. Synthetic drugs often come with a range of side effects, some of which can be severe or life-threatening (Singh 2010). Additionally, the emergence of drug resistance most notably in the case of antibiotics has raised global concerns. Many infectious diseases that were once easily treatable are becoming resistant to conventional drugs, rendering them less effective. Moreover, the high costs associated with developing, producing, and accessing synthetic drugs pose significant barriers to healthcare, particularly in low- and middle-income countries (Chinemerem *et al.*, 2022).

These limitations have prompted a resurgence of interest in plant-based medicines, especially in contemporary research. Researchers and healthcare professionals are increasingly recognizing the need for alternative, more sustainable

therapeutic options that can complement or replace synthetic drugs in certain cases. Plant-based compounds offer several advantages, including a lower risk of side effects, reduced likelihood of drug resistance, and greater accessibility in terms of cost and availability (Hamidi *et al.*, 2022). Furthermore, plants are an abundant source of bioactive compounds, many of which have been used traditionally for centuries, providing a rich foundation for scientific exploration and validation (Riaz *et al.*, 2023).

In recent years, there has been a growing trend toward investigating plant-derived bioactive compounds as potential therapeutic agents. The focus on natural products is driven by their relative safety, affordability, and wide array of pharmacological activities (Shoaib *et al.*, 2023). Natural products often possess complex chemical structures that can target multiple biological pathways, offering a holistic approach to disease management. This is in contrast to many synthetic drugs, which are designed to target specific molecular pathways and may not address the multifaceted nature of chronic diseases (Wainwright *et al.*, 2022). Among the natural products gaining attention, alkaloids naturally occurring nitrogenous compounds are particularly promising due to their ability to exert therapeutic effects in various disease models. Alkaloids are a diverse group of compounds with potent biological activities, including anti-inflammatory, antimicrobial, antidiabetic, and anticancer properties. Well-known alkaloids such as morphine, quinine, and caffeine have long been used in modern medicine, and new alkaloids continue to be explored for their therapeutic potential. As a result, the exploration of plant-based alkaloids as novel drug candidates has become a critical area of research, with scientists seeking to harness their medicinal properties for the development of safer, more effective treatments for a wide range of diseases (Atanasov *et al.*, 2021).

This renewed interest in plant-based compounds is not just a return to traditional practices but a recognition of their potential to address modern health challenges. Researchers are combining the knowledge of traditional medicine with advanced technologies, such as molecular biology and bioinformatics, to uncover the mechanisms behind the therapeutic effects of plant-based compounds and optimize their use in modern healthcare. By identifying bioactive molecules like alkaloids, and understanding their pharmacological actions, researchers aim to create a bridge between the ancient wisdom of plant-based remedies and the precision of modern drug development.

Trigonelline, a pyridine alkaloid, has emerged as a particularly interesting compound because of its diverse biological activities and potential therapeutic applications in modern medicine. The growing interest in trigonelline is rooted in its abundance in common plants such as coffee beans, fenugreek seeds, and other

legumes, as well as its demonstrated ability to modulate key metabolic processes in the body (Zhou *et al.*, 2012). Unlike many other alkaloids, trigonelline is water-soluble and highly bioavailable, making it easier to absorb and utilize in the human body. Recent studies have highlighted its potential in addressing a variety of health conditions, including diabetes (Haxhiraj *et al.*, 2024), neurodegenerative diseases (Farid *et al.*, 2020), and sarcopenia (Membrez *et al.*, 2024). This renewed focus on plant-based compounds, including trigonelline, reflects the increasing demand for safer, more sustainable therapeutic options in modern healthcare. The therapeutic, pharmacological applications, and a complete knowledge on the metabolic properties of Trigonelline is need for the researcher. In this chapter, author overview the pharmacological properties and applications of Trigonelline is attempted.

2. Structure of Trigonelline

Trigonelline is an alkaloid chemically classified as N-methylpyridinium-3-carboxylate, with a molecular weight of 137.138 g/mol. Its molecular formula is $C_7H_7NO_2$, indicating the presence of carbon, hydrogen, nitrogen, and oxygen in its structure, as shown in Figure - 1 (https://pubchem.ncbi.nlm.nih.gov/). The structure of trigonelline consists of a pyridine ring substituted with a methyl group at the nitrogen atom and a carboxyl group (-COOH) attached to the third position of the ring. This makes trigonelline the N-methyl derivative of niacin (nicotinic acid or vitamin B3), an important compound involved in cellular energy metabolism. The presence of the quaternary ammonium group (a positively charged nitrogen atom) and the carboxylate group ($-COO^-$) gives trigonelline distinctive chemical behavior. Due to these functional groups, trigonelline behaves similarly to amino acids and can exist as a zwitterion, a molecule that carries both positive and negative charges simultaneously. In this form, the molecule has an internal balance of charge, which can affect its solubility, stability, and interactions within biological systems. Trigonelline has been described to have a bitter taste (Ashihara *et al.*, 2015).

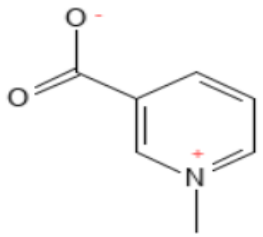

Figure - 1. Structure of Trigonelline

3. Metabolism of Trigonelline

Trigonelline accumulate in mature seeds of a number of plant species, including coffee (Matsui *et al.*, 2007). During germination of coffee seeds, limited amounts of trigonelline are catabolized and used as a substrate for the synthesis of nitrogen containing compounds (Shimizu and Mazzafera 2000). It has been supposed that nicotinic acid, which is a precursor of trigonelline synthesis, originates from two distinct routes: catabolism of NAD, and the de novo synthesis of NMN from amino acid precursors via quinolinic acid. The pyridine nucleotide cycle, which comprises the catabolism and regeneration (salvage) pathways of NAD, differs considerably between organisms. In animals, some bacteria and fungi, nicotinamide, which is a catabolite of NAD, is converted to Nicotinamide Mononucleotide (NMN) by nicotinamide phosphoribosyl transferase (EC 2.4.2.12) and is utilized for regeneration of NAD. Formation of NMN from nicotinamide riboside by nicotinamide riboside kinase (EC 2.7.1.22) has recently been discovered in yeast and humans, in which nicotinamide and nicotinamide riboside are both utilized for NAD synthesis via NMN. In plants, nicotinamide is not salvaged directly, as nicotinamide phosphoribosyl transferase is not present. Nicotinamide formed by NAD catabolism is converted into nicotinic acid by nicotinamidase (EC 3.5.1.19), and nicotinic acid is salvaged to nicotinic acid mononucleotide (NaMN) by nicotinate phosphoribosyl transferase (EC 2.4.2.11). During in situ tracer experiments with [14C] nicotinamide in coffee leaves, temporary accumulation of radioactivity was observed in nicotinic acid riboside (NaR). Nicotinamide riboside deaminase and nicotinate riboside kinase activity has recently been observed in plants, and an alternative pathway has been proposed, as follows: NAD - NMN - nicotinamide riboside - NaR - NaMN - nicotinic acid adenine dinucleotide – NAD.

a) Anabolism of Trigonelline

From the metabolic fate of [14C] nicotinamide, Matsui *et al*. (2007) proposed that plants can be grouped into three types, according to the synthetic ability of nicotinic acid conjugates: trigonelline-forming plants (type 1), nicotinic acid N-glucoside forming plants (type 2), and plants forming both conjugates (type 3). These differences seem to arise because of the presence or expression of Trigonelline synthase (SAM: nicotinic acid N-methyltransferase) and UDP glucose: nicotinic acid glucosyltransferase. Type 1 plants include Rice (*Oryza sativa*), *Lotus japonicus*, *Trifolium incarnatum*, *Medicago sativa* and *Raphanus sativus*. Trigonelline synthesis from nicotinamide is generally greater in leaves than in roots. Tobacco and possibly Arabidopsis thaliana are categorized as Type 2, although trace amounts of trigonelline have been detected in *A. thaliana* leaves as a metabolite of [14C]

nicotinamide in leaves. In contrast, *Chrysanthemum coronarium* and *Theobroma cacao* are of Type 3.

Although the major source of nicotinic acid for trigonelline synthesis appears to be produced via the pyridine nucleotide cycle, the direct pathway of nicotinic acid formation from NaMN derived from quinolinic acid appears to be particularly active in organs which synthesize large amounts of trigonelline. In vitro and in situ experiments using enzyme extract and tissues suggest that the NaMN → Na-riboside → nicotinic acid → trigonelline pathway is operative (Ashihara 2008). Nicotinic acid is utilized for trigonelline synthesis in many plant species, but some of it has another fate. Some plant species, including tobacco, produce nicotinic acid N-glucoside (Matsui *et al.*, 2007; Ashihara *et al.*, 2008). Nicotinic acid O-glucoside is also produced when a high concentration of nicotinic acid is supplied to tobacco cultures (Ohshima *et al.*, 1997).

b) Catabolism of Trigonelline

In planta, limited amounts of trigonelline appear to be demethylated to nicotinic acid and utilized for NAD synthesis. Trigonelline demethylating activity has been found in extracts of some plant leaves, including those of pine (Taguchi, & Shimabayashi 1983). Shimizu and Mazzafera (2000) studied changes in the trigonelline content of coffee seeds during the very early stages of germination. Trigonelline accumulated in seeds is converted to nicotinic acid during germination and is used for NAD synthesis. Trigonelline acts in this case as a reservoir of nicotinic acid in plants. Compared with trigonelline, nicotinic acid N-glucoside is more easily converted to nicotinic acid, because the reaction catalysed by UDP-glucose: nicotinic acid transferase (EC 2.4.1.196) is reversible (Upmeier *et al.*, 1988). Some of the nicotinic acid formed from trigonelline or nicotinic acid N-glucoside appears to be further degraded. Willeke *et al*. (1979) stated that degradation of nicotinic acid could be observed only in cell cultures producing the sugar conjugates of nicotinic acid, and that nicotinic acid degradation does not involve free 6-hydroxynicotinic acid. The degradation route of the pyridine ring of trigonelline in plants is still unclear.

4. Pharmacological Properties and Applications of Trigonelline

Trigonelline is clinically employed in management of diabetes and some central nervous system disorders. The literature suggests its therapeutic efficacy as a neuroprotective, anticancer, hypoglycemic, hypolipidemic, sedative, memory-enhancing, antibacterial, antiviral, and antitumor agent (Nguyen *et al.*, 2024).

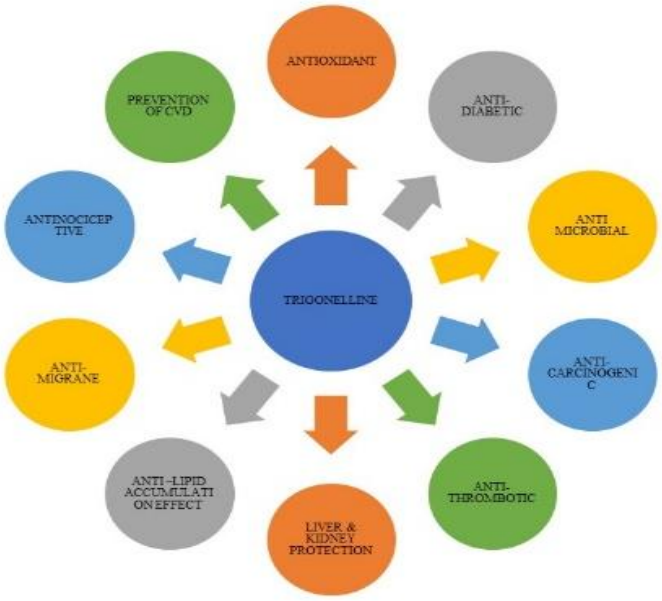

Figure - 2. Properties of Trigonelline

a) Antidiabetic Activity

Diabetes mellitus is a chronic metabolic disorder characterized by elevated blood glucose levels due to impaired insulin secretion, insulin action, or both. The global prevalence of diabetes has reached alarming levels, affecting over 463 million individuals worldwide, with projections indicating that this number will exceed 700 million by 2045 (Saeedi *et al.*, 2019). The condition is primarily categorized into two types: Type 1 Diabetes (T1D), which results from autoimmune destruction of insulin-producing β-cells in the pancreas, and Type 2 Diabetes (T2D), characterized by insulin resistance and relative insulin deficiency (Khawandanah, 2019). Both types of diabetes pose significant health risks, including cardiovascular diseases, kidney failure, neuropathy, and retinopathy, necessitating effective management strategies. Current treatment options for diabetes include lifestyle modifications, oral hypoglycemic agents, and insulin therapy (Davies *et al.*, 2022). Oral medications for T2D encompass various classes, including biguanides (e.g., metformin), sulfonylureas, DPP-4 inhibitors, and SGLT2 inhibitors, each targeting different mechanisms to lower blood glucose levels. While these treatments have demonstrated efficacy, they are often accompanied by side effects, limited long-term effectiveness, and potential issues related to drug resistance. Consequently, there is a pressing need for novel therapeutic agents, particularly those derived from natural sources, to enhance diabetes management and improve patient outcomes (Chaudhury *et al.*, 2017).

Research has demonstrated that trigonelline exhibits significant anti-diabetic effects through various mechanisms, making it an attractive alternative or adjunct to conventional therapies. The anti-diabetic effect of trigonelline was evident from a study involving Trigonelline and nicotinic acid treatment. Studies have shown that trigonelline administration leads to a marked reduction in blood glucose levels. For instance, in a study involving KK-Ay obese mice, treatment with trigonelline and nicotinic acid resulted in improved glucose tolerance during Oral Glucose Tolerance Tests (OGTT). Notably, these treatments also decreased fasting serum insulin levels and enhanced the liver glucokinase/glucose-6-phosphatase ratios, indicating improved hepatic glucose metabolism. These findings suggest that trigonelline may facilitate better glycemic control in diabetic conditions by Yoshinari and Igarashi (2010). Additionally, Gong *et al*. (2023) conduct the in vivo experiment in mice model, trigonelline has been found to inhibit Epithelial-Mesenchymal Transformation (EMT) in proximal tubule epithelial cells, thereby mitigating kidney complications often associated with diabetes. This action is linked to the modulation of the TGF-beta signaling pathway, further highlighting trigonelline's protective effects against diabetic complications.

In further investigations involving streptozotocin-nicotinamide-induced diabetes in rats, trigonelline demonstrated a significant antihyperglycemic effect when administered both alone and in combination with sitagliptin. This combination therapy resulted in a notable reduction in serum glucose levels, increased insulin secretion, and improved peripheral glucose utilization, showcasing trigonelline's potential to enhance the effectiveness of existing diabetic medications. Moreover, trigonelline's ability to reduce Endoplasmic Reticulum (ER) stress in β-islet cells underscores its protective role in preserving pancreatic function (Rani *et al*., 2019). Peerapen *et al*. (2024) demonstrate that trigonelline treatment leads to significant reductions of oxidative stress, Mitochondrial dysfunction, and impaired angiogenesis along with improvements in blood glucose homeostasis and human endothelial EA. hy926 cells.

b) Hepatoprotective activity

The liver, as the central organ in metabolic regulation, detoxification, and synthesis of essential biomolecules, plays a pivotal role in maintaining overall health. However, it is highly susceptible to damage from various agents, including toxins, drugs, infections, and oxidative stress. Conditions such as liver cirrhosis, hepatitis, and Non-Alcoholic Fatty Liver Disease (NAFLD) have become increasingly prevalent, often progressing to severe complications like liver failure and hepatocellular carcinoma. Given the liver's vital functions and its vulnerability to damage, the search

for effective strategies to protect and restore liver function is of paramount importance (Allameh *et al.*, 2023).

In modern medicine, hepatoprotective therapies include the use of synthetic drugs like ursodeoxycholic acid, and corticosteroids (Li *et al.*, 2022). While these agents can mitigate liver damage, they are often associated with side effects and limited long-term efficacy. This has sparked growing interest in natural compounds with hepatoprotective potential, especially those derived from medicinal plants. Plant-based therapies have long been used in traditional medicine to protect the liver and promote its recovery, offering promising avenues for the development of safer, more sustainable treatments (Benić *et al.*, 2022). Among the various bioactive compounds investigated for hepatoprotective activity, alkaloids like trigonelline have gained attention due to their potent antioxidant and anti-inflammatory properties. Trigonelline, in particular, has shown the ability to protect liver cells from oxidative stress and toxic insults, highlighting its potential as a therapeutic agent in preventing liver damage and supporting liver regeneration.

The hepatoprotective activity of Trigonelline was explained by Hamden *et al.* (2013), clinical in alloxan-induced diabetic rats. The AST, ALT, LDH, and GGT activities in the liver of diabetic rats increased in serum by 88, 83, 63, and 44 %, respectively. Interestingly, the injection of trigonelline to diabetic rats that survived the condition reversed this rise and improved all indicators of liver impairment caused due to diabetes. Similar, hepatoprotective activity is established by Dong-Fang Zhang *et al.* (2015). Their study revealed that trigonelline intervention in test animal, with the dosage of 40 mg/kg/d for 8 weeks had much less hepatic steatosis and partially visible hepatic lobules than the control group, which received equal intragastric administration of saline, according to a histopathologic study. While the change in the levels of TG and HDL-C was not statistically different, the levels of ALT, AST, TC, and LDL-C in the serum of the rats in the trigonelline group were dramatically decreased. SOD levels significantly increased, TG, TC, and MDA levels significantly decreased.

Moreover, Hamden *et al.* (2013) observed trigonelline protected the liver function efficiently, which was evident as trigonelline reduced Serum Aspartate Transaminase (AST), Alanine Transaminase (ALT), Gamma-Glutamyl Transpeptidase (GGT), and Lactate Dehydrogenase (LDH) activities and creatinine, albumin, and urea rates in administrated rats. Zhang *et al.* (2015) observed the levels of ALT, AST, TC and LDL-C in the serum of rats in the trigonelline group were significantly reduced, while the change in the levels of TG and HDL-C was not significantly different. The levels of TG, TC and MDA in the liver tissues were

significantly decreased, while the level of SOD significantly increased; the expression of Bcl-2 protein in the liver tissues of rats in the trigonelline intervention group was significantly increased, while the expression of Bax protein significantly decreased. Concluding that non-alcoholic fatty liver diseases trigonelline showed therapeutic effects by increasing the expression of Bcl-2 protein and decrease in the expression of Bax protein in the liver tissues, thereby protecting the liver.

Further, the effect of trigonelline in the molecular switch of Bcl-2/Bax in favour of liver cells is clinically proved by Lindvist *et al*. (2014). These are the genes that are responsible for the on-off mechanism of apoptosis. Bcl-2, resist the stimulation of apoptosis and thus play the role of protection for cells, whereas high expression of Bax gene is the indication of apoptosis. In normal cells the ratio of Bcl-2/Bax is balanced. Bcl-2 protein expression significantly increased while Bax protein expression significantly decreased in the liver tissues of rats receiving trigonelline intervention. This suggests that the trigonelline could have an impact on the relative expression of Bcl-2 and Bax in the liver tissues and thus reduce the hepatocyte apoptosis and realize the treatment of NAFLD.

c) Anti-Cancer Activity

Trigonelline were highlighted in cancer treatment by its influence on Nrf2-dependent proteasome activity and its role in countering resistance to both Tumor Necrosis Factor-Related Apoptosis-Inducing Ligand (TRAIL) and drug-induced apoptosis in pancreatic carcinoma cell lines (Panc1, Colo357, MiaPaca2) and H6c7 pancreatic duct cells, as reported by Arlt *et al*. (2012). Chemosensitive MiaPaca2 and H6c7 cells showed low basal but strong tert-butylhydroquinone (tBHQ)-induced Nrf2 activity and drug resistance, whereas chemo-resistant Panc1 and Colo357 cells demonstrated high constitutive Nrf2 activity. Trigonelline significantly reduced nuclear accumulation of the Nrf2 protein and decreased both basal and tBHQ-induced Nrf2 activity across all cell lines. Beyond Nrf2 inhibition, trigonelline also suppressed the expression of Nrf2-dependent proteasomal genes, such as s5a/psmd4 and 5/psma5, leading to reduced proteasome activity in all tested cell lines. Likewise, trigonelline inhibit the Nrf2 and also induce caspase mediate apoptosis and limitation of cycloin D1 and Bcl2 in lung cancer (Hamzawy *et al*., 2022). Further, trigonelline increased the sensitivity of all cell lines to anticancer medicines and TRAIL-induced apoptosis, depending on the expression of the Nrf2 and proteasomal genes. Liao *et al*., 2015 noticed that trigonelline inhibits metastasis of tumor cells by protein kinase Ca (PKCa) and Raf/ERK/Nrf2 signaling pathway and MMP-7 gene expression, in their study on hepatocellular carcinoma in Hep3B cell lines. The inhibitory effect was mediated by down regulation of nuclear factor E2- related factor 2-dependent

antioxidant enzymes. Nobuhiro Hirkawa *et al*. (2005) have also represented the anti-invasive activity of trigonelline and niacin in hepatoma cell lines. They have shown a suppressive activity against ROS generating system. Even chitosan incorporated with nanoparticles of trigonelline have shown a minimal cytotoxic effect against CT 26 cells and a slight inhibitory effect on tumor cell proliferation, whereas, a significant inhibitory effect of the nanoparticle on metastasis of tumor cells has been registered in Matrigel invasion assay.

d) Gastroprotective Properties

The effectiveness of trigonelline gastroprotective properties has been assessed using an indomethacin-induced ulcer model. Analysis of antioxidants, cytokines, adhesion indicators, and levels of apoptosis has been done to determine the molecular mechanism behind trigonelline action. Gastric lesions significantly decreased by 81.71% in rats pretreated with trigonelline (45 mg kg^{-1}). Leukotriene B4 (LTB4), Lipid Peroxidation, and Myeloperoxidase (MPO) levels are increased after indomethacin treatment, but levels of Prostaglandin E2, Superoxide Dismutase (SOD), Catalase (CAT), and Glutathione Peroxidase (GSH-px) are noticeably decreased. On the other hand, PGE2 and antioxidant levels were increased in trigonelline (45 mg kg^{-1}) pretreated mice, while LTB4, lipid peroxidation, and MPO levels significantly decreased. The pro-inflammatory cytokines interleukin-6 (IL-6), interleukin-1 (IL-1), Tumor Necrosis Factor (TNF), and Interferon (IFN) were all markedly increased in indomethacin-induced rats. and decreases of anti-inflammatory cytokines such as interleukin-10 (IL-10) and interleukin-4 (IL-4). Treatment with trigonelline further diminished microvascular permeability induced by indomethacin in the test animal (Lee *et al*., 2020).

e) Nephroprotective Activity

Trigonelline is also proved to exhibit protective activity against chronic kidney disease by inhibiting the epithelial to mesenchymal transition (EMT) of renal epithelial tubular cells, which otherwise may lead to fibrosis. In a study involving oxalate induced EMT, pre-treatment with trigonelline showed significant inhibitory effect by inhibiting the MAPK mediated activation of TGFβ induced EMT, which is activated by increased ROS produced by oxalate via EMT inducer protein snail1 (Cichon and Radisky, 2014). Moreover, Trigonelline has also clinically proved to suppress oxidative stress mediated DNA damage in cells (Xue *et al*., 2011). Oxalate mediates fibrosis by activating cell migration and suppression of Nrf2 both of which are inhibited by trigonelline pre-treatment, further establishing the nephron-protective function of trigonelline. Trigonelline inhibits cell migration leading to fibrogenesis.

Further, activation of Nrf2 is essential mechanism for protecting the cells against oxidative stress induced damage. Trigonelline ameliorates the effect of Nrf2 mediated cellular damage due to oxidative stress.

f) Anti-degranulation Effect

Trigonelline possess anti-degranulation leading to allergic response. The anti-allergic property of trigonelline was evaluated *in vitro* and *in vivo* in rat basophilic leukemia cell line, RBL-2H3 using β-hexaminadase as the biomarker. The antigen-antibody interaction between DNP-HAS antigen and IgE results in allergic response due to degranulation of mast cells by a cascade of pathways (Nugrahini *et al.*, 2020). Trigonelline was found to inhibits PI3 mediated Ca_2^+ release and degranulation of mast cell by inhibiting the PI3K and inhibition of phosphorylation of PLCγ1/2. Inhibition of PI3K by trigonelline also inhibits the DAG mediated activation of protein kinase C, which signals the activation of transcription factors for the synthesis of proinflammatory cytokines. The study also proved that trigonelline inhibits degranulation by inhibiting the action of pro-esterase by the ag-ab complex, which is responsible for the aggregation of microtubules in the cytosol of mast cell (Jin *et al.*, 2020; Zhang *et al.*, 2021).

g) Antibacterial Activity

Trigonelline, a naturally occurring alkaloid found in coffee and various plants, has shown promising antibacterial properties. Research highlights its ability to disrupt bacterial communication pathways, such as quorum sensing in Pseudomonas aeruginosa (Kar *et al.*, 2024), and inhibit biofilm formation in enterobacteria (Almeida *et al.*, 2006), thereby reducing bacterial virulence. Moreover, da Silva *et al.* (2004) revealed that aqueous extracts and bioactive chemical compounds of Coffea canephora like trigonelline has ability to inhibit the dental caries and periodontal disease causing microorganisms. These findings suggest trigonelline as a potential natural agent for combating bacterial infections and related biofilm-associated conditions.

h) Lipid Accumulation

The inhibitory action of trigonelline on lipid accumulation and adipocyte development was shown in a cell line study (3T3-L1). Trigonelline inhibited the accumulation of lipid droplets in a concentration-dependent manner (between 75 and 100 M). Diminished expression of mRNA, PPAR (peroxisome proliferator-activated receptor) and CCAAT element binding protein (C/EBP) was seen on the 5th and 10th day of differentiation which further reduced the expression of other related genes like

adiponectin, adipogenin, leptin, resistin, and adipocyte fatty acid binding protein (aP2) (Ilavenil *et al.*, 2014). Research has also shown that trigonelline inhibits the production of TMAO (trimethyl amine N – oxide), a dietary choline breakdown product that could otherwise increase foam cell formation, raise LDL levels, and act as a pro-atherosclerotic metabolite causing cardiovascular diseases. Further Love Sharma *et al* (2018), proved that TG have a negative effect on lipid accumulation and lipotoxicity in the palmitic acid-induced AML-12 cell lines.

i) Nervous System

Numerous clinical studies also reveal the dose dependent effect of trigonelline (0.5 – 200 mg/kg body wt) on the nervous systems of rats and mice, including antinociception (the action of reducing sensitivity to painful stimuli by sensory neurons) (Mandegary *et al.*, 2012). Additionally, Aktar *et al*. (2024) demonstrate that natural compounds (Trigonelline) for mitigating age-related cognitive decline, with trigonelline (TG) showing promising effects. In a study using a senescence-accelerated mouse model (SAMP8), TG (5 mg/kg/day) improved memory and spatial learning after 30 days of treatment, as evidenced by the Morris Water Maze test. Further molecular analysis revealed that TG modulates inflammation, enhances neurotransmitter levels, and influences pathways associated with neural development and mitochondrial function, highlighting its potential for supporting healthy aging show in the Figure 3.

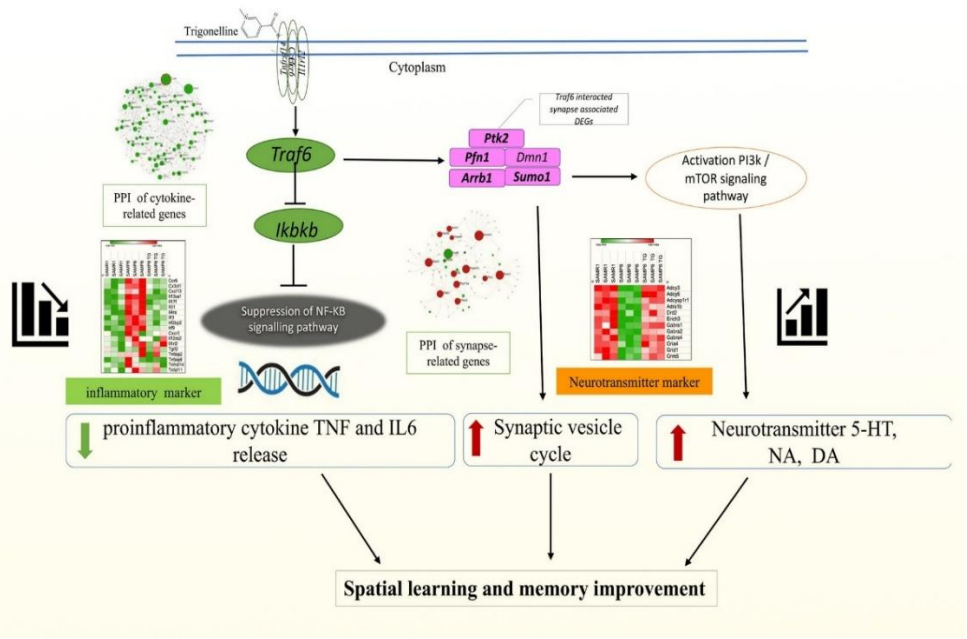

Figure - 3. Trigonelline target the Traf6 and its downstream target to inhibit the pro-inflammatory cytokines and induce the neurotransmitter serotonin (5-HT), noradrenaline (NA), dopamine DA in learning and memory decline (Aktar *et al.*, 2024)

5. Conclusion

In this chapter, we overviewed the trigonelline has emerges as a naturally occurring alkaloid with remarkable therapeutic potential, driven by its diverse metabolic products and their wide-ranging effects on human health. Its metabolism in the liver and intestines leads to bioactive compounds, including nicotinic acid, which are involved in critical physiological processes such as glucose and lipid metabolism, as well as neuroprotection. The growing body of evidence supporting trigonelline's anti-inflammatory, antioxidant, antidiabetic, neuroprotective, and anticancer properties highlights its potential for addressing metabolic disorders, neurodegenerative diseases, and cancer. By modulating oxidative stress, reducing inflammation, and improving insulin sensitivity, trigonelline stands out as a promising candidate for the development of novel therapeutic strategies targeting chronic diseases. This chapter underscores the need for further research to fully harness trigonelline's therapeutic capabilities and explore its potential Clinical and pre-clinical studies.

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Chapter - 4

Phytomedicine Innovations: The Future of Plant – Based Therapies
ISBN: 978-81-977907-4-4
First Edition
Chapter – 4, Page: 49 - 68

4

COAGULANT PROPERTY IN *Moringa oliefera* LEAVES ANALYSED IN POULTRY BLOOD

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Abstract

Blood clotting has emerged as one of the most serious side effects associated with Corona virus, along with the high level of cholesterol and triglycerides in the blood. Consequently, the utilisation of physiologically safe medicinal plants that contain anti-clotting compounds has become imperative. More recently, researchers have focused on learning more about the phytochemical compositions, qualities, and possible uses of these extracts in a variety of contexts, including foods, medicines, cosmetics, and other industries. The aqueous Moringa *oleifera* leaf extracts in this study were subjected to quantitative test, phytochemical analysis using gas chromatography-mass spectrometry (GCMS) and also to evaluate the effect of the test sample extract on blood clotting activity in the chicken blood sample by the determination of prothrombin time (PT).The quantitative analysis reveals that the total phenol content (µg/g GAE) contain 52.08 ± 0.21 µg/g, total flavonoid content (µg/g QE) contain 116.93 ± 1.22 µg/g and Total Tannin content (µg/g) has 86.91±0.42 µg/g in aqueous extract of Moringa *oleifera*. The extract of Moringa *oleifera* leaves contained 20 major compounds of which the maximum quantum was 2-(3,4 – dihydroxyphenyl)- trihydroxychromen-4-one, 3TMS derivative (38.9Percentage) followed by 1H-Indene, 2-butyl-5-hexylocta hydro (15.29 Percentage) then followed by 3-(2-aminoethyl)-1H-indol-5-ol (7.46Percentage).thus the result from the data analysis reveals that the fastest blood coagulation time occurred in the group of concentration of 100Percentage Moringa *oleifera* leaves extract with significant differences compared to other treatment extract resulting shorterand average blood coagulation time.

Keywords: *Moringa oleifera*, Phytochemical test, GC-MS and Blood Clotting activity.

1. Introduction

For thousands of years, nature has been a fantastic supply of medicinal remedies, and a startling number of modern medicines have been derived from natural sources. Since the beginning of time, plant extracts have been highly valued for their vast medical potential. More recently, researchers have focused on learning more about the phytochemical compositions, qualities, and possible uses of these extracts in a variety of contexts, including foods, cosmetics, and other industries (Nitesh Bhalla *et al.*, 2021). The widespread use of plants is still very significant today. According to the World Health Organisation, 80 % of the world's population uses traditional medicine to manage their health issues because they often do not have access to modern medicinal products, and also these medicinal plants can be highly effective (Novais, 2004). In fact, most modern medications are derived from or based on their models (active ingredient synthesis or chemical semi-synthesis). Herbal medicine has developed into a brilliant science where the active ingredient is found directly in the plant. The usage of traditional herbal remedies can be explained by socio-cultural norms, the high expense of pharmaceuticals, the absence of necessary medications, and inadequate health care (Atchade Pascal *et al.*, 2018).

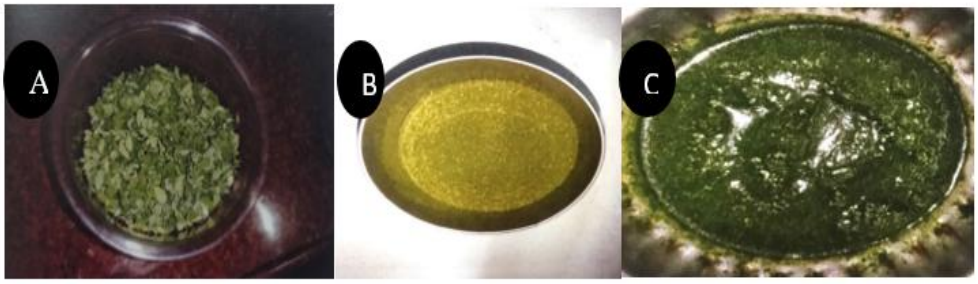
It is important to emphasize that using medicinal herbs as an alternative for modern medicine is appropriate in such a scenario. It is vital and ongoing to understand, advance, and value the usage of therapeutic plants. In this regard, *Moringa oleifera* is a drought resistant fast-growing perennial plant belong to the family Moringaceae. It is one of the plants used in treatment for various parts such as leaves, roots, seed, fruits, flowers and immature pods act as circulatory stimulants, possess antitumor, antipyretic, antiepileptic, anti-inflammatory (Kumar *et al.*, 2009). The *Moringa* tree contains the majority of the phytochemicals. Indeed, it is generally believed that the presence of these phytochemicals is responsible for varies range of biological activities and disease-prevention potential of *Moringa*. Therefore, it is quite promising that future studies will be able to use the chemical diversity of *Moringa* phytochemicals to treat illnesses and promote better health (Bohn *et al.*, 2012). In southern Asia it also utilized as an indigenous of medicine system for treatment of antiulcer, antispasmodic diuretic, antihypertensive, cholesterol lowering antioxidant, antidiabetic, hepatoprotective (Shunmugapriya *et al.*, 2017). Plant extracts are immediately used in traditional medicine as food, tonics, external application to improve the immunity and vigor since ancient time (Ullah *et al.*, 2020).

In fact, using the vital power of nature is crucial to prevent rapidly growing proliferating diseases such as cancer, heart attacks, diabetes, and rapid ageing of the skin, as well as emerging forms of alarming new health concerns like COVID-19, (Nitesh Bhalla *et al.*, 2021). Because of their impact on biological processes, plants may offer up novel possibilities for the creation of cutting-edge anticoagulant drugs. Medicinal drugs made from plants have a wide range of activity with a focus on preventive action, in addition to being easy to use and effective. There is compelling scientific evidence that indicates the consumption of dietary anticoagulants or phytochemicals with anticoagulant activity gradually reduce blood clotting or eliminate the risk of thromboembolic diseases (Al-Saadi, 2011). Anticoagulants are a class of medicines that prevent the formation of a clot in the blood vessels by affecting platelets and blood coagulation factors' availability or activation. However, life-threatening adverse effects such thrombocytopenia, bleeding episodes, and osteopenia are often brought on by these medications (Kumar *et al.*, 2011). Consequently, the hunt for novel, alternative agents derived from natural sources has been sparked by the concerning limitations of the anticoagulants already in use (Manicam *et al.*, 2010). The present work was conducted to identify and quantify the presence of various compound by using GC-MS in Moringa leaves for anti-coagulant and to evaluate the effect of aqueous *Moringa oleifera* leaves extract on blood clotting activity in the chicken blood sample by the determination of Prothrombin time (PT).

2. Materials and Methods

2.1. Plant Collection and Extract Preparation

The plant utilized in this study was analysed first to distinguish that the leaves were without a doubt Moringa *oleifera*. After the assessment and recognizable proof, the leaves were brought to the research centre to be handled. *Moringa oleifera* leaves were softly eroded in deionized water by which the dust particles were removed. The leaves were dried to a constant weight at 18 °C in an enclosed air-conditioned research laboratory for 72 hours. Dried leaves were grounded using mortar and pestle. After the process of grinding, the leaves powder was sieved to get very fine particles of uniform size. The powdered (100 gm) was extracted by cold percolation method with 300 ml of distilled water. After Maceration cycle of powder was dissipated utilizing the rotating evaporator gadget, creating glue structure extricate. The *Moringa oleifera* leaves glue separate was then put away at -20 °C and store till use for the further process as shown in Plate - 1 (A, B, and C).



A) Collected and air dry of *Moringa oleifera* leaves in room temperature B) Dried leaves were Grounded into powder C) Aqueous Extract of *Moringa oleifera*

Plate - 1: Preparation of *Moringa oleifera* Leaves Aqueous Extraction

a) ***Phytochemical Screening Preliminary:*** Phytochemical screening was carried out on the crude aqueous extracts of *Moringa oleifera* leaves using standard procedures as described by Trease and Evans (1989); Sofowora (1993); Ushie *et al*. (2016); Santhi *et al*. (2016).

b) ***Detection of Alkaloids:*** The test sample extracts were dissolved in dilute hydrochloric acid and then filtered. The filtrates were used to test the presence of alkaloids. Mayer's Test. The Filtrates samples were treated with Mayer's reagent. Formation of a yellow cream precipitate signify the presence of alkaloids.

c) ***Detection of Flavonoids by Lead Acetate:*** The test samples extracts were treated with few drops of lead acetate solution. Formation of yellow color precipitate imply the presence of flavonoids.

d) ***Detection of Phenols using Ferric Chloride Test:*** 10 ml of each extract was treated with few drops of ferric chloride solution and evolve the bluish black color indicates the presence of phenol

e) ***Detection of Tannins:*** 1 ml of each of the extracts was mixed with water and heated on a water bath. The mixture was distilled and ferric chloride was added into it. Then formation of a dark green color reveals the presence of tannins.

f) ***Detection of Saponins (Foam Test):*** 1 ml of test sample extracts was shaken with 5 ml of the distilled water. Formation of stable persistent foam express the presence of saponins.

g) ***Detection of Glycosides:*** Take 0.5 ml of each extract was dissolved in 1 ml of water and then aqueous NaOH solution was added. Formation of yellow color imply the presence of Glycosides.

h) ***Detection of Steroids:*** 2 ml of acetic anhydride was added to 0.5 ml of each extract in a test tube, followed by the addition of 2 ml of sulfuric acid. The color changes from violet to blue or violet to green indicates the presence of steroids.

i) ***Detection of sterols (Chloroform and sulfuric acid test):*** Add 5 ml of chloroform to 2 ml of plant extract, then carefully add 1 ml of concentrated sulfuric acid along the walls of the tube. A reddish-brown color in the lower layer indicates the presence of sterols.

j) ***Detection of Anthraquinones:*** 2 ml of each of the plant extracts was boiled with 10 ml of sulfuric acid (H_2SO_4) and was filtered while hot. Two ml of chloroform were shaken with the filtrate. One ml of diluted ammonia was introduced to a test tube containing the chloroform layer using a pipette. Colour variations in the resultant solution were monitored.

k) ***Detection of Carbohydrates:*** Add equal volume of Fehling's (A & B) solution to 2 ml of extract, then heat for five minutes. A dark red precipitate reveals the presence of carbohydrates.

l) ***Detection of Amino acid:*** A few drops of the 2 % Ninhydrin solution must be added to the test solution. The test tube must be kept in a warm water bath for approximately 5 minutes. The development of a deep blue or violet colour indicates the presence of amino acids.

m) ***Detection of Terpenoids (Salkowski s Test):*** 0.5 ml of each extract was mixed with 2 ml of Chloroform, and 3 ml of Concentrated H_2SO_4 was carefully added to form a layer. An appearance of a reddish-brown color interface indicated the presence of Terpenoids.

n) ***Detection for Reducing Sugars:*** 1 ml of the analyte sample must be mixed with 2 ml of Benedict's reagent and heated in a bath of boiling water for 3 to 5 minutes. The development of a brick-red coloured precipitate of cuprous oxide confirms the presence of reducing sugars in the analyte.

o) ***Quantitative Analysis of the Phytochemicals:*** Quantitative analysis of plant extracts is a method for determining the amount or concentration of phytochemicals in a plant sample. It can be used to study drug discovery, standardize herbal drugs, and determine toxicity levels in plants.

p) ***Estimation of Tannins:*** According to Rahman Gu *et al*. (2017), the tannins were determined by Folin-Ciocalteu method. A volumetric flask (10 ml) with 7.5 ml of distilled water, 0.5 ml of Folin-Ciocalteu phenol reagent, 1 ml of 35 % Sodium carbonate solution, and 10 ml of distilled water was diluted with approximately 0.1 ml of the sample extract. After giving the mixture an adequate shake, it was left at room temperature for a half-hour. Tannic acid reference standard solutions (20, 40, 60, 80, and 100 µg/ml) were made using the same technique earlier mentioned. Using a UV/visible spectrophotometer,

the absorbance of the test and standard solutions was measured at 700 nm in relation to the blank and repeat the process in triplet and calculate tannin.

q) ***Total Phenolic Content:*** The Folin-Ciocalteu (FC) reagent was used to calculate the Total phenolic content (Mallick and Singh, 1983). Two millilitres of 20 % Na_2CO_3 were added after the plant extract (0.5 ml) and 0.5 ml of FC reagent (1:1 diluted with distilled water) were combined and incubated for five minutes at 22 °C. After 90 minutes of additional incubation at 22 °C, the mixture's absorbance at 650 nm was determined. Gallic acid served as a standard in the calculation of the Total phenolic content (mg/ml).

r) ***Total Flavonoid Content:*** The Aluminium chloride ($AlCl_3$) technique was used to calculate the Total flavonoid content (mg/ml) (Riya Kadia *et al.*, 2022). The assay mixture, consisting of 0.3 ml of 5 % $NaNO_2$, 0.5 ml of distilled water, and 0.5 ml of the plant extract, was incubated for 5 min at 25 °C. Following that, 0.3 ml of 10 % $AlCl_3$ was added immediately. After adding 2 ml of 1 M NaOH to the reaction mixture, the absorbance at 510 nm was calculated. The standard used was Quercetin.

3. GCMS Analysis

The analysis of extracted phytochemicals of *Moringa oleifera* leaves were done using GC-MS Agilent Technologies-7820A GC system. Gas Chromatogram coupled with Mass Spectrometer of Agilent Technologies-5977MSD equipped with an Agilent Technologies GCMS capillary column HP-5MS (30 m, 0.25 mm, ID 0.25 m) composed of 5 % Diphenyl, 95 % Dimethyl polysiloxane. An electron ionization system with ionizing energy of 70 eV was used. Helium gas (99.99 %) was used as the carrier gas at constant flow rate 1 ml/min and an injection volume of 1 ml was employed at split ratio of 50:1, injector temperature was at 60 °C and ion source temperature was at 250 °C. Mass spectra were recorded using voltage of 70 eV. The relative percentage amount of each component was calculated by comparing its average peak area to the total areas, software of GC-MS Mass Hunter used for Spectra and Chromatograms analysis.

a) Blood Plasma Preparation

The whole blood sample of the chicken was collected and immediately transfer into two other blood tubes, each holding 10 ml of 3.2 % anticoagulant trisodium citrate at a 9:1 ratio (Adcock *et al.,*1997). To avoid blood clotting, the blood and trisodium citrate were well mixed by constantly flipping the blood tubes. Using a refrigerated centrifuge, cells are extracted from plasma by centrifuging at 1,000 – 2,000 rpm for 10 minutes. The plasma sample's platelet content is reduced by centrifugation for 15 minutes at 3,000 rpm. The resulting supernatant is designated as Pure Platelet Plasma

(PPP). After centrifugation, it is essential to quickly put the liquid component (plasma) into a sterile microcentrifuge tube using a pipette. The samples should be handled with a temperature between 2 °C and 8 °C. If the plasma is not going to be investigated immediately, it must be transported and kept at –20 °C or lower. It is important to avoid repeated freeze-thaw cycles. Samples that are lipemic, icteric, or hemolyzed can invalidate some assays (Nurul Huda Mohd Nor *et al.*, 2019).

Plate -3 Prepared the blood sample in five groups for Centrifugation

Plate- 4 Separation of Plasma and Serum Pure Platelet plasma(PPP)

b) Coagulation Test

Using the Prothrombin Time test, the length of the blood coagulation process was determined. Each subject's measurement was divided into five study groups for a total of two cycles. Five groups were created using 0.1 ml of PPP (Pure Platelet Plasma) in test tubes. After that, the tubes were incubated for 180 seconds at 37 °C.

i) Group 1: 0.1 ml of PPP with addition of 0.3 ml $CaCl_2$ (Positive control)
ii) Group 2: 0.1 ml of PPP (Negative control)
iii) Group 3: 0.1 ml of PPP with addition of 0.05 ml 25 % Concentrate of *Moringa oleifera* leaves extract + 0.3 ml $CaC1_2$.
iv) Group 4: 0.1 ml of PPP with addition of 0.05 ml 50 % Concentrate of *Moringa oleifera* leaves extract + 0.3 ml $CaCl_2$.
v) Group 5: 0.1 ml of PPP with addition of 0.05 ml 100 % Concentrate of *Moringa oleifera* leaves extract + 0.3 ml $CaC1_2$.

Every ten seconds, each tube was gently shaking and assessed to see if a plasma clot had formed. Using a digital stopwatch, the length of the coagulation process was determined from the start of the shaking procedure to the development of a plasma clot.

4. Results

4.1. Phytochemical Screening done in Aqueous Extract of *Moringa oleifera* Leaves

The results obtained following the phytochemical screening of the leaves of *Moringa oleifera* are recorded in the above table. We thus note in the *Moringa oleifera* leaves has a very strong presence of flavonoids and tannin, a weak presence of reducing sugar, terpenoids carbohydrate and sterols, a strong presence of reducing compounds such as Amino acid, steroids, glycosides, saponins, alkaloids and phenol and no results found in anthraquinones compound in the aqueous extraction of *Moringa oleifera* leaves as shown in the Table - 1.

Table - 1: Results of phytochemical screening of *Moringa oleifera*

S.No	Phytochemical Test	Aqueous
1	Alkaloids	++
2	Flavonoids	+++
3	Phenol	++
4	Tannins	+++
5	Saponins	++
6	Glycosides	++
7	Steroids	++
8	Sterols	+
9	Anthraquinones	-
10	Carbohydrate	+
11	Amino acid	++
12	terpenoids	+
13	Reducing sugar	+

+: Low presence,++:strong presence ,+++Very strong presence, -:Absence

4.2. Quantitative Analysis

The total phenol content (µg/g GAE) in *Moringa* expressed in GAE was 52.08 ± 0.21 µg/g in aqueous extract (Figure - 1). The total flavonoid content (µg/g QE) in *Moringa* expressed in quercetin equivalents was 116.93 ± 1.22 µg/g in aqueous extract (Figure - 1). The Total Tannin content (µg/g) in *Moringa* was 86.91±0.42 µg/g in aqueous extract as shown in the Figure - 1 respectively.

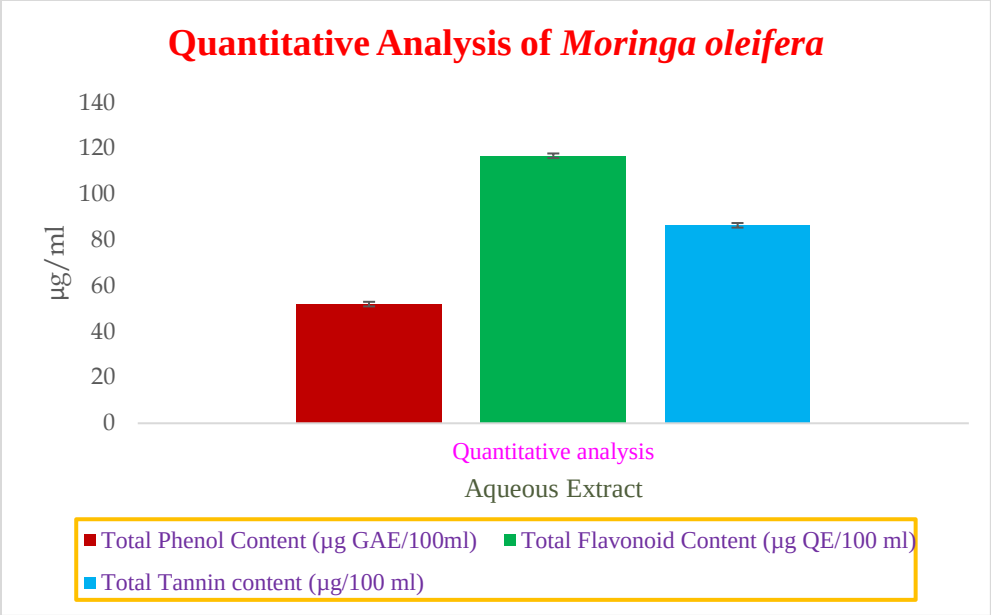


Figure 1: The total amount of Tannin, Phenolic and Flavonoid compounds of Aqueous extracts of *Moringa oleifera* leaves

4.2. Phytocomponent Identification by GC–MS analysis of Aqueous extract of *Moringa oleifera* Leaf

Analysis of the mass spectrum The National Institute of Standards and Technology (NIST) database, which contains more than 65,000 patterns, was used for GC-MS analysis. A comparison was made between the spectrum of the unknown component and the known components kept in the NIST collection. We determined the components of the test materials' names, molecular weights, and structures. GC-MS analysis was used to identify the twenty main chemicals found in the aqueous extract of Moringa *oleifera* leaves. The compounds applications, concentration (Percentage), retention period, molecular formula, and molecular weight of the active principles are displayed in (Table - 2 and Figure - 2). The extract of *Moringa oleifera* leaves contained 20 major compounds of which the maximum quantum was 2-(3,4 – dihydroxyphenyl)- trihydroxychromen-4-one, 3TMS derivative (38.9 %) has effective in anti-cancer, antioxidant and also gives anti-arthritis, antihistamine effects followed by 1H-Indene, 2-butyl-5-hexylocta hydro (15.29 %) activate in antioxidant and anti-lung cancer properties, and may also protect skin cells from UV radiation next followed by 3-(2-aminoethyl)-1H-indol-5-ol (7.46Percentage). referred to as the "happy chemical" since it promotes happiness and well-being, its found in the brain, intestines, and blood platelet. It Assist with mood regulation and memory, sleep, sexual function, bone health and blood coagulation.

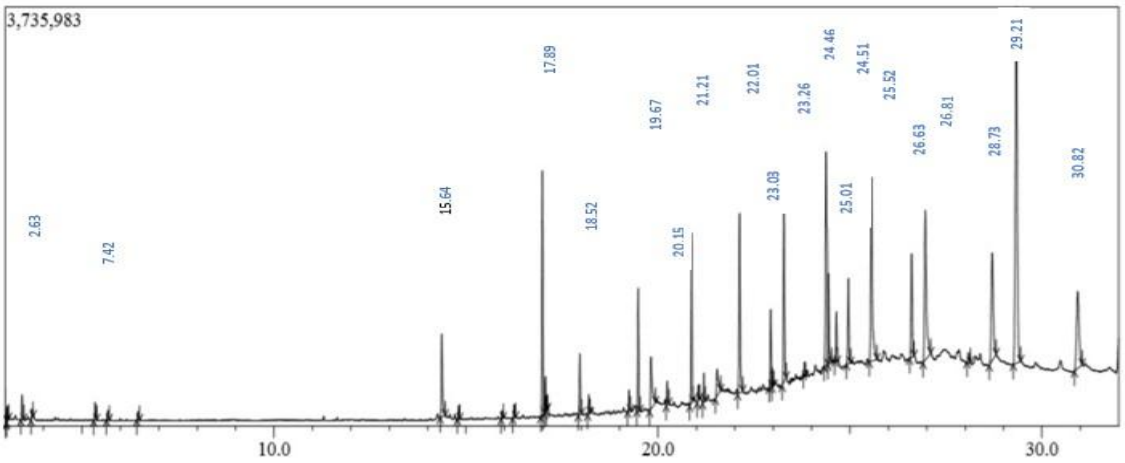


Figure – 2: GC-MS Analysis of *Moringa oleifera* Aqueous Extract

S. No	Compound Name	R. Time	Peak Area %	Molecular Formula	Molecular Weight (g/mol)	Uses
1	5-Nonanol–dibutylcarbinol	2.63	0.65	$C_9H_{20}O$	144.25	It has a role as a pheromone and an animal metabolite.
2	Carbamic acid	7.42	0.36	CH_3NO_2	61.04	It is insecticides, herbicides, and fungicides are used to protect crops and gardens and to protect human and animal health from insect-borne diseases (Horacio Heinzen and María Verónica Cesio 2024)
3	n-Hexadecanoic acid	15.64	1.53	$C_{16}H_{32}O_2$	256.43	Anti- inflammatory, neurotrophic, Antibacterial, Antioxidant, Nematicides Hypocholesterolemia, and Pesticides (Vasudevan Aparna *et al.*, 2012)
4	4H-Pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl-	17.89	2.97	$C_6H_8O_4$	144.12	Strong Anti-oxidant (Yu *et al.*, 2013; Čechovská *et al.*, 2011)
5	1, 2-epoxyhexadecane (oxirane)	18.52	1.55	$C_{16}H_{32}O$	240.42	It used as a diluent for UV-curable coatings (Atul Kumar *et al.*, 2022)
6	Azetidin-2-one 3,3-dimethyl-4-(1-aminoethyl)-	19.67	1.89	$C_7H_{14}N_2O$	142.20	Anti-inflammatory, analgesic and ulcerogenic activities (Siddiqui *et al.*, 2010)
7	1-Propanamine, 3-propoxy	20.15	0.51	$C_6H_{15}NO$	117.19	Textile resins, Drugs, Pesticides (Odochi Chukwu *et al.*, 2024)
8	3-(2-aminoethyl)-1H-indol-5-ol	21.21	7.46	$C_{10}H_{12}N_2O$	176.22	Assist with mood regulation and memory, sleep, sexual function, bone health and blood coagulation (Shubhada Tayade *et al.*, 2022)
9	Dodecyl-	22.01	1.93	$C_{12}H_{26}O$	288.38	It is used in plant and marine-derived antimalarial agents (Marjan Talebi *et al.,* 2023)

10	Butanedioic acid, 2-hydroxy-2-methyl-, (S)-	23.07	2.01	$C_5H_8O_5$	134.087	Mobilize the soil Phosphates for agricultural applications (Leila Rezakhani *et al.*, 2019)
11	L-Galactose, 6-deoxy-	23.26	3.24	$C_6H_{12}O_5$	164.16	It is a mediate cell-cell recognition and adhesion-signaling pathways. Blood transfusion reactions and also a tool to determine cancer diagnosis, prognosis (Jiawei Meng *et al.*, 2023)
12	D-Mannoheptulose	24.46	4.71	$C_7H_{14}O_7$	210.18	D-Mannoheptulose widely studied for its activity against breast cancer and to suppress the D-glucose induced insulin release (Al-Ziaydi *et al.*, 2020)
13	Propenamide	24.51	0.84	C_3H_7NO	73.09	Propenamide derivatives studied for antimicrobial and antiviral efficacy (Nitesh Bhalla *et al.*, 2021)
14	Z-10-Tetradecen-1-ol acetate	25.01	1.56	$C_{16}H_{30}O_2$	254.41	It is an insect pheromone used for therapeutics
15	2-Ethylacridine	25.52	2.14	$C_{15}H_{13}N$	207	Anti-inflammatory anticancer, antimicrobial, antiparasitic, antimalarial, antiviral and fungicidal activities (Upe Francisca *et al.*, 2017)
16	Pentadecanoic acid	26.73	2.44	$C_{15}H_{30}O$	242.3	Antimicrobial activity (Mujeeb *et al.* 2014)
17	Tetra acetyl-d-xylonic nitrile	26.85	3.93	CHNO	342.29	Anti-tumor and Anti-oxidant (Kanhar and Sahoo, 2018)
18	Cis-Octadecenoic acid	28.73	5.99	$C_{18}H_{34}O_2$	282.46	Prevents the function of protein kinase C lymphocytes, releases myeloperoxidase and chemotaxis in human neutrophils (Igwe *et al.*, 2015)
19	2-(3,4 – dihydroxyphenyl)-trihydroxychromen-4-one	29.21	38.9	$C_{15}H_{11}O$	302.238	It is an effective antioxidant and anti-arthritis effects. It has anticancer characteristics, which might help prevent malignant cells from tumor formation. It also helps in neurodegenerative illnesses and efficient antihistamine (Younis Khalaf *et al.* 2021)
20	1H-Indene, 2-butyl-5-hexyloctahydro	30.82	15.3	$C_{19}H_{36}$	264.48	Antioxidant and anti-lung cancer properties, and also protect skin cells from UV radiation (Pichnaree Kraokaew *et al.*, 2022)

4.3. Blood Coagulation activity

Formation of blood clot was seen when the test tubes were inverted. In negative control, plasma dropped when the test tube was rearranged. In this gathering no plasma clump happened. The plasma in sure control, 25 %, half, and 100 percent concentrate bunch the plasma didn't drop at the point when the test tubes were upset

which implies the plasma clumps were shaped. Each gathering had different length of plasma cluster arrangement the blood coagulation season of two subjects in two cycles.

Table - 3: The Mean Difference of Blood Clotting Time

Mean time of Blood Coagulation (Seconds)					
	Positive Control	**Negative Control**	**25 % Concentration**	**50 % Concentration**	**100 % Concentration**
Mean Time	215.66±4.19	373.33±2.41	181.66±9.55	125.33±7.23	103.33±8.93

Mean of Blood coagulation time in short order and Standard Deviation (SD) in each gathering as follows: Positive control was 215.66 plus/minus 4.19 seconds, Negative control showed plasma coagulation in 373.33 plus/minus 2.41 seconds gathering of centralization of 25 % was 181.66 plus/minus 9.55 seconds, gathering of centralization of half was 125.33 plus/minus 7.23 seconds, and the gathering of centralization of 100 % was 103.33 plus/minus 8.93 seconds. *Moringa oleifera* leaves showed the briefest length of plasma coagulation in 100 % as shown in Table – 3.

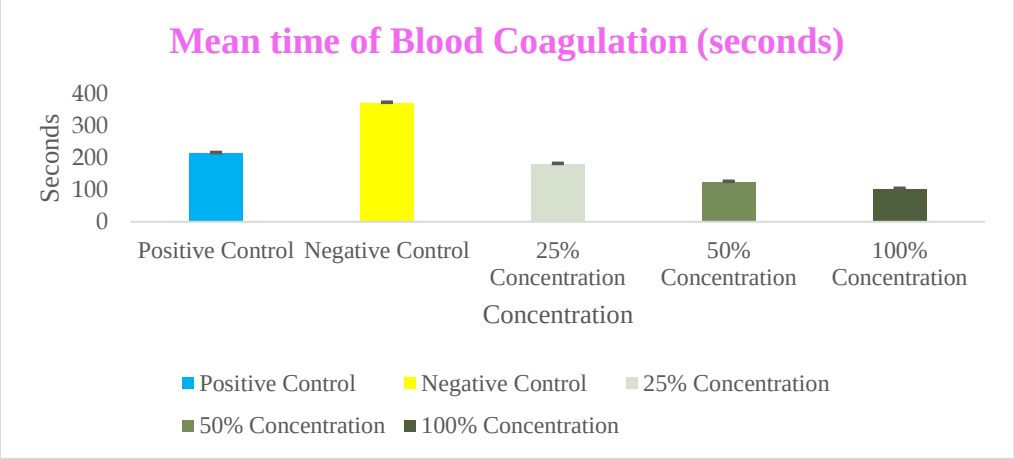


Figure - 3: The Mean difference of Blood Clotting Time

The average blood coagulation time of the positive control group was 155 seconds longer compared to the group of 100 % concentrate; 1.96 times increased the blood coagulation time, 140 seconds longer than the group of 50 % concentrate; 1.8 times increased the blood coagulation time. The positive control group and the group of 25 % concentrate showed no significant difference (P>0.05) with an average blood coagulation time 18 seconds longer than the positive control group; 1.06 times increased the Blood coagulation time (Plate - 5 and 6).

Table - 4: Mean Difference for Test Groups

Groups	Concentrations	Mean Difference
Positive Control	100 %	112.33
	50 %	90.33
	25 %	34
100 %	50 %	-22
	25 %	-78.33
50 %	25 %	-56.33

From the data analysis, the fastest Blood coagulation time occurred in the group of concentration of 100 % *Moringa oleifera* leaves extract with significant differences compared to other treatment extract resulting shorter average blood coagulation time shown in Plate - 7 and Table – 4.

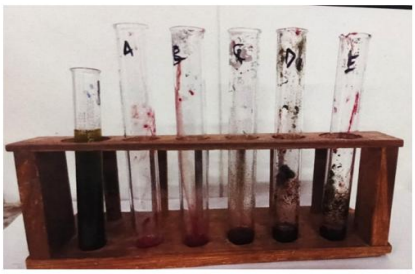


Plate -5 Coagulation Formation

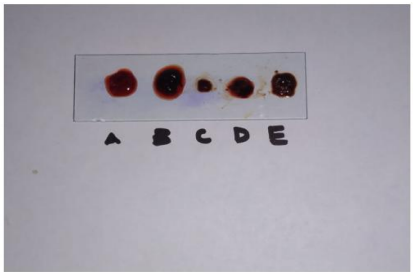


Plate -6 Blood clot formation Process

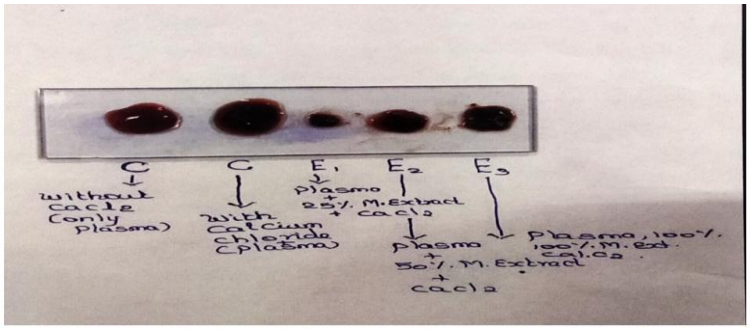


Plate -7 Blood clot after coagulation test with Aqueous *Morienga oleifera* Leaves Extract

5. Discussion

The majority of traditional healers' knowledge of medicinal plants comes from oral tradition, and many are unaware of the active elements in herbal treatments. Accurately identifying herbal material and active components is crucial for quality assurance, safety and effectiveness, public acceptance, and potential integration with the national healthcare system (Abideen Adeyinka Adekanmi *et al.*, 2020). The

potential of plants to produce aromatic compounds is actually limitless. This includes phenolics and polyphenols such as quinine, phenolic acids, flavonoids, and flavanols, as well as tannins, coumarins, terpenoids, essential oils, alkaloids, lectins, and polypeptides (Cowan, 1999). In regards, several experiments relying on the chemical analysis of secondary metabolite content of plants in general and the plant species being studied in particular were carried out.

Alkaloids are nitrogen containing organic compounds present in plants and derived from amino acids metabolism (Cheraghi *et al.*, 2017). Fresh *Moringa* leaves are also known as pro-vitamin which are rich source of β-carotene. *Moringa* has been found to be a rich source of polyphenols (flavonoids, phenolic acids and tannins) that containing all phenolic molecules in a sample including those found in extractable proteins (Saini *et al.*, 2016). Glucosinolates are an extensive category of glycosidic chemicals prevalent in many plant families that include sulphur and nitrogen. The Moringa plant's roots, stem, leaves, and pods were all found to include a variety of glucosinolate chemicals (Maldini *et al.*, 2014). There are also plenty of tannins compounds in Moringa leaves. Moringa leaves also contain an appreciable amount of tannins. These are complex polyphenol molecules that can bind to and precipitate protein, amino acids, alkaloids and other organic molecules in aqueous solutions (Teixeira *et al.*, 2014).

In recent years, Gas Chromatography and Mass Spectroscopy (GC–MS) has been applied unambiguously to identify the structures of different phytoconstituents from plant extracts and biological samples with great success (Pichnaree Kraokaew *et al.*, 2022). Gas Chromatography and Mass Spectrum is a reliable technique to identify the phytoconstituents of volatile matter, long chain branched hydrocarbons, alcohols, acids and esters (Shubhada Tayade *et al.*, 2022).

Still medicinal plants are used significantly in healthcare by different populations throughout the world (Majeed *et al.*, 2012). The natural compounds extracted from medicinal plants have been used as conventional or complementary remedies for both treatable and untreatable diseases (López D *et al.*, 2009). Yet, these natural products are considered to possess a good source of several kinds of chemicals that exhibit various biological properties, that can help build complementary medicines. For instance, it is believed that herbal remedies made from the plant *Allium sativum* L. (garlic) are supposed to inhibit platelet activation (Zhang *et al.,* 2013). Also, other herbs such as *Salix alba* L. are ethnomedicinally used as an anti-inflammatory agent. Later on, the extracted salicylic acid from the second plant species was transformed into a powerful anti-platelet drug acetylsalicylic acid that also called aspirin (Rahman and Billington, 2000). Out of all the plants studied, *Strophanthus*

hispidus proved to be the most effective. The dose-response profiles obtained showed that the increased clotting time was due to different processes for the different plant extracts (Peter Houghton and Karl Skari, 1994).

In vitro activity of *Aizoon hispanicum* L. (Aizoaceae), *Centaurea hyalolepis* Boiss. (Asteraceae), *Heliotropium maris-mortui* Zohary. (Boraginaceae), *Parietaria judaica* L. (Urticaceae), *Polygonum arenarium* Waldst. & Kit. (Polygonaceae), and *Verbascum sinuatum* L. (Scrophulariaceae) on blood coagulation was estimated and it is apparent that these plants should be cautiously consumed with anticoagulant drugs (*e.g.* Heparin) and stops their consumption before surgery (Lubna Abdallah *et al.*, 2022).

For that reason, the current research worked on *Moringa oleifera* plant species was selected for this research according to their medical histories in various fields (Vane and Botting, 2003). The quality features, data, and therapeutic potential of these medicinal plants can be obtained from the phytochemical tests of *Moringa* leaves. However, there are no previous studies on the effect of these plant species on blood coagulation, which is closely related to thromboembolic diseases. This study is trial lab research utilizing *Moringa oleifera* leaves removed as a lab test. Estimation of Blood coagulation time relates to an extraneous fountain of coagulation to assess the coagulant impact estimated by Prothrombin Time (PT) testing technique. A positive benchmark group, 25 %, half, and 100 % removed bunch, PPP, was added with $CaC1_2$ going about as a recalcification agent on Chicken Blood Plasma, hence, animating the typical development of a Blood coagulation.

The outcomes show that the treatment gathering of *Moringa oleifera* leaves concentrate of 25 %, half, and 100 % has a more limited Blood coagulation time than the positive benchmark group was 1.64 times, 1.27 times, and 1.08 times separately. The higher the level of *Moringa oleifera* leaves separate, the more limited Blood coagulation time was acquired than the positive control bunch (Ahmed Sabo *et al.,* 2022). The higher level of *Moringa oleifera* leaves separate had a more limited blood coagulation time than the lower level of *Moringa oleifera* leaves remove. It may very well be closed if an expansion in fixation leads to a Swiffer plasma cluster arrangement. *Moringa oleifera* leaves separate demonstrates that it assumes a part in speeding up human blood coagulation. There calcification process happens by changing coagulation time in human blood plasma tests, portrayed by the arrangement of blood clumps through platelet actuation and the coagulation overflow.

The quickest Blood coagulation time happened in the 100 % concentrate of *Moringa oleifera* leaves remove contrasted with other treatment gatherings; 1.64 times increment the blood coagulation time contrasted with the positive control, going about as expected new human blood plasma *in vitro*. *Moringa oleifera* leaves extricate has a fantastic capacity to abbreviate the coagulation season of new human ordinary blood plasma (Goldhaber, 1992).

Coagulation factor testing, a kind of blood test, looks at one or more of your clotting factors to determine whether you: suffering clotting factor levels that are unusually high or low. Our blood contains chemicals released by the platelets that activate the clotting factors. A more robust blood clot that will adhere to its location is formed when the clotting elements combine in a cascade (Martin N. Raber. 1990). Plasma is produced when whole blood is collected in tubes that are treated with an anticoagulant. The blood does not clot in the plasma tube. The cells are removed by centrifugation. The supernatant, designated plasma is carefully removed from the cell pellet using a Pasteur pipette (Thavasu *et al*., 1992).

6. Conclusion

Moringa oleifera has many properties such as Anti-Inflammatory Anticancer, Antimicrobial, Antiparasitic, Antimalarial, Antiviral, Fungicidal, Neurotrophic, Antioxidant, Nematicides, Hypocholesterolemia and Pesticides activities According to the present study results to a research reveals that *Moringa oleifera* leaves also contain anti-coagulating properties and more research is needed to ascertain its molecular characterization, substrate specificity, and activity. For brief experiment can be done in chronic study for future work.

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Eco-friendly housefly repellents from two invasive plants: Lantana camara L. and Eichhornia crassipes (Mart.) Solms-Laub.

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Chapter - 5

Phytomedicine Innovations: The Future of Plant – Based Therapies
ISBN: 978-81-977907-4-4
First Edition
Chapter – 5, Page: 69 - 86

5

ECO-FRIENDLY HOUSEFLY REPELLENTS FROM TWO INVASIVE PLANTS: *Lantana camara* L. AND *Eichhornia crassipes* (Mart.) SOLMS-LAUB

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Abstract

The present study developed eco-friendly housefly repellents using extracts and powders from two invasive plants, *Lantana camara* L. and *Eichhornia crassipes* (Mart.) Solms, combined with elephant and cow dung separately. Various formulations were prepared in the form of dhoop and extract cards and tested against houseflies. With the combination of elephant dung and plant powders proving most effective, followed by plant extracts. Results showed that the type of dung and the form of the plant material significantly impacted repellency, with elephant dung and plant powders being superior. These findings highlight the potential of these invasive weeds as sustainable, economical alternatives to synthetic insecticides, offering effective housefly management solutions and reducing environmental impact.

Keywords: Housefly repellent, Eco-friendly, Dhoop, Weeds, Invasive and Formulations.

1. Introduction

Houseflies (*Musca domestica*) are among the most common and widespread pests globally, posing significant health risks to humans and animals by transmitting numerous diseases, including typhoid fever, dysentery, cholera and parasitic worm

infections (Olsen, 1998). Their omnipresence and ability to breed in various organic materials make them persistent nuisances in both urban and rural settings, necessitating effective control measures. Traditional chemical insecticides have been the primary method for managing housefly populations; however, these chemicals often lead to environmental contamination, adverse health effects and the development of resistance among target insect populations (Kumar *et al.*, 2012).

Given the growing concerns over the environmental and health impacts of synthetic insecticides, there is an increasing need for alternative, eco-friendly solutions for pest control. One promising approach is the utilization of natural bioactive compounds derived from plants. Plants have evolved various defense mechanisms against herbivores and pathogens, producing a wide array of secondary metabolites with insecticidal and repellent properties (Isman, 2006). Among the many plants studied for their pesticidal potential, invasive species such as *Lantana camara* L. and *Eichhornia crassipes* (Mart.) Solms stand out due to their abundance and bioactivity. *Lantana camara*, commonly known as wild sage, is a perennial shrub native to the tropical and subtropical regions of the Americas. It has become a widespread invasive species in many parts of the world, often outcompeting native vegetation and disrupting local ecosystems (Sharma *et al.*, 2005). Despite its notoriety as a weed, *L. camara* contains various bioactive compounds, including terpenoids, flavonoids and phenolic acids, which have shown potential as natural insecticides and repellents (Day *et al.*, 2003). Similarly, *Eichhornia crassipes*, known as water hyacinth, is an aquatic plant native to the Amazon basin that has become one of the most invasive species globally. It forms dense mats on water bodies, impeding water flow and affecting aquatic life. *E. crassipes* also contains a range of bioactive compounds with potential pesticidal properties (Gunnarsson and Petersen, 2007).

The utilization of these invasive plants for pest control offers a dual benefit: managing the negative impact of these species on ecosystems while providing sustainable solutions for pest management. Many literature studies have demonstrated the potential of plant-based products in repelling or killing various insect pests (Dubey *et al.*, 2011; Pavela, 2016). However, the specific application of *L. camara* and *E. crassipes* for housefly repellency has not been extensively explored. Hence this study aims to develop novel housefly repellent products using extracts and powders from *L. camara* and *E. crassipes*, combined with organic substrates like elephant dung and cow dung. These substrates were chosen due to their natural availability and potential to enhance the effectiveness of the plant extracts and powders. Various formulations were tested to evaluate their repellent efficacy in the form of dhoop and extract cards, as a novel delivery method for the repellent compounds. By investigating the repellent properties of these formulations, this study seeks to identify effective and

environmentally friendly alternatives to synthetic insecticides. The findings could contribute to sustainable pest management practices and provide a practical use for invasive plant species, thereby addressing both ecological and public health concerns.

2. Materials and Methods

2.1. Plant Collection and Identification

The plant material for the present study was collected from in and around Pollachi. The collected specimen was identified as *Lantana camara* L. and *Eichhornia crassipes* (Mart.) Solms- Laub with the help of Flora of presidency of Madras by Gamble and Indian biodiversity portal. The leaf materials of both the plants were thoroughly washed in running tap water in order to remove debris.

2.2. Preparation of powder

The leaves of *Lantana camara* L. and *Eichhornia cressipens* L. were shade dried for two months to remove all the moisture content and to preserve maximum of the bioactive compounds. The dried leaves were cut down into small pieces of size up to 1 – 2 cm. The cut down leaves were crushed using a laboratory blender and then sieved through a mesh size of 3 mm in order to remove the coarse materials. The fine powder was then packed in an airtight container.

2.3. Preparation of extract

Lantana camara and *Eichhornia cressipens* leaf powder were subjected to methanol extraction using Soxhlet apparatus for a period of 72 hrs at 40 – 60 °C. Excess solvent was removed by keeping in water bath at 40 °C for 2 hrs. Stock solution was prepared from crude extracts by dissolving 2.5 mg of solvent extract in 25 ml of methanol to get a solution of 10 percent concentration (Adlin *et al.*, 2023).

2.4. Collection of Dung

Elephant dung was collected from the natural forest of Kallapuram, Udumalpet, Pollachi. The elephant dung was spread as thin layer and dried under sunlight for 48 hours, after drying the elephant dung was powdered using mixy. The fresh cow dung was collected and stored before few hours of formulation and used.

2.5. Preparation of Dhoop using Elephant Dung and Plant Extract

Five gram of dried elephant dung and 5 ml of extract of each selected plant was taken and mixed well and dhoops were prepared in required size and shape. After preparation of dhoop, it was allowed for sun drying.

2.6. Preparation of Dhoop using Elephant Dung and Plant Powder

A mixture of powdered elephant dung and each plant powder was added separately in the ratio 1:1 and then hot water was added to the elephant dung mixture and it was mixed well until it forms a dough consistency. Finally, the dough was mould in to required shape and dried under sunlight.

2.7. Preparation of Dhoop using Cow Dung and Plant Leaf Extract

Dhoop was prepared by using fresh Indian cow dung and leaves extract of each selected plant separately. For this preparation, 5 ml of each plant extract separately were added to 5 gm of freshly collected Indian cow dung. After preparation, the dhoop were allowed for sun drying. The completely dried dhoop were used to evaluate housefly repellent activity.

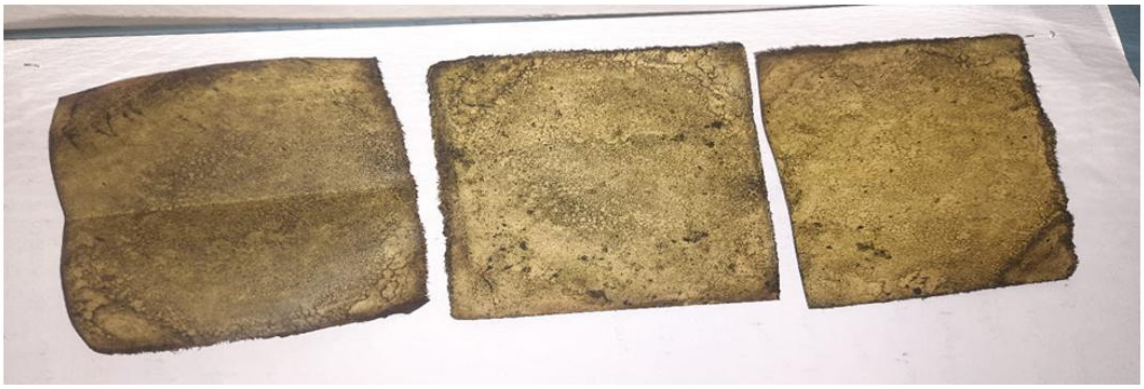
2.8. Preparation of Dhoop using Cow Dung and Leaf Powders

Four grams of Plant powder of each plant was taken separately and it was added with 5 grams of fresh cow dung and mixed well to get a dough form. After 10 minutes the dough was molded in to required size and shape and allowed to dry.

2.9. Preparation of Extract Cards

Extract papers were prepared by using Whatman no.1 filter paper. These papers were soaked in each extract and dried. The dried paper is an extract card (Asmitha *et al.*, 2018).

Elephant dung + Extract | **Elephant dung + Powder** | **Cow dung + Extract** | **Cow dung + Powder**



Extract Cards

2.10. Collection of Houseflies

Houseflies were collected using sugar solution from houses, dairy farms and public places and carefully left in the pin holed container for aeration. Collected Houseflies were of different age groups. Mixed population of house flies were used to study activity.

2.11. Preparation of Cage

The glass cage of 20 × 15 × 22 (Length × Breadth × Width) was prepared and used as cage. The houseflies were left inside the cage in order to test the repellent activity of dhoops and extract cards.

2.12. Testing the efficiency of formulated dhoop and extract card

The efficiency of the dhoop was tested by burning the elephant dung and cow dung-based Dhoop, extract card individually with *L. camara* and *E. crassipes* extract and leaf powders. The burning ability such as initial burning, final burning, time interval flammability and ash content were recorded. Samples were prepared in different ratios and the tests was conducted as per the standard protocols and the result were recorded at different time intervals (Hazarika *et al.*, 2019).

2.13. Burning time

Burning time is a time interval between the initial burning to the final burning. The time taken for burning was calculated by the following formula, (Das *et al.*, 2019)

$$\text{Burning time (min)} = FB - IB$$

Where, IB = Initial burning, FB = Final Burning and the results were expressed in minutes.

2.14. Burning rate

Burning rate was calculated by recording the initial mass of product (M_1) and the time (T_1) and then after burning the formulations, final Mass (M_2) and time (T_2) was recorded. The recorded time mentioned in hours and mass in grams. The formula for calculating the burning rate was,

$$\text{Burning rate} = M2\text{-}M1 \ / T2\text{-}T1$$

2.15. Mortality Rate

The toxicity of the dhoop was tested against the housefly using well closed containers. Housefly was released inside the containers and the filter paper impregnated with extracts was attached to the inner side of cage door and thin layer of cotton was used to avoid escaping of houseflies. Both the repellent dhoops and extract cards were tested using this method and the mortality rate was observed for every one hour (Das *et al.*, 2003).

2.16. Smoke Toxicity Test

Experiments were conducted in a glass chamber which has a measuring window situated at the mid-bottom of one side of the chamber. The experiment chamber was tightly closed smoke and toxicity was tested with herbal housefly repellant at different time intervals by observing the dead dropped down housefly (Gopeswar and Sandipan, 2019).

2.17. Smoke Emission Test (%)

A smoke emission test was conducted to measure the Carbon monoxide and Carbon dioxide level of the organic herbal housefly repellant by using a carbon monoxide detector and carbon dioxide meter. A smoke meter was used to measure the amount of carbon dioxide and carbon monoxide emission from both the elephant dung based housefly repellent and cow dung based repellent (Ramya *et al.*, 2019). It was carried out by use of an approved and calibrated smoke meter.

2.18 Public Survey

Public volunteer survey carried out in locality of college and nearby places to study safety and efficacy of the formulations. The formulation was distributed to volunteers and feedbacks were collected. The data was collected and studied statistically (Kuntal *et al.*, 2016).

2.19. Field Experiments

The field experiments were conducted at dairy farm, fruit shops and houses. This dairy farm was sited on 1 acres of land and housed with cows and calves. The cow shed comprised of closed shed, a dump site and an open area. The dump site was a breeding ground for flies and the closed shed was infested with a high density of flies. Experiments were conducted in the closed shed. The study was performed using a formulation of dhoop and extract cards. The efficacy of the formulated product was assessed by calculating the percentage reduction in the number of flies visiting the treated area compared with the control area. The percentage reduction in flies visiting the designated area was calculated as:

$$\% \text{ IR} = \text{Cv} - \text{Tv}/\text{Cv} \times 100$$

where Cv is the number of flies/h visiting the untreated(control) plots and Tv is the number of flies/h visiting the treated plots.

3. Results and Discussion

3.1. Cage Test

Cage test was performed to check the housefly repellent activity of the prepared different formulations of dhoop and extract card. Housefly was left inside the glass cage and the each formulated housefly repellents were burnt inside the cage separately to check the repellence activity and it is recorded in table.

Fig 1: Elephant dung + Powder

Fig 2: Elephant dung + Extract

Fig 3: Cow dung + Powder

Fig 4: Cow dung + Extract

Fig 5: Extract card

Table - 1: **The Repellency Percentage of Formulations in first 5 minutes**

Product	Total	Trial 1			Trial 2			Trial 3		
		D	S	A	D	S	A	D	S	A
Elephant dung+ *L.camara* + *E.crassipes* powder	30	0	2	28	0	0	30	0	0	30
Elephant dung + *L.camara* extract +*E.crassipes* extract	30	0	7	23	1	9	20	0	6	24
Cowdung + *L.camara* + *E.crassipes* powder	30	0	1	29	0	0	30	0	1	29
Cowdung + *L.camara extract* + *E.crassipes* extract	30	0	0	30	0	0	30	0	0	30
Extract card	30	0	0	30	0	0	30	0	0	30

D= Dead; S= Seduced; A= Active

Table - 2: **The Repellency Percentage of Products in first 10 minutes**

Product	Total	Trial 1			Trial 2			Trial 3		
		D	S	A	D	S	A	D	S	A
Elephant dung + *L. camara* + *E. crassipes* powder	30	0	6	24	0	6	24	0	9	21
Elephant dung + *L. camara* extract + *E. crassipes* extract	30	1	7	22	1	10	19	2	7	21
Cowdung + *L. camara* + *E. crassipes* powder	30	0	3	27	2	7	21	0	6	24
Cowdung + *L. camara extract* + *E. crassipes* extract	30	0	2	28	0	0	30	0	1	29
Extract card	30	0	0	30	0	1	30	0	1	30

Table - 3: **The Repellency Percentage of Products in first 15 minutes**

Product	Total	Trial 1			Trial 2			Trial 3		
		D	S	A	D	S	A	D	S	A
Elephant dung + *L. camara* + *E. crassipes* powder	30	3	11	16	2	9	19	1	9	20
Elephant dung + *L. camara* extract + *E. crassipes* extract	30	4	12	14	3	10	17	6	12	12
Cowdung + *L. camara* + *E. crassipes* powder	30	0	4	26	2	7	21	0	9	21
Cowdung + *L. camara extract* + *E. crassipes* extract	30	0	3	27	0	1	29	0	1	29
Extract card	30	0	1	29	0	0	30	0	0	30

Table - 4: **The Repellency Percentage of Products in first 20 minutes**

Product	Total	Trial 1			Trial 2			Trial 3		
		D	S	A	D	S	A	D	S	A
Elephant dung + *L. camara* + *E. crassipes* powder	30	3	11	16	2	11	17	2	9	19
Elephant dung + *L. camara* extract + *E. crassipes* extract	30	6	12	16	6	11	13	6	13	11
Cowdung + *L. camara* + *E. crassipes* powder	30	1	4	25	2	7	21	0	9	21
Cowdung + *L. camara extract* + *E. crassipes* extract	30	0	3	27	0	1	29	0	1	29
Extract card	30	0	1	29	0	0	30	0	0	30

Table - 5: **The Repellency Percentage of Products in first 25 - 30 minutes**

Product	Total	Trial 1			Trial 2			Trial 3		
		D	S	A	D	S	A	D	S	A
Elephant dung + *L. camara* + *E. crassipes* powder	30	4	11	15	2	11	17	2	10	18
Elephant dung + *L. camara* extract + *E. crassipes* extract	30	15	12	3	11	13	6	14	8	8
Cowdung + *L. camara* + *E. crassipes* powder	30	0	8	22	2	7	21	0	11	19
Cowdung + *L. camara* extract + *E. crassipes* extract	30	0	3	27	0	2	28	0	1	29
Extract card	30	0	1	29	0	0	30	0	0	30

Cage test was performed by leaving 30 houseflies inside the glass cage and the test was triplicated. Each housefly repellents were burnt inside the cage separately to check the repellence activity and the number of active, died and seduced houseflies were recorded for every trials.

From 0 to 5 minutes of time duration and in each trial, none of the houseflies were dead or seduced when burning any of the formulations of dhoop and extract cards but about 6-9 number of houseflies were seduced by the smoke formed from Elephant dung + *L. camara* extract + *E. crassipes* extract in all the three trials. Elephant dung + *L. camara* + *E. crassipes* extract and Cow dung + *L. camara* extract + *E. crassipes* powder has seduced only few numbers of houseflies. After 10 minutes of burning, could able to see about 7-10 houseflies were seduced in the cage when burning the dhoop and extract card composed of Elephant dung + *L. camara* extract + *E. crassipes* extract and it headed as dominant repellent. After 5 minutes of burning, Elephant dung + *L. camara* extract + *E. crassipes* extract showed increased number of seduced houseflies inside the cage *i.e.,* about 12 - 17 houseflies were seduced and 4 - 6 houseflies were died. Elephant dung + *L. camara* extract + *E. crassipes* powder has also increase the seduced houseflies number to 9-11 and dead houseflies number to 1-3 in every

trials. Cowdung + *L. camara* + *E. crassipes* powder has also shown repellency property by seducing 4 - 9 houseflies.

In the next 5 minutes, the number of seduced houseflies increased to 11-13 in the cage with dhoop made of Elephant dung + *L. camara* extract + *E. crassipes* extract, and the number of dead houseflies for the same formulation was 6. During this time, there were not many changes in repellency shown by the other dhoop formulations. In the following 10 minutes, there was a rapid increase in the number of dead houseflies to 15, 11, and 14 and seduced houseflies to 12, 13, and 8 in trials 1, 2, and 3, respectively, for the formulation Elephant dung + *L. camara* extract + *E. crassipes* extract. Elephant dung + *L. camara* + *E. crassipes* powder also showed good results, with the number of seduced houseflies being 11, 11, and 10 and the number of dead houseflies being 4, 2, and 2 for trials 1, 2, and 3, respectively. The cage with Cow dung + *L. camara* + *E. crassipes* powder had about 8-11 seduced houseflies across the 3 trials. The Cow dung + *L. camara* extract + *E. crassipes* extract and extract card had only a few (1-3) seduced houseflies even after 30 minutes and were not effective against housefly repellency. The greatest and most immediate response of repellency was shown by Elephant dung + *L. camara* + *E. crassipes* powder.

4. Testing the Efficiency of Formulated Dhoop and Extract Card

4.1. Burning time of dhoop

Table - 6: **Formulated products and its burning time**

Product	Initial burning (time)	Final burning (time)	Burning time in minutes (FB-IB)
Elephant dung + *L. camara* + *E. crassipes* powder	11:05 A.M	11:33 A.M	28 min
Elephant dung + *L. camara* extract + *E. crassipes* extract	12:00 P.M	12:20 P.M	20 min
Cowdung + *L. camara* + *E. crassipes* powder	11:15 A.M	11:41 A.M	26 min
Cow dung + *L. camara* extract + *E. crassipes* extract	1:00 P.M	1:40 P.M	40 min
Extract card	3:30 P.M	3:50 P.M	20 min

4.2 Burning rate of Dhoop and Extract Card

Burning rate of dhoop and extract card was calculated by recording the initial mass of product (M_1) and the time (T_1) and then after burning the dhoop, final Mass (M_2) and time (T_2) was recorded. The recorded time mentioned in hours and mass in grams.

Table - 7: Burning rate of Formulated Dhoop and Extract card

Formulations	M2-M1/T2-T1	Burning rate
Elephant dung + *L. camara* + *E. crassipes* powder	2.607- 0.360/28	0.0802
Elephant dung + *L. camara* extract + *E. crassipes* extract	1.114-0.130/20	0.0492
Cowdung + *L. camara* + *E. crassipes* powder	1.453-0.256/26	0.0460
Cowdung + *L. camara* extract + *E. crassipes* extract	1.559-0.142/40	0.0354
Extract card	0.526-0.098/20	0.0214

The result showed the burning rate of Elephant dung + *L. camara* + *E. crassipes* powder shown highest burning rate which has a lasting smell and effectiveness in repellency, followed by Elephant dung + *L. camara* extract + *E. crassipes* extract with 0.0492 Cow dung + *L. camara* + *E. crassipes* powder with 0.0460 as burning rate. The burning rate was low for both the formulation of Cowdung + *L. camara* extract + *E. crassipes* extract and extract card which gave a result that these products are a failure. Similar to our result, Nelly *et al*. (2022) observed the prepared candles while burning. It was noticed that they burned with a yellow, long and steady flame suggesting a complete combustion. The fragrance of the candle started diffusing after ten minutes of burning. The burning rate results are 6.97 5.46 7.94 (g/h).

Table - 8: **Product weight and Ash content**

Product	Weight in grams	Ash content (g)
Elephant dung + *L. camara* + *E. crassipes* powder	2.607 g	0.360 g
Elephant dung +*L. camara* extract + *E. crassipes* extract	1.114 g	0.130 g
Cowdung + *L. camara* +*E. crassipes* powder	1.453 g	0.256 g
Cow dung + *L. camara* extract + *E. crassipes* extract	1.559 g	0.142 g
Extract card	0.526 g	0.098 g

The data represents observations on the weight in grams and ash content of various products derived from combinations of elephant dung, cow dung, *Lantana camara* L., and *Eichhornia crassipes* (Mart.) Solms. Five different combinations were examined: elephant dung with *L. camara* and *E. crassipes* powder, elephant dung with *L. camara* extract and *E. crassipes* extract, cow dung with *L. camara* and *E. crassipes* powder, and cow dung with *L. camara* extract and *E. crassipes* extract and an extract card was included for comparison. The weights of the products ranged from 1.114 g to 2.607 g, while the corresponding ash content varied between 0.130 g and 0.360 g. On comparing the ash content with the other repellent produced against insects the ash content odd dhoops is more. These findings suggest differences in the composition and potentially the efficacy of these combinations, highlighting the importance of further investigation into their respective properties and applications.

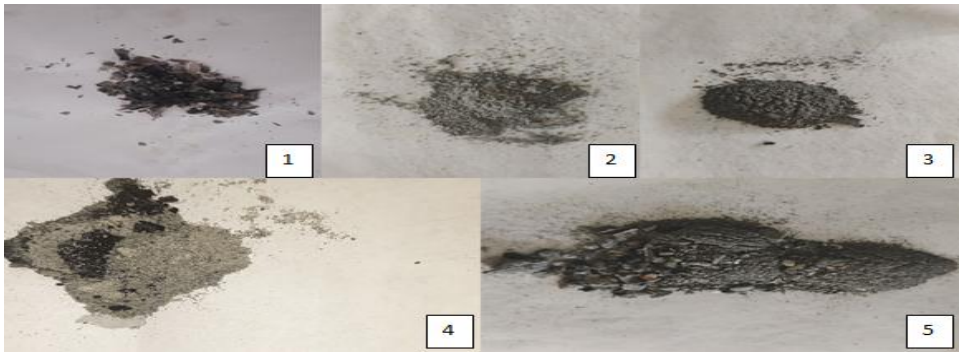


Figure – 6: (1) Ashes of Extract card; (2) Elephant dung + Plant extracts; (3) Cow dung + Plant powder; (4) Cow dung + Plant extracts; (5) Elephant dung + Plant powder

4.3. Mortality rate

The toxicity of the dhoop was tested against the housefly using well closed containers. Housefly were released inside the cage and the extract card impregnated with test compound was attached to the kept and burnt inside the cage. The repellent dhoops were also tested using this method to test the mortality of housefly and was observed after one hour. From the data collected the mortality rate of houseflies was less and shows a standard deviation of ±1.699755 for the formulation Elephant dung + *L. camara extract* + *E. crassipes* extract. This reveals that this formulation has a great repellency property compared with other products. The mortality rate of Elephant dung + *L. camara* + *E. crassipes* powder and Cowdung + *L. camara* + *E. crassipes* powder has shown an average repellency and mortality rate which has a value of mortality as ±0.942815. Cowdung + *L. camara* + *E. crassipes* extract and extract card has shown zero mortality rate that is no houseflies were repelled using this products.

Table - 9: Mortality rate of Housefly against Dhoops

Formulations	Mortality rate
Elephant dung + *L. camara* + *E. crassipes* powder	2.66 ± 0.942815
Elephant dung + *L. camara* extract + *E. crassipes* extract	13.3 ± 1.699755
Cowdung + *L. camara* + *E. crassipes* powder	0.66 ± 0.942815
Cowdung + *L. camara* extract + *E. crassipes* extract	00
Extract card	00

4.4 Public survey

Public survey was conducted based on preparing questionnaire after distributing the products in markets, homes, fruit shops, college and stationary stores. The questions were answered by each person who used the dhoops and extract cards from which the results were gathered. The above results with questions and related graphs were the results obtained from the google sheets based on the answers given by the individual for the particular questions given by the researcher.

Figure – 7: Elephant dung + *L. camara* extract + *E. crassipes* powder

Figure – 8: Elephant dung + *L. camara* + *E. crassipes* extract

Figure – 9: Cowdung + *L. camara* + *E. crassipes* powder

5. Smoke Emission Test

Smoke emission test was done at college inside the class room and in an open space. The aim of the test was to detect the presence of carbondioxide and carbon monoxide present in the dhoops and extract cards. If the carbon dioxide or carbon monoxide was present more than the desired value, the product smoke seems to be toxic to breath. The amount of carbon dioxide more than 1000 ppm is toxic whereas for carbon monoxide according to EPA (Environmental Protection Agency) established the National Ambient Air Quality Standards (NAAQS) to protect public health at outdoor for 1 hour 35 ppm is average amount of carbon-monoxide than can be emitted and at indoor generally to be maintained to zero. According to the reading taken by the smoke emission detector and readings taken The carbon monoxide

emitted was about 030-040 ppm by all the formulations in 30 minutes and carbon dioxide emission was about 015-028 by the formulations in 30 minutes and the result obtained was these products were safe to use and not toxic.

Table - 10: Carbon mono oxide and Carbon-dioxide emission from formulated products

Product	Carbon monoxide emission in ppm	Carbon dioxide emission in ppm
Elephant dung + *L. camara* + *E. crassipes* powder	039	016
Elephant dung + *L. camara extract* + *E. crassipes* extract	031	028
Cowdung + *L. camara* + *E. crassipes* powder	031	015
Cowdung + *L. camara* extract + *E. crassipes* extract	032	000
Extract cards	000	000

Figure - 10: Smoke Emission Test

Fig - 10: Elephant dung + *L. camara* + *E. crassipes* powder; Fig – 11: Elephant dung + *L. camara* + *E. crassipes* powder; Fig – 12: Cow dung + *L. camara* + *E. crassipes* powder

Table - 11: Field Experiment Test done using Formulated products

Product	Untreated area (CV)	Treated area (TV)	CV	TV	% IR
Elephant dung + *L. camara* + *E. crassipes* powder	90 - 100	5 – 10	95	7	92.6 %
Elephant dung + *L. camara* extract + *E. crassipes* extract	125 - 130	30 – 40	127	35	72.4 %
Cow dung + *L. camara* + *E. crassipes* powder	10 - 20	3 - 5	15	4	73.3 %
Cow dung + *L. camara* extract + *E. crassipes* extract	100 - 110	105	105	105	0 %
Extract cards	50 - 55	30 - 35	53	33	37.7 %

5. Conclusion

The study evaluated the effectiveness and toxicity of various dhoop formulations made from combinations of elephant dung, cow dung, *Lantana camara* L. and *Eichhornia crassipes* (Mart.) Solms against houseflies. The formulations tested included powders and extracts, with an extract card used for comparison. The weights of the products ranged from 1.114 g to 2.607 g, and ash content varied between 0.130 g and 0.360 g. The data revealed significant differences in burning rates and repellent effectiveness. The formulation of Elephant dung + *L. camara* extract + *E. crassipes* extract demonstrated the highest burning rate and superior repellent properties, as evidenced by a higher standard deviation in housefly mortality rates (±1.699755). The powders of Elephant dung + *L. camara* + *E. crassipes* and Cow dung + *L. camara* + *E. crassipes* showed average repellency and mortality rates (±0.942815). In contrast, Cow dung + *L. camara* extract + *E. crassipes* extract and the extract card exhibited zero mortality, indicating ineffectiveness in repelling houseflies. These findings highlight the potential of specific formulations, particularly those involving elephant dung and extracts, as effective insect repellents. However, the variability in results suggests a need for further investigation into optimizing the composition and application methods to enhance efficacy. Future research should also explore the long-term effects and environmental impact of these natural repellent products. In summary, even though certain dhoop formulations showed promising result as natural insect repellents, additional research is necessary to thorough understand of their potential and refine their use for practical applications.

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Phytomedicine and Human Health

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Chapter - 6

Phytomedicine Innovations: The Future of Plant – Based Therapies
ISBN: 978-81-977907-4-4
First Edition
Chapter – 6, Page: 87 - 103

6

PHYTOMEDICINE AND HUMAN HEALTH

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Abstract

Phytomedicine, which involves the use of medicinal plants and their extracts, has been a cornerstone of traditional medicine for centuries. Recent research highlights its significant role in modern healthcare. Phytomedicines are known for their potential to treat a variety of health conditions, including chronic diseases like cancer, heart disease, diabetes and infections.Plant preparations use for medicinal purposes. It is refers to use of naturally occurring products to cure human health. Natural products have the advantages of causing minimum side-effects, being available, economical and biocompatible. Phytomedicine contain Antioxidant and anti-inflammatory properties. It also potential in addressing mental health disorder such as anxiety, depression. It has applications in wound healing and skin conditions.

Keywords: Phytomedicine, Traditional medicine, Human health and Natural product.

1. Introduction

There is a tremendous use of medicinal plant products. Phytomedicine involves plants and their extracts to treat and prevent various health conditions. Ancient civilizations relied on plants for their medicinal properties to treat ailments and maintain health. *Moringa oleifera,* is a type of local medicinal Indian herb which shows anti-inflammatory effects, antioxidant properties as well as anti-cancerous properties. Proteolytic enzyme in pineapple plant like bromelain has various applications in antimicrobial efficacy, therapeutic, dental and synergistic effects. Stress, anxiety, mood disorder, sleep problems can be cured by many plants such as *Ginkgo biloba*, lavender, rosemary, lemon, *Schisandra chinensis*, saffron. In

Cymbopogon genus, lemongrass shows anti-bacterial and antifungal effect. It also shows anti-diabetic and anti-inflammatory effect.

Oral squamous cell carcinoma can be cured by *Angelica keiskei*, is hardly perennial that grows mainly in Asian countries, including Korea, China, Japan. It is used as anti-aging agent and general health enhancer. Joint disorders like osteoarthritis and rheumatoid arthritis cured by *Curcuma* spp., *Equisetum arvense*, *Herpagophytum procumbens*, *Panax notoginseng*. Since centuries phytomedicine has been used as traditional medicine. *Cimicifuga racemosa* which is extensively used to treat women health related issues and also carries a lot of traditional uses. Since forty years in Europe this plant is used for treatment of menstrual pain. Alovera gel, Cannabis, Echinacea, Garlic, Ginkgo, Ginseng, Devil's claw, Tumeric, Green tea has medicinal properties to cured inflammatory disease.

2. Phytomedicine

Phytomedicine, also known as herbal medicine or phytotherapy which involves the use of plants or herbs to treat or prevent health conditions. Phytomedicine has become an increasingly important treatment option for patients in western world. It includes the use of various plant parts, like leaves, flowers, roots and seeds to create medicinal products. The use of plants for medicinal purposes is beneficial for health. For example, the anti-maralial drug artemisinin was derived from the plant Artemisia annua, which was used in traditional Chinese medicine to treat fever. In the United States, they are often sold as dietary supplements. Phytomedicine is widely used, but there is still need research for safety and efficacy of many herbal remedies. It represents a fascinating intersection of traditional knowledge and modern science.

3. Phytomedicine and Human Health

3.1. *Moringa oleifera*

Moringa (*Moringa oleifera* Lam). is a type of local medicinal Indian herb which has turn out to be familiar in tropical and subtropical countries. The other terms used for *Moringa* are Horseradish tree, Mulangay, Drumstick tree, Kelor, Mlonge, Benzolive , Sajna and Marango. *Moringa oleifera* is scientific division to become from Kingdom: Plantae, Division: Magnoliphyta, Genus: *Moringa*, Species: *M. oleifera* (Fahey, 2005). *Moringa* was found to contain many essential nutrients, for instance, vitamins, minerals, amino acids, beta-carotene, antioxidants, anti-inflammatory nutrients and omega 3 and 6 fatty acids (Fahey, 2005; Hsu, 2006; Kasolo *et al.*, 2010). Nutrition content of plant plays an essential function in medicinal, nutritional and therapeutic properties. It is believed that Moringa leave to consist high source of

vitamin C, calcium, beta-carotene, potassium as well as protein. It works as an effective source of natural antioxidants. Antioxidant compound such as flavonoids, ascorbic, carotenoids and phenolics.

- *Anti-fibrotic/Ulcer* - It is a natural drugs to treat liver fibrosis. It was recently discovered that the *Moringa oleifera* seed extract exhibited and anti-fibrotic effects on liver fibrosis.
- *Anti-inflammatory* - *Moringa* has been practically used in medicinal field, throughout the decades to heal a huge amount of acute and chronic conditions. The properties of its phytochemicals, such as flavonols and phenolic acids were related to heal a huge amount of acute and chronic conditions. It also possessed anti-inflammatory properties against CC14-induced liver damage and fibrosis.
- *Antimicrobial and Anti-oxidant* - *Moringa's* morphological parts such as seed cotyledon, seed coat, bark, Stem, leaves, root bark shows antimicrobial properties. It treats on certain bacterial infections. It shows activity against gram positive than gram negative bacteria. The leaves of the *Moringa oliefera* tree have shown antioxidant activity due to its high amounts of polyphenols. Plant extracts of both mature and tender leaves exhibit strong antioxidant activity against free radicals, major biomolecule prevents from oxidative damage, protection against oxidative damage.
- *Anti-hyperglycemic and Anti-tumor* - Diabetic patients exhibit a stage of chronic hyperglycemia and glucose tolerance impairment (Tiwari and Roa, 2002). Diabetes mellitus is a chronic metabolic disorder. *Moringa oleifera* is used ti treat diabetes mellitus since it is traditional method. As it shows blood glucose lowering activities. Hypoglycemic and anti-hyperglycemic activity of the leaves of *Moringa oleifera* may probably due to the presence of terpenoids, which appears to be involved in the stimulation of the beta-cells and the subsequent secretion of preformed insulin (Tende, 2011). *Moringa* also shows anti-tumor as it found bioactive compound, Niazimicin.
- *Anti-cancer* - *Moringa* is revealed to potential therapeutic effects to fight cancer, rheumatoid arthritis, diabetes and some other aliments. *Moringa oleifera* Lam pod is chemopreventive agent. Glutathione and GST activity loss was restored by the *Moringa* pod extract in which these enzymes offer a major protection role against the effects of carcinogens (Sharma, 2012).

Figure – 1: *Moringa oleifera* powder

Figure – 2: *Moringa oleifera*

3.2. *Cymbopogon* genus

The *Cymbopogon* genus is belongs to the Andropoganeae family of the family Poaceae. It has high essential oil concentration. It has diverse applications in cosmetic, phytotherapy and pharmaceuticals. *Cymbopogon* mainly contained flavonoids and phenolic compounds, which were the crucial pharmacological active ingredients when combined with the complex beta- cyclodextrin. *Cymbopogon* is known with various names, lemongrass, barbed wire grass, silky heads, cochin grass, Malabar grass, oily heads, citronella grass or fever grass. It is diverse in terms of names, species, and uses with almost all of them being aromatic. It consists of 144 species, some of which include *Cymbopogon nardus* (L.) Rendle (C. nardus), *Cymbopogon citratus* (DC) Stapf (*C. citratus*), *Cymbopogon flexuosus* (Nees ex steud.) W. Watson (*C. flexuous*), *Cymbopogon martini* (Roxb.) W. Watson (*C. martini*). Different parts of the *Cymbopogon* plant consist of bioactive chemicals which shows the anti- inflammatory, antiseptic, anti- dyspeptic and anti-fever actions, antispasmodic, analgesic, antipyretic, tranquilizer, anti-hermetic and diuretic characteristics of the plant (Ademuyiwa, 2015; Bayala, 2018).

- *Antiprotozoal effect* - Citral is the major component of *C. citratus* and *C. flexuosus* essential oils. Myrcene and citral shows anti-leishmanial effect on different species like *Leishmania infantum, Leishmania tropica* and *Leishmania major*. Citral also shown to exert anti-trypanosoma cruzi activity and inhibit the anatomic and ultrastructural changes of *Leishmania amazonesis* without cytotoxicity. *Entamoeba histolytica* active in broth culture from *Cymbopogon* essential oil (Dutta, 2016).
- *Anti-bacterial and Antifungal effect - C. citratus* has been used to isolate, characterize and analyze essential oils like citral (geranial) and citral (neral), which have been shown to be antibacterial chemicals that are active against both Gram-positive and Gram negative microorganisms (Soares, 2013). This herb treats against bacterial infections like meningitis, pneumonia, impetigo, cellulitis, folliculitis and food poisoning. Myrcene shows low antibacterial activity but is very active when combined with other essential. *C. martini* shows antibacterial activity against *Staphylococcus aureus, S. pyogens, E. coli* and *Corynebacterium ovis. C. citratus* can prevent fungal infections like athlete's foot, ringworm, jock itch, yeast infection and keratinophilic fungi (Abe, 2003).
- *Anti-cancer and Anti-inflammatory effect - C. flexuosus* oil triggered apoptosis in Human leukemia cell lines (HL-60 cells) effect was seen on human cancer lines of colon, liver, cervix and neuroblastoma. The oil treatment of *C.densiflorus* is to shows antitumor effects on TP53 wild-type and mutated bladder cancer cells. Therefore *C. flexuosus* and *C. densiflorus* maybe the reasonable alternative for novel antineoplastic drug. The essential oil of *C. flexuosus* with high citral content reduce numerous inflammatory biomarkers in human skin cells. It also used in many ointments and lotions to treat tropical inflammation.
- *Anti-malarial effect* - The essential oils of *C. giganteus*, *C. nardus* and *C. schoennanthus* shows effect against *Trypanosoma brucei* and *Plasmodium falciparum.*
- *Anti- diabetic and Antinociceptive effect - C. nardus* shows maintaining blood glucose levels. *Cymbopogon* used as a traditional medicine to relieve pain and anxiety. Essential leaf oil of *C. winterianus* exhibits antinociceptive effects through the inhibition of prostaglandin synthesis (Leite,2010).
- *Insecticidal activity* - Essential oil from different *Cymbopogon* spp. can controlled pathogen and insects like, piperitone from *C. schoenanthus* is proven to be strong repellant against *Crematogaster* spp. and *Callosobruchus maculates. C. citratus, C. nardus, C. martini* is efficient against *Anopheline* mosquitos*, Anopheline culicifacies.*

- *Anti-HIV Effect* - In HIV/AIDS patients, citronella oil extracted from *C. citratus* leaves was reported to heal oral thrush caused by *Candida albicans* in 1 - 5 days (Wright, 2009).

Figure – 3: *Cymbopogon citratus*

Figure – 4: *Cymbopogon martini*

3.3. Pineapple plant

Pineapple plant possesses therapeutic characteristics. It contains an additional proteolytic enzymes such as comosain, ananain and bromelain is most studied. This proteolytic enzyme (protease) catalyzes the breakdown of proteins into amino acids. It belongs to the Bromeliaceae family. Bromelain has ubiquitous nature and is used as a phytomedicine. Its fibrinolytic, antifungal, antibacterial, antithrombotic and anti-inflammatory effects are well established. It also shows anti-cancer functions. Chemical constituents, such as tannins, saponins, flavonoid and several enzymes, present in bromelain exert antibacterial characteristics to it. Bromelain's antiadhesion capability has been suggested to prevent bacteria from adhering to surfaces, resulting anti-bacterial action. It has efficacy to treat infections caused by *Vibrio cholera, E. coli,*

helminthic and chronic disease such as Crohn's disease, ulcerative colitis, UTI, sinus infections and prostatitis. It also has therapeutic applications. It is used to treat burns, allergies, blood coagulation, inflammation, antibiotic enhancement, blocked sinuses, cardiovascular disorders, diarrhea and cancer. It works as fibrinolytic agent because it promotes the conversion of plasminogen to plasmin. It increases antibiotic absorption, which is effective drug diffusion in tissue and reduce the toxicity-related adverse effects. Bromelain acts on the immune system by enhancing the production of Tumor Necrosis Factors, Interferons, Granulocyte-Macrophage Colony-Stimulating Factors (GMCSF), and Interleukins (IL-1, IL2, IL-3, IL-6). CD4+ helper T-lymphocytes activation is limited by bromelain thereby decreasing CD25 and CD44 expression. Bromelain serve as anti-inflammatory agent by decreasing bradykinin production in the Kinin-Kalli-Krein pathway. Bromelain has dental applications. The dental bleaching action is aided and accelerated by bromelian when used in combination with hydrogen peroxide. It used after acid etching to improve the bond strength of adhesive systems. It reduce in microleakage of tooth-colored restorations. Bromelain enzyme acts on the pre-degraded collagen networks of the carious lesion, it softens them and promotes their easy removal. Bromelain and pineapple fruit demand has been rising around the world because of their advantages in maintaining human health and uses. As it shows anti-inflammatory capabilities. It is synthetically produced medications because it is natural and harmless substance.

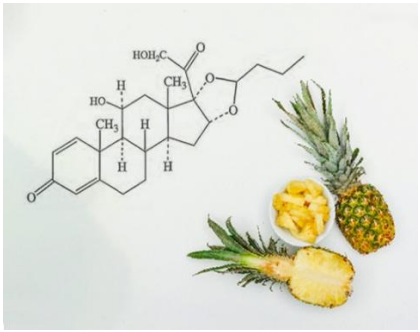

Figure – 5: Bromelain Structure

Figure – 6: Pineapple Plant

3.4. *Cimicifuga racemosa* and *Angelica keiskei*

Menopause is a natural health concern among women of all over the world. It is characterized by hormonal changes. Low estrogen levels show ovarian dysfunction are characteristic feature found in postmenopausal women. The variation in hormones may lead to diverse range of indications, collectively called Postmenopausal Syndrome (PMS). Therefore, attention needs to paid to women health in order to improve quality of life after menopause. Hormonal replacement therapy commonly known as menopausal hormone therapy, is an extensively used treatment for postmenopausal syndrome, but its associated risks outweigh the benefits in long-term use. Therefore, phytomedicine has been used in medicine.

Cimicifuga racemosa (CR) is extensively used to treat women's health-related issues and also carries a lot of traditional uses. CR has been used for over years to treatment of menstrual pain. It is also distributed in Canada and China and cultivated in Europe. It also called as black cohosh, rattle weed, snakeroot, squaw root. CR is widely used to mitigate menopausal symptoms like sleep disturbance, hot flashes, night sweats, nervousness, mood swing, vertigo and vaginal dryness associated with postmenopausal females. This herbaceous plant has history of treating varieties of aliments with global demand. It is herbal remedy for the treatment of menopausal symptoms. It has been suggested that CR possesses direct estrogenic activity it is widely used by menopausal women considering its estrogenic activity, as it possesses functions similar to estrogen like deficiency of hot flashes, the reduction of depression and the protection against bone loss.

Angelica keiskei which belongs to the family Umbelliferae, plant that grows mainly in Asian countries, including China, Korea and Japan. It is known as Shin-Sun ho, which means to 'a precious herb used by God'. It is also called as tomorrow's leaf because of its quick growth and regeneration capacity. *A. keiskei* has been used as an anti-aging and health enhancer. This plant extracts induced apoptotic cell death in various human cancer cell lines including breast cancer (MDAMB-231) (Jeong and Kang, 2011), leukemia, melanoma, lung cancer, as it shows anti-tumor and anti-mutagenic activity. Powder of *A. keiskei* improved blood glucose control and moderately and safely reduced blood glucose as it shows anti-diabetic activity. It shows anti- bacterial activity against *Helicobacter pylori*, preventive agent for gastritis. Also control mouth odor by an anti-bacterial activity against *Fusobacterium nucleatum. Angelica keiskei* also shows anti-inflammatory, anti-obesity, anti-hyperlipidemic activity.

Oral Squamous Cell Carcinoma (OSCC) is the malignancy. Traditional OSCC therapies, including surgery, radiotherapy and chemotherapy have advanced but not improved survival due to the aggressive characteristics of OSCC. Xanthoangelol (xanol) isolated from *A. keiskei*. Xanol has protective effects against allergic diabetes, inflammation, infection, neurodegeneration, muscle loss, tumor growth, stress. Xanol exerts anti-cancer activity by inhibiting the AKT signaling pathway in human OSCC. Xanol shows effects in suppressing the proliferation, migration, invasion and tumorigenesis of human OSCC.

Figure – 7: ***Cimicifuga racemosa***

Figure – 8: ***Angelica keiskei***

4. Disease Cured by Phytomedicine

4.1. Joint Disorders

Chronic joint inflammatory disorders such as osteoarthritis and rheumatoid arthritis common in increase of inflammation and stress, resulting in histological alterations and disabling symptoms. Use of traditional herbalism, medicinal plants are a promising alternative with lower rate of adverse events and efficiency frequently comparable with that of conventional drugs. Osteoarthritis is one of the most common musculoskeletal disorder, in this irreversible destruction of articular cartilage and bone erosion, induced by pro-inflammatory cytokines i.e. interleukin 6 (IL-6), interleukin 1

(IL-1), and Tumor Necrosis Factor - Alpha. Rheumatoid arthritis (RA) is a chronic systematic autoimmune disease. It increased the risk of cardiovascular disease, lymphoma as well as death. It is associated with high levels of oxidative stress and inflammatory mediators. RA is currently treated with steroids/ nonsteroids and anti-inflammatory drugs. Among nonsteroidal anti-inflammatory drugs, acetaminophen is most frequently used in very high doses (4000 mg/day). In painkillers, tramadol is highly recommended. Anakinra and methotrexat are other therapeutic drugs. Unfortunately, the use of standard drugs has numerous serious side effects like gastrointestinal ulceration, hemorrhagic events, infusion hypersensitivity reactions. Therefore, biologic therapies have proven to be highly effective in the majority cases of RA.

Boswellia serrata (BS) yields a gum resin, known as frankincense, efficacious in the treatment of inflammatory disorders, particularly arthritis. A BS preparation enrichred in active principles was able to hinder cartilage breakdown by metalloproteinase-3 (MMP-3) and to block intercellular Adhesion Molecule 1 (ICAM-1) and thereby the inflammatory reaction. A mixture of *Curcuma longa* and *Boswellia serrata* has been shown to be more efficient than a standard dose of celecoxib in the treatment of osteoarthritis. *Curcuma domestica* extracts have been shown to be useful in knee osteoarthritis, reducing the pain. Beta-Elemene, found in *Curcuma wenyujin*, an herb used in Traditional Chinese Medicine for the treatment of rheumatoid arthritis. *Harpagophytum procumbens* (HP), also known as devil's claw, a medicinal plant native to Africa, is a 'celebrity' among anti-osteoarthritis natural remedies. The major phytochemicals responsible for the anti-osteoarthritis effect are the iridoid glycosides, which are found in a higher amount in tubers and root.

*Panax notoginseng (*PN), known as sanqi in Chinese, use for the treatment of traumatic injuries, swellings and pains. Saponins are considered the main osteo-active phytochemicals from PN. Sesame oil (SO) extracted from *Sesamum indicum* (SI) has been used in various Asain traditional medicines to alleviate pain in inflammatory conditions of joints, teeth, skin. *Symphytum officinalis*, also known as comfrey, is a medicinal plant used for the treatment of inflammatory disorders. *Zingiber officinalis* (ZO), also known as ginger, is a common spice used for diseases. In Ayurveda, Ashwagandha is a potent anti-osteoarthritic and anti- inflammatory plant.

Figure – 9: ***Boswellia serrata***

Figure – 10: ***Panax notoginseng***

Figure – 11: ***Sesamum indicum***

4.2. Mental Health

Stress, anxiety, mood disorders, sleep problems and cognitive dysfunction are the most common mental health problems. In this, herbal products constitute treatment with minor side effects and low toxicity. Many herbal drugs from medicinal

plants with clinical effects in mild depression, anxiety, cognitive impairment, insomnia and fatigue contain triterpenoid saponins (Radix Astragali, Radix ginseng, Radix polygalae) steroid saponins (Radix Polygonatae, Semen Foenugraeci). Saponins have benefits in many diseases. *Trigonella foenum-graecum* L. and *Polygonatum sibiricum* Redoute are medicinal plants with effects on mental health that contain substantial amounts of steroidal saponins. *P. sibiricum* extract increased probiotic bacteria and decreased the harmful species. *Astragalus membranaceus* root contain triterpene saponins with the marker compound astragaloside IV, in addition to various compound classes such as flavonoids, polysaccharides and amino acids.

Leaf extract of *Gynostemma pentaphyllum* Makino, another mental health-related, triterpene saponin-rich medicinal plant. It increases in potentially health-beneficial bacteria and significantly reduced sulfate-reducing bacteria. The aerial parts of *Centella asiatica*, a herbal brain tonic for mental disorders and reduced stress-related depression and anxiety. The best examined medicinal drug influencing the brain and nervous system is ginseng root from Asain ginseng or American ginseng. Orange, lavender, lemon verbena and rosemary are shows anxiety, insomnia, anxiolytic and sleep-promoting effects. Extracts of *Ginkgo biloba*, leaves are used worldwide. These are applied to neurological disorders connected to impaired cognitive functions and have been considered for anxiety and depression. Saffron (*Crocus sativas*) is also used in mood disorders, anxiety and mild depression.

Schisandra chinensis and *Eleutherococcus senticosus* has role in mental health including, behavioral disorder, anxiety, depression, memory and attention. Glycine max, a medicinal and food plant which is rich in isoflavones shows beneficial effects on mental health in menopausal women. The female infloresesence of *Humulas lupulus* are used as herbal medicinal products for anxiety, mood disorders and sleep disturbance. Mulberry leaf extract improved working memory and cognitive function in clinical trails. Green tea, prepared from unfermented leaves of *Camellia sinensis* has beneficial effects including the modulation of cognitive function and mood disorder, reduced anxiety, improved attention and prevent cognitive impairment. Compounds present in unfermented green tea leaves which active mental health are methylxanthines (caffeine), amino acid, flavan-3-ols.

A medicinal herb commonly used to treat depression is *Hypericum perforatum*, this plant in the treatment of mild to moderate depression because it has shown comparable efficacy, fewer side-effects and lower risk of discontinuation. It shows antidepressant effects such as hyperforins, polyphenols. The root of *Rhodiola rosea* are used as traditional medicinal for their positive mental health effects on anxiety, stress, fatigue and depression. *Cannabis sativa* for chronic pain and chemotherapy-induced nausa and

vomiting as well as secondary sleep disturbance. Traditional medicines rich in polysaccharides that are used to promote mental health include the rhizomes of Dioscorea opposite and the fruits of *Lycium barbarum*.

Figure – 12: ***Ginkgo biloba***

Figure – 13: ***Cannabis sativa***

Figure – 14: ***Gynostemma pentaphyllum***

Figure – 15: ***Schisandra chinensis***

4.3. Inflammatory Disease

Inflammatory diseases occur when the body's immune system mistakenly attacks its own tissues, causing inflammation. This can lead to various chronic conditions such as, Rheumatoid arthritis, Crohn's disease, Ulcerative colitis, Psoriasis and Lupus. Inflammation may be acute or chronic. Acute inflammation is a normal response to injury or infection, while chronic inflammation can persist for months or years and may require medical treatment. Plant preparations use for medicinal purposes. It refers to use of naturally occurring products to cure human health.

Common cold prevent and treated by herb and roots of several *Echinacea* species. Root extract of *Echinacea purpurea* contain alkylamide content because of immune stimulating effect, *Echinacea* products are contraindicated for patients with autoimmune disease or immune modulating therapy, based on theoretical consideration. *Echinacea* root extracts are considered as safe, regarding pharmacokinetic interaction. Devil's claw originating from southern Africa, root of this plant is traditionally used to treat digestive disorders and mild articular pain. Aqueous extracts have been shown anti-inflammatory and antioxidant effects.

Garlic is an herbal drug widely used to prevent atheroscelerosis and treat common cold. *Allium sativum* containing at least 0.45% allicin. Clinical data suggest favourable influence of garlic on risk factors for atherosclerosis, such as blood pressure and hypercholesterolemia. It also shows antimicrobial properties. There are tablets and capsules with garlic powder. Allicin has been suspected to be the main active coumpound, due to its instability, enteric coated products containing alliin and alliinase were used to enable allicin formation in the intestine.

Medicinal products based on ginkgo are used to treat dementia, vertigo and peripheral arterial disease. Ginseng is among the most popular herbs and applied by healthy, mostly elder person as well as patients with chronical diseases. This termed ginseng, used for several drugs. Most often it refers to Panax ginseng roots. They can be differentiated into dried (white ginseng) and steamed (red ginseng). The intake of beverages prepared from green tea from unfermented leaves of *Camellia sinensis,* has been part of food culture in East Asia for centuries. In modern times, it has gained popularity worldwide. Tea has been suggested to have health benefits in prevention of cardiovascular disease, cancer and neurodegenerative diseases and is part of supplements advertised for weight control. The leaves contain flavonoids and catechins, the most active and abundant as it contains epigallocatechin-3-gallate (EGCG). The risk is higher when the supplement is taken under fasting conditions and as single bolus instead of split doses due to higher EGCG bioavailability. Tumeric shows anti-inflammatory properties as its main active substance is curcumin. Willow bark and Meadowsweet herb both drugs contain flavonoids and salicylates and are traditionally used to treat fever and pain. Systemic inflammatory disease and women health are treated by evening primrose oil. *Aloe barbadensis* leaves contain a gel rich in mono- polysaccharides that is used in cosmetics and food flavor. It is suspected to have anti-inflammatory properties.

Figure – 16: ***Camellia sinensis***

Figure – 17: ***Echinacea purpurea***

Figure – 18: ***Allium sativum***

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Chapter - 7

Phytomedicine Innovations: The Future of Plant – Based Therapies
ISBN: 978-81-977907-4-4
First Edition
Chapter – 7, Page: 104 - 116

7

ETHNOPHARMACOLOGICAL SURVEY OF MEDICINAL HERBS IN BHIL AND BHILALA TRIBE OF SENDHWA REGENCY OF BARWANI, MADHYA PRADSH, INDIA

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Abstract

Within the gift time name for of plants can be very high just so those plant lives are the most extensively used plant products. Extensive ethnopharmacological survey has been done in awesome seasons from 2022 to 2023 through manner of properly-deliberate time table. A observes became finished to analyse floristic range of Sendhwa block of Barwani district of Madhya Pradesh. Sendhwa is surrounded through way of Satpuda hill tiers in south and Vindhyanchal hill tiers in north. Goi River is the main river fallowing in this location that is tributary of Narmada River. The forests and a hill of this location is a treasure house of medicinal flora. Biodiversity of Sendhwa is representing the richness of various existence forms starting from climber, shrubs and timber, which may be annual to perennials. Present observe facts a complete of 185 ethnopharmacological species which is probably distributed in 139 genera and 48 families. Exclusive life paperwork diversity is Herbs (111), Shrubs (21), trees (29) and climbers (24). Jacard's generic coefficient is 75.13. Maximum species is used for wound in this area fallowed with the aid of skin care (19 species), irritation and fever (34 species), stomachache 13, asthma and ulcer (20 species) tonic (8 species) snake bite (6 species) indigestion (5 species) & diarrhea (4 species).

Keywords: Ethnopharmacological, Narmada River, Satpura ranges, Goi River, Jaccard's generic coefficient.

1. Introduction

The tribal live in woodland environments and close affiliation with plants. The tribal experimented with plants to therapy several illnesses despite the development of chemotherapy and radiotherapy. Most of the people of tribal are nevertheless sticking to their age old conventional drug treatments, the know-how of which got here from their forefathers inside the form of oral folklores (Sainkhediya and Trivedi, 2021). Ethno botany is observed of the interactions between plants and people over the years and area. Therefore, plants are important to the functioning of all social societies and to the operation of all ecosystems (Sainkhediya and Rawat, 2022). In our planet, tens of tens of millions of species are grown. guy has surveyed one among a type wooded area regions in addition to certainly one of a type galaxies however he does now not enough to everywhere to complete a taxonomic catalogue (Sainkhediya *et al.,* 2022)

The recipes used inside the traditional medicinal drug of India had been passed down from the forefathers by way of oral lifestyle and this as disappeared from our cutting-edge-day society (Sainkhediya *et al.,* 2022). India has a completely wealthy history of conventional healthcare gadget for livestock through Ayurveda, Unani and Homeopathic system of medicine which has been used considering the fact that time immemorial and there may be some other device of medicine parallel to this that is known as folks medicinal drug, tribal medicinal drug or ethno medicinal drug (Trivedi *et al.,* 2024). Botanists have been exploring the floristic areas as well as medicinal flowers of the world for numerous centuries and their efforts have succeeded excellent in getting ready an extra sensible taxonomic account of the plants of India (Sasidharan, 2002). The biodiversity discovered on the planet in recent times which encompass many masses of thousands of great organic species that's the fabricated from almost 3.5 billion years of evolution and got here into life, flourished and vanished due to various reasons (Sainkhediya and Ray, 2014). The richness of flowering flora makes India one of the mega range international locations inside the global with 4 biodiversity hotspots and 3 mega centers of endemism (Pachaya and Sainkhediya 2015). Biodiversity keeps the ecological strategies in a balanced nation that is vital for human survival and fitness advantages also (Kaur and Sharma 2014).

The cutting-edge international context of gradual financial growth, social inequality and environmental degradation is growing remarkable challenges for the worldwide network. The time period organic variety became used first by means of manner of natural world scientist and conservationist Raymond F. Dasmann in the 1968 in reference to the richness of living nature that conservationists should shield in

his book "A exclusive sort of U. S." the term Biodiversity become coined through Walter G. Rosen in 1985 Eric A Davidson is a professor on the Appalachian Laboratory of the University of Maryland Centre for Environmental era. He has stated in his eBook entitled 'you couldn't devour GNP: Economics as even though Ecology mattered' that a healthy economic device relies upon on a healthy surroundings - a notion we are able to't afford to push aside. This eBook offers a blueprint for a really sustainable financial device that acknowledges the herbal resources (like water, air, and soil) on which we in the end depend. You comprehend peace can't be carried out without bringing the pieces together likewise; sustainability can't be done without a synergic mutual balanced method the various social, financial and ecological pillars of sustainability.

Natural variety approaches the range amongst dwelling organisms from all assets and the ecological complexes of which they are an element; this consists of variety inner species, amongst species and of ecosystems. India is a mega range state which means that that it harbors most of the people of the earth's species and is consequently considered extremely biodiversity. India constitutes most effective 2.4 % of the arena's land vicinity however having 11 % of plant life and 6.5 % of the fauna of the sector. India incorporates 2.9 % of the IUCN-exact threatened species. India has 350 species of mammals, 1200 species of birds, 453 species of reptiles and 45000 plant species of which maximum are angiosperms. in line with the worldwide Union for Conservation of Nature (IUCN), there are approximately eight.7 million species on earth, but most effective 1.2 million of those species were scientifically defined and catalogued. In India, the expected extensive variety of species is spherical 90,000, with round 50,000 species of plants and 20,000 species of animals. The closing species consist of fungi, and microorganisms. Biodiversity plays a crucial function in preserve the stability of our planet's surroundings and the survival of the existence on the earth. However, due to human sports activities consisting of deforestation, pollution, introduction of invasive species, climate change, and over-exploitation of natural assets, biodiversity is under risk.

Biodiversity is formally described by the convention on biological diversity (CBD) as: "the variety among dwelling organisms from all property at the side of, among others, terrestrial, marine and different aquatic ecosystems and the ecological complexes of which they are element; this includes range inside species, among species and of ecosystems" (Kumar and Verma, 2017).Biodiversity is the result of the evolutionary plasticity of living organisms and increase geometrically via 2.5 billion years proliferating through trial and blunders managed with the resource of herbal pick out filling nearly every one of the livable ecological niches created in a likewise evolving international surroundings. Biodiversity is measured with the aid of major

additives which can be Species richness and Species evenness. Species richness is the diploma of the quantity of species placed in a community and Species evenness is a degree of the relative abundance of the distinct species making up the richness of a place. Low evenness suggests that some species dominate the web page. Diploma of variety consists of Alpha variety, beta variety and gamma range. Alpha range refers to the variety inner a specific location is generally expressed thru the wide form of medicinal species in that ecosystem. Beta biodiversity is a contrast of variety among ecosystems, normally measured because the exchange in the amount of specie. Sendhwa has wealthy and varied flowers due to its diverse floral elements beneath well covered forests areas. The forests and a hill of this place is a treasure residence of medicinal plants. A small work completed on this vicinity through Sainkhediya and Patil (2019); Sainkhediya and Ray, (2014); Ray and Sainkhediya (2012); Sisodiya and Sainkhediya (2018); Ahirwar and Sainkhediya (2021).

2. Study Area

Sendhwa location is positioned on the southern western a part of Madhya Pradesh. It lays on 21°41'North latitude and 75°6 E Longitudes. The call Sendhwa modified into derived after the rulers Sendhwa at duration of Holkars (Sisodiya and Sainkhediya 2018). Sendhwa castle have become built in 10th Century. It's far located in middle of metropolis. it is classical example of 4 directional Gates with Temple at important access gate. Topographically the vicinity is bounded by the Rajpur tehsil to the north, Warla tehsil in south, Niwali to west, and Khargone district to east. The jap part of the district is covered with the useful resource of Satpura hill ranges and northern part of Malwa plateau, and Narmada valley. Satpura plateau covers 20.33 part of the south-Western a part of Nimar. Sendhwa, come beneath Satpura hill tiers. Important part of Khargone and Barwani occurs in Narmada valley (Sainkhediya and Ray, 2012). Narmada and Goi is the fundamental river flowing in the region. Phytogeographical the check location is close to Gujarat nation and bordering Maharashtra. The aridity and dryness of the climate, unique topography of the place i.e. Junction of Vindhyan and Satpura hill levels and exceptional River Narmada provides a very good ground for the diverse ecological habitats with overlapping flowers pattern and unique floral factors. Nagalwadi has a wealthy pocket of vegetation and dense woodland. The land surface attains a most altitude of 409 m (1,342 ft) above imply sea level. Demographically Sendhwa had a populace of 56,485 (census 2011) Bhil and Bhilala tribe are denominated inside the area. Sendhwa has a mean literacy price of 63 %, better than the national not unusual of 59.5.

3. Methodology

In depth and big Ehnopharmacological survey of medicinal herbs in Bhils and Bhilala tribe of Sendhwa regency of Barwani, Madhya Pradesh, India for the duration of the 365 days 2022-2023.The random sampling approach are used for the collection of samples. Ehnopharmacological surveys are involved with an assessment of species composition of flowers, rather than the structure. Those are desired for large-scale research of a detailed botanical nature. The facts may be included for large region research. Manage the spanned phrases as you need. Sure, surveys of vegetation frequently require facts on species composition further to, or instead of, structural or physiognomic descriptions. Such studies incorporate the identification of individual species and moreover the assessment of abundance of species. The gathering of information at the species diploma is vital to biogeography and ecology and medicinal residences. Individual plant species are the constructing blocks of plant communities and exceptional survey and clarification of the distribution of groups further to character species calls for floristic description. Additionally precise appreciation of plant-environmental relationships and the consequences of control of flora via man can often handiest be absolutely understood thru an ethnopharmacological survey. The ethnopharmacological survey carried in considered one of type seasons. All tribes of the observe vicinity surveyed carefully. The vegetation and distribution sample of the plants were studied. Plant series and herbarium guidance changed into finished by brand new technique (Jain and Rao, 1977). Identification of flora done with the assist of flowers (Verma *et al.*, 1993; Mudgal *et al.*,1997; Khanna *et al.,* 2001; Shah, 1978; Hooker, 1872-1897; Naik, 1998) and one of a kind taxonomic literature. For determination of widespread coefficient, the following gadget turned into used:

Familiar coefficient = No. of Genus/No. of species × 100

4. Results and Discussion

Present look at critiques 185 plant species which is distributed in 48 families 139 genera. Dicotyledons consist of 158 species with 114 genera and 41 families and monocotyledons are composed 27 species, 25 genera and 7 families (Table – 1 & Figure - 1). Our test critiques 185 species and 139 genera which appear to be a remarkable instance of the flora for a small region. Totally, 48 families, 139 genera and 185 species had been recorded. Established coefficient is 75.13. Monocotyledons percent 7 households (14. 8 %), 25 genera (18 %) and 27 species (14.6 %) and Dicotyledons percentage 41 families (85.1 %), 114 genera (82 %) and 158 species (85 %), (desk-2). The Table - 3 confirmed the list of Ehnopharmacological plant of Sendhwa district Barwani, Madhya Pradesh, India. Maximum species is used for

wound in this region fallowed by means of skin care (19 species), inflammation and fever (34 species), stomachache 13, bronchial asthma and ulcer (20 species) tonic (8 species) snake bite (6 species) indigestion (5 species) and diarrhea (4 species).

Borassus flabellifera L. species have been decided to be unusual within the place. character One medicinal species is used for exclusive disease like that Anemia, Colds, Cooling, Digestive sickness, Diuretic, Dysentery, Gastritis disorders, will increase power, Infertility, Jaundice, Joint ache, Kidney stone, Liver tonic, Muscle pain, Pneumonia, Rheumatism, Ringworms, Sexual debilities. Medicinal species are used for exceptional disease like that Antidiabetic, Antifertility, Burns, Conjunctivitis, Diabetes, Menstrual problems, Nerves disorders, Swelling, Toothache. Antibacterial, Constipation, Cough, Headache. Medicinal species is used for Diarrhea disease. Medicinal species is used for Indigestion. Medicinal species is used for Snake bite. Medicinal species is used for Tonic. Medicinal species is used for bronchial asthma. Medicinal species is used for Ulcer. Thirteen medicinal species is used for Stomachache. Medicinal species is used for Fever. Medicinal species is used for inflammation. Medicinal species is used for pores and skin care. Medicinal species is used for Wound. In view of the severe problem that the price of eroding biodiversity is growing and its miles estimated that nearly 10 % of the recorded organic wealth is at the verge of extinction (Raj, 2010), because of care and motion have to be taken on precedence foundation for the conservation of unusual, species. Within the take a look at location five biggest families are as fallowed Leguminosae is the most important family in the location fallowed via way of Poaceae, Dipterocarpaceae, Compositae, and Apocynaceae. The jacard's common coefficient it truly is hundred instances the reciprocal of average number of species per genus speaks of immoderate commonplace diversification of the species quota of every genus being near one, famous diversification displays heterogeneity, antiquity and species impoverishment of the community. There's an urgent want to optimize 'nature's economic system' simply so there's an enhancement in the species diversification ok to restore the winning woodland-ecosystems inside the Sendhwa district Barwani.

Table - 1: Distribution of Taxa in Sendhwa

		Species	**Genera**	**Families**
Dicotyledons	Polypetalae	91	63	23
	Gamopetalae	50	40	12
	Monochlamydeae	17	11	6
	Total	158	114	41
Monocotyledons		27	25	7
	Grand total	**185**	**139**	**48**

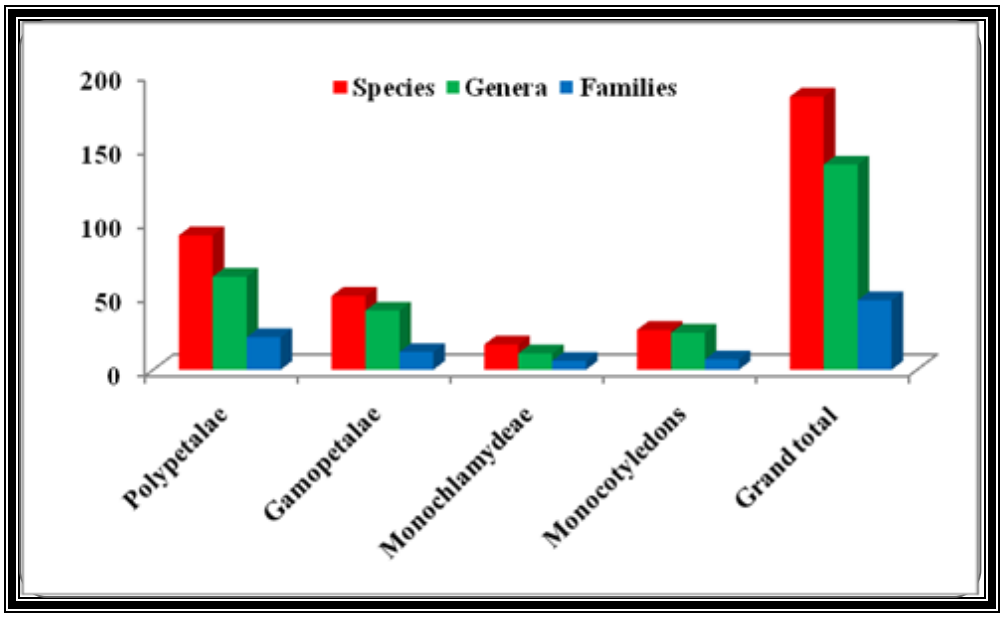

Figure - 1: Distribution of Taxa

Table - 2: Diversity of Family, Genera and Species

Angiosperm	Species	%	Genera	%	Families	%
Dicotyledons	158	85.4	114	82	41	85.1
Monocotyledons	27	14.6	25	18	7	14.8
Jaccard's generic coefficient	75.13					

Table - 3: Ehnopharmacological Used Plants in Sendhwa Dist. Barwani (M.P.), India

Families	Botanical Name	Ethnopharmacological uses in different disease
Annonaceae	*Annona reticulata* L.	Inflammations
	Annona squamosa L.	Wounds
Menispermaceae	*Cissampelos pareira L.*	Snakebite
	Cocculus hirsutus (L.) Theob.	Skin care
	Tinospora sinensis (Lour.) Merr.	Wounds
Papaveraceae	*Argemone mexicana* L.	Wounds
Capparaceae	*Capparis decidua* (Forssk.) Edgew.	Inflammations
	Capparis grandis L.	Asthma
	Capparis sepiaria L.	Stomachache
Cleomaceae	*Cleome gynandra* L.	Inflammations
Polygalaceae	*Polygala arvensis* Willd.	Fever
	Polygala erioptera DC	Wounds
Dipterocarpaceae	*Shorea robusta* Gaerth	Ulcers
Malvaceae	*Abutilon hirtum* (Lam.) Sweet.	Ulcers
	Abutilon indicum (L.) Sweet	Increases strength
	Bombax ceiba L.	Fever
	Corchorus aestuans L.	Inflammations
	Corchorus fascicularis Lam.	Anemia

	Corchorus olitorius L.	Tonic
	Grewia flavescens Juss.	Wounds
	Grewia hirsuta Vahl.	Indigestion
	Grewia sapida Roxb. ex DC.	Inflammations
	Sida acuta Burm. F.	Inflammations
	Sida cordata (Burm f.) Borss. Waalk.	Asthma
	Sida cordifolia L.	Headache
	Triumfetta malebarica Koenig ex Rottb.	Skin care
Malpighiaceae	*Hiptage benghalensis* (L.) Kurz	Wound
Zygophyllaceae	*Tribulus terrestris* L.	Diuretic
Oxalidaceae	*Biophytum reinwardtii* (Zucc.) Klotzsch.	Wound
	Biophytum sensitivum (L.) DC.	Stomachache
	Oxalis corniculata L.	Fever
Rutaceae	*Aegle marmelos* (L.) Correa	Antifertility
	Murraya paniculata (L.) Jack	Stomachache
Simaroubaceae	*Ailanthus excelsa* Roxb.	Antifertility
Meliaceae	*Azadirachta indica* Juss.	Fevers
	Melia azedarach L.	Skin care
Rhamnaceae	*Ventilago denticulata* Willd.	Wounds
	Ziziphus jujuba Mill	Stomachache
	Ziziphus nummularia (Burm. f.) Wight & Arn.	Liver tonic
Vitaceae	*Ampelocissus latifolia* (Roxb.) Planch.	Wounds
Sapindaceae	*Cardiospermum halicacabum* L.	Diarrhea
Anacardiaceae	*Mangifera indica* L.	Diarrhea
Leguminosae	*Abrus precatorius* L.	Fever
	Aeschynomene aspera L.	Stomachache
	Aeschynomene indica L.	Wounds
	Alysicarpus bupleurifolius (L.) DC.	Stomachache
	Alysicarpus tetragonolobus Edgew.	Wounds
	Butea monosperma (Lam.) Taub.	Skin care
	Cajanus platycarpus (Benth.) Maesen	Wounds
	Cajanus scarabaeoides (L.) Thouars	Wounds
	Clitoria annua J. Graham	Asthma
	Clitoria ternatea L.	Tonic
	Crotalaria albida Roth.	Tonic
	Cullen corylifolium (L.) Medik.	Skin care
	Dalbergia latifolia Roxb.	Indigestion
	Dalbergia sissoo DC.	Inflammations
	Desmodium dichotomum (Willd.) DC.	Stomachache
	Desmodium scorpiurus (Sw.) Desv.	Fever
	Indigofera trifoliata var. *duthiei* (Naik) San.	Fever
	Indigofera linifolia (L.f.) Retz.	Wounds
	Indigofera linnaei Ali	Antibacterial
	Indigofera tinctoria L.	Skin care
	Lathyrus aphaca L.	Toothache
	Pongamia pinnata (L.) Pierre	Ulcer
	Rhynchosia minima (L.) DC.	Inflammations
	Rhynchosia bracteata Baker	Inflammations
	Tephrosia pumila (Lam.) Pers.	Wounds
	Tephrosia purpurea (L.) Pers.	Fever
	Zornia gibbosa Span.	Diabetes

	Bauhinia purpurea L.	Antidiabetic
	Caesalpinia bonduc (L.) Roxb.	Inflammation
	Cassia fistula L.	Tonic
	Senna alata (L.) Roxb.	Skin care
	Senna alexandrina Mill.	Constipation
	Senna occidentalis (L.) Link	Fever
	Tamarindus indica L.	Stomachache
	Acacia leucophlaoe (Roxb.) Willd.	Wounds
	Acacia nilotica (L.) Del.ssp. indica (Ben.) Bren.	Stomachache
	Albizia amara (Roxb.) B.Boivin	Diarrhea
	Albizia lebbeck (L.) Benth.	Asthma
	Mimosa rubicaulis Lam.	Ringworms
	Pithecellobium dulce (Roxb.) Benth.	Constipation
	Prosopis cineraria (L.) Druce	Anti -bacterial
Myrtaceae	*Syzygium cumini* (L.) Skeels	Ulcers
Onagraceae	*Ludwigia octovalvis* (Jacq.) Raven	Dysentery
Cucurbitaceae	*Citrullus colocynthis* (L.) Schrad.	Indigestion
	Coccinia grandis (L.) Voigt	Asthma
	Ctenolepis garcini (L.) Clarke	Fever
	Luffa echinata Roxb.	Stomachache
	Luffa tuberosa Roxb.	Muscle pain
Apiaceae	*Centella asiatica* (L.) Urb.	Skin care
Rubiaceae	*Spermacoce articularis* L.	Jaundice
	Spermadictyon suaveolens Roxb.	Diabetes
Compositae	*Ageratum conyzoides* (L.)	Wounds
	Blumea eriantha DC.	Skin care
	Blumea fistulosa (Roxb.) Kurz	Burning sensation
	Conyza japonica (Thunb.) Less. ex Less.	Pneumonia
	Cyathocline purpurea (Buch. Ham. Don) Kun.	Swelling
	Eclipta prostrata (L.)	Skin care
	Sonchus asper (L.) Hill	Indigestion
	Sonchus brachyotus DC.	Ulcers
	Tridax procumbens (L.)	Wounds
	Xanthium strumarium L.	Ulcers
Sapotaceae	*Madhuca longifolia* var. *latifolia* (Roxb.) Chev.	Skin care
Oleaceae	*Nyctanthes arbor-tristis* L.	Skin care
Apocynaceae	*Nerium oleander* L.	Ulcers
	Tabernaemontana divericata (L.)	Headache
	Hemidesmus indicus (L.) R. Br. ex Schult.	Fever
	Calotropis gigantea (L.) Dryand.	Fever
	Calotropis procera (Aiton) Dryand.	Snake bite
	Pergularia daemia (Forssk.) Chiov.	Menstrual complaints
	Telosma cordata (Burm. f.) Merr.	Conjunctivitis
Gentianaceae	*Canscora diffusa* (Vahl)	Sexual debilities
	Enicostema axillare (Poir. ex Lam.)	Fever
	Exacum tetragonum Roxb.	Stomachache
	Exacum pedunculatum L.	Cough
	Hoppea dichotoma Willd.	Snake bite
Boraginaceae	*Bothriospermum tenellum* (Hor.) Fisch. & Mey.	Anti bacterial
	Cynoglossum zeylanicum (Vahl) Brand	Wounds
Convolvulaceae	*Argyreia bella* Raizada	Wounds

	Ipomoea hederifolia L.	Inflammations
Solanaceae	*Datura stramonium* L.	Toothache
	Physalis minima L.	Tonic
	Solanum anguivi Lam.	Ulcer
	Solanum incanum L.	Wounds
	Withania somnifera (L.) Dunal	Asthma
Acanthaceae	*Barleria cristata* L.	Snake bite
	Gantelbua urens (Hey.ex Roxb.) Bremek.	Kidney stone
	Haplanthodes tentaculatus (L.) Maj.	Colds
	Haplanthodes verticillatus (Roxb.) Maj.	Skin care
	Hemigraphis hirta (Vahl) Anderson	Inflammations
	Rungia pectinata (L.) Nees	Swelling
	Rungia repens (L.) Nees	Inflammations
	Thunbergia fragrans Roxb.	Fever
Verbenaceae	*Lantana aculeata* L.	Skin care
Lamiaceae	*Hyptis suaveolens* (L.) Poit.	Headache
	Leucas aspera (Willd.) Link	Snake bites
	Leucas biflora (Vahl) Sm.	Conjunctivitis
	Ocimum basilicum L.	Coughs
	Ocimum americanum L.	Rheumatism
Nyctaginaceae	*Boerhavia diffusa* L.	Inflammation
	Boerhavia repens L.	Skin care
Amaranthaceae	*Achyranthes aspera* L.	Menstrual disorders
	Achyranthes aspera var. *porphyristachya* (Wall. ex Moq.) Hk.f.	Abdominal pain
	Aerva lanata (L.) Juss.	Abdominal pain
	Amaranthus viridis L.	Asthma
	Celosia argentea L.	Wounds
Aristolochiaceae	*Aristolochia bracteolata* Lam.	Snake bite
Euphorbiaceae	*Acalypha indica* L.	Wounds
	Euphorbia caducifolia Haines	Skin disease
	Euphorbia chamaesyce L.	Asthma
	Euphorbia hirta L.	Fever
	Jatropha curcas L.	Skin disease
	Jatropha gossypiifolia L.	Digestive disease
Phyllanthaceae	*Phyllanthus emblica* L.	Indigestion
Moraceae	*Ficus hispida* L. f.	Ulcers
	Ficus religiosa L.	Asthma
Hypoxidaceae	*Curculigo orchioides* Gaertn.	Tonic
Asparagaceae	*Asparagus racemosus* Willd.	Tonic
Commelinaceae	*Commelina benghalensis* L.	Infertility
	Commelina diffusa Burm	Burns
Arecaceae	*Phoenix sylvestris* (L.) Roxb.	Cooling
	Borassus flabellifera L.	Gastritis disorders
Araceae	*Amorphophallus bulbifer* (Roxb.) Blume	Asthma
Cyperaceae	*Bulbostylis barbata* (Rottb.) Clarke	Stomachache
	Cyperus alopecuroides Rottb.	Skin disease
	Cyperus rotundus L.	Inflammation
	Cyperus triceps (rottb.) end.	Antidiabetic
Poaceae	*Alloteropsis cimicina* (L.) Stapf	Fever
	Andropogon pumilus Roxb.	Nerves disorders

	Apluda mutica L.	Nerves disorders
	Bambusa bambos (L.) Voss	Tonic
	Commelina benghalensis L.	Inflammation
	Cynodon barberi Rang. & Tadul.	Diarrhea
	Cynodon dactylon (L.) Pers.	Cough
	Dactyloctenium aegyptium (L.) Willd.	Wounds
	Digitaria ciliaris (Retz.) Koeler	Ulcer
	Dinebra retroflexa (Vahl) Panz.	Skin care
	Echinochloa colona (L.) Link	Constipation
	Eragrostis ciliaris (L.) R.Br.	Fever
	Heteropogon contortus (L.) Beauv	Joint pain
	Isachne globosa (Thunb.) Kuntze	Skin care
	Polytrias indica (Houtt.) Veldkam.	Inflammation
	Sorghum halepense (L.) Pers.	Stomachaches
	Tripogon jacquemontii Stapf	Wounds

5. Conclusion

The existing take a look at gives Ehnopharmacological documentation and analysis on the medicinal texa utilized by the traditional healer Bhil and Bhilala tribe of Sendhwa regency of Barwani, Madhya Pradesh, India to remedy special diseases. The goal to extract Ehnopharmacological as well as cover of a diverse range and differentiate it effectively through deep gaining knowledge of algorithms has been finished. Although the outcomes of the take a look at encourage sensible use of medicinal plants, investigations are required at the pharmacological efficacy of diverse ethno drug treatments used by them. The life depends on flora starting from meals, safe haven, clothing to medical studies. The arena health enterprise estimates that 80% human beings in developing international rely on conventional tablets derived from flora. Biodiversity has taught us that the green Planet isn't always a reservation of guy handiest due to the truth all residing beings are as high-priced to mom earth as man who's at the top of all living beings. A human is used at least 40,000 species of flora on a day-by-day basis. The medicated claims incorporated within the look at want to be evaluated via phytochemical and pharmacological investigations to discover their potentiality as capsules. The medicinal vegetation finest rate is but unknown and scientist determined best 20 % of predicted to exist and diagnosed which is costing 5 to 30 % GDP, 11 % of worldwide financial device and 26 trillion dollars.

Medicinal texa of residing being are misplaced at alarming quotes, such a lot of; in fact biologist estimates that 3 species cross extinct every 12 months. Scientist spherical the world is cataloguing and analyzing global. From wild-life factor of view, India might be very wealthy from medicinal texa issue of view; Indian forests maintain a specific characteristic inside the worldwide. In India, now not simplest wild plant life display mega-range but cultivated vegetation show immoderate variety. Those are 30000 to 50000 species of rice, one-of-a-kind meals grains, stop end result and vegetable in traditional agricultural flora determined in India. The high-quality biodiversity in those floras is decided in Western Ghats, northern Himalayas. In this place confined take a look at within the field of forestry. Similarly, just a few

information was documented on plant life of Sendhwa block. Floristic stock is used to estimate the wooded region's biophysical houses, and it is been broadly used over the last little a long term.

Acknowledgement

The authors are grateful to Bhil and Bhilala tribe of Sendhwa regency of Barwani, Madhya Pradesh, India for all sorts of cooperation. The conventional healers of Sendhwa gram panchayat additionally deserve thankful appreciation for sharing their information sooner or later of challenge work.

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Current Advancement and Future Challenges for Phytomedicines

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Chapter - 8

Phytomedicine Innovations: The Future of Plant – Based Therapies
ISBN: 978-81-977907-4-4
First Edition
Chapter – 8, Page: 117 - 132

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CURRENT ADVANCEMENT AND FUTURE CHALLENGES FOR PHYTOMEDICINES

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Abstract

Over the years, medicine derived from plants have been in demand to cure many diseases. In ancient times, drugs extracted from medicinal plants have been reliving mankind from ailments. Health professionals and scientists acknowledge therapeutic values and lesser side-effects given by the phytomedicines compared to modern medicines. Advancements in science and technology has brought in a new era for phytomedicine through the wider interdisciplinary approach, combining phytomedicine with nanotechnology, regenerative medicine, bioinformatics etc. These fields help enable much more precise, efficient and target based drug delivery for major diseases like cancer, diabetes, cardiovascular disorders, Alzheimer's and other neurogenerative diseases. Allicin from *Allium sativum,* Mangiferin from *Mangifera indica,* Carnosol, Rosemarinic acid from *Rosemarinus officinalis* etc. are a few phytochemicals extracted from plants possessing anti-inflammatory and anti-oxidant properties. In a study, it was found that curcumin in the form of silk fibroin nanoparticles showed enhanced tumour-specific toxicity in neuroblastoma cells. With the development in the field, artificial intelligence and personalized medicine will emerge as the future pillars and will shape the therapeutics for the betterment of the mankind. However, challenges shall arise in regulatory framework and socio-economic and ethical issues. This review highlights the historical influence on modern phytomedicine, current advancements and future challenges and prospects of phytomedicine and its potential to transform healthcare through plant-based therapies.

Keywords: Phytomedicine, Nanotechnology, Regenerative Medicine, Bioinformatics, Artificial Intelligence and Personalized Medicine.

1. Introduction

Plants have been an important source of medicines since years. Many pharmaceutical products have been formulated from various plant sources based on the traditional knowledge. The world is moving towards the use of herbal or phytomedicines combining the knowledge of our ancestors and modern research to strengthen the immune system of the body and destroy pathogens, with no side effects (Pandey *et al.*, 2011). The term phytomedicine dates back to 1913, given by a French physician, Henri Leclerc. Phytomedicine is a branch of plant pathology dealing with the medicines derived from herbal plants. In future, there might be challenges regarding drug potency, cost-effectiveness, drug-resistance etc. traditional phytomedicine is on a rise with new concepts and changes. Phytomedicine is closely related to phyto-pharmacology and phyto-therapy within a specific field (Kurhekar, 2020). The increased interest in this area demonstrates a larger movement toward merging traditional wisdom with modern scientific studies in order to develop more comprehensive healthcare remedies. The combination of conventional herbal medicine with contemporary scientific methods has resulted in substantial progress in the industry, providing fresh perspectives on the development of medications for the treatment of diseases.

Compared to the synthetic compounds available in the market, phytochemicals have been a major preference these days because of their low side effects. Alkaloids extracted have a wide range of biological activities including antimalarial, antibacterial, analgesic, anticancer, anti-diabetic, anti-hyperglycimic, anti-asthma etc. (Umashankar, 2020). Allicin from *Allium sativum,* Mangiferin from *Mangifera indica,* Carnosol, rosemarinic acid from *Rosemarinus officinalis* etc. are a few phytochemicals extracted from plants possessing anti-inflammatory and anti-oxidant properties. These compounds have been substantially studied for their therapeutic potential, leading to the development of numerous pharmaceutical products derived from plant sources. Nanoparticle based drug delivery system are in use because of high bioavailability and précised drug delivery at the diseased target size (Tiwari *et al.*, 2023). Regenerative medicines also uses plant secondary metabolites as medicine. Bioinformatics provides a viable route to tackling global health concerns in an era of precision medicine and sustainable healthcare practices, as well as to fully realize the therapeutic potential of medicinal plants, by fusing traditional knowledge with contemporary computational techniques. This interdisciplinary approach allows researchers to analyse complex data sets and discover new insights into plant therapeutic mechanisms.

Phytomedicines show a promising future in the field of healthcare. Human Mesenchymal stem cells, when treated with herbal extracts may provide therapies and tissue replacements for diseases like Parkinson's disease, osteoporosis, heart disease and cartilage replacement. In regenerative medicine, even as a treatment for attaching gels and scaffolds, herbal products may be used (Udalamaththa *et al.*, 2016). The uprising of Artificial Intelligence will be helpful in the field of phytomedicine. With proper training and validation, commercial Artificial Intelligence tools may offer proper performance and convenience (Daynac *et al.*, 2015). Although, phytomedicines have great potential but they have certain challenges too like regulatory hurdles and ethical issues. There are many phyto-compounds that aren't classified neither drug nor dosages. This causes safety issues, dosage standardizing issues, biopiracy of the traditional knowledge, irrational use of the drug etc. (Fokunang *et al.*, 2020; HOSSAIN *et al.*, 2022). By harnessing the therapeutic challenges of medicinal plants and addressing current challenges, phytomedicine can revolutionize healthcare by providing safe and effective treatments for a wide range of diseases. This chapter outlines the future prospects and hurdles in establishing phytomedicine as a mainstream component of global healthcare.

2. Historical Evolution

Phytomedicine has played a vital part in the healthcare of human civilisation for years now. History suggests that plants have been used for medical reasons all over the world. The evolution of phytomedicine, from ancient writings and oral traditions to modern scientific study, illustrates a captivating transition from traditional practices to contemporary medicinal uses.

2.1. Traditional Phytomedicine

Pre-historic findings and ancient texts also has evidence of uses of herbal plants as medicine. Early humans used plants for their medicinal properties more than they used them as food. This knowledge has been passed from generation to generation giving rise to traditional medicine system. In Nagpur, India, an old written manuscript was found referring to the usage of herbal plants in the preparation of medicines imprinted on a Sumerian clay slab. In this book, there has been a mention of around 12 drug preparation using 250 varieties of plant has been mentioned (Kurhekar, 2020). Folk medicine is an ancient medical profession which has primarily focussed on therapeutic and preventive characteristics of crude drugs, which developed gradually over generations from sources like early people involved with herbal medicines, Ayurveda, and other scripts written on temples, monuments, caves, scriptures decoded by scholars over a period of time (Kurhekar, 2020). One of the examples of traditional

folk medicine is shilajit. Traditional Indian knowledge suggests that shilajit functions as a laxative, diuretic, anti-bilious agent, tonic, immuno-modulator, expectorant, lithotriptic, and anti-hypertensive when administered internally, while exhibiting antiseptic, analgesic, deobstruent, and germicidal properties when applied externally. To control diabetes, shilajit is administered alongside milk, and to treat fractures, shilajit is prescribed with *Commiphora wightii* (Arn.) Bhand. (guggulu) to promote callus formation (Wilson *et al.*, 2011).

Mishing community followed traditional healing and folk practice. Powdered bark of Bagouri (*Zizyphus maurtiana*) is taken with warm water to treat stomach ache. Leaf juice extracted from Bhang (*Cannabis sativa L.*) is taken orally to treat loose motion. Paste prepared from the leaf from (*Chromelaena adorata L.*) is applied to cut areas to prevent clotting of blood (Shankar *et al.*, 2012). These examples highlight on the rich history of phytomedicine and its relevance to healthcare and research.

2.2. Transition to Modern Phytomedicine

The transition to modern phytomedicine from traditional phytomedicine shows a great evolution in the plant-based therapeutics. This transition occurred due to advancements in analytical techniques, knowledge and growing interests in this field. Traditional phytomedicine depended on the knowledge passed down from generations, while using the whole plant or complex formulas. While, modern phytomedicine depends on advanced techniques based on isolation, identification and characterization of the bioactive compounds extracted from the plant making it more precised therapeutic treatment. A few examples of extracted compounds from Chinese herbal medicines on the traditional basis are, Artemisinin from *Artemisia annua* L. for anti-malarial property, Puerarin from *Pueraria lobata* for diabetic property, Romidepsin from *Chromobacterium volaceum* for its Anti-tumor property etc (Zhong *et al.*, 2014). According to a study, an aqueous extract of Coriander (*Coriandrum sativum*) at 100 mg/kg showed anxiolytic effect in mice (Mahendra and Bisht, 2011). This has resulted in enhanced scientific rigor in phytomedicine, with randomized controlled trials and pharmacological research now common practice.

3. Current Advances in Phytomedicine

Recent advancements in the field of phytomedicine includes nanotechnology for improved drug delivery, regenerative medicine using bioactive compounds extracted from plants and bioinformatics for easy and fast drug discovery. Phytomedicine shows promise in tissue generation, targeted drug-delivery, precision medicine, ligand-receptor interaction, finding treatments for diseases like diabetes, cancer, cardiovascular diseases, neurodegenerative diseases etc.

3.1. Nanotechnology in Phytomedicine

Nanotechnology has been a powerful tool in the field of phytomedicine. Combination of nanotechnology and plant-based extracted drugs, "nano-phytomedicine" may help overcome the challenges associated with conventional herbal medicines. One of the major benefits of nanoformulations is that it can improve the bioavailability of the phytochemicals and enhance its efficacy. Nanocarriers like liposome, phytosome, nanosphere, dendrimers and polymeric micelles encapsulate phytochemicals to increase their stability and solubility. Other benefit can be targeted and controlled release of the drugs (Tiwari *et al.*, 2023). Few of the nanotechnology-based plant-derived medicines are mentioned in Table - 1.

Table - 1: Nanoformulations from Plant-derivatives

Phytochemical	Plant	Nanocarrier	Function	Reference
Curcumin	*Curcuma longa*	Liposome	Anti-cancer Anti-inflammatory	Jalili *et al*. (2023)
		Phytosome	Anti-inflammation Anti-anxiety	
		Solid nano particles	CNS disease Anti-cancer Hodgkin's lymphoma Anti-oxidant	
		Nanosphere	Anti-cancer	
		Nanocapsule	Neuroprotective Anti-malarial	
		Dendrimer	Anti-cancer	
		Polymeric micelles	Anti-bacterial	
Naringin	Rutaceae plant	Chitosan nanoparticle	Bone regeneration	Nath *et al*. (2024)
Baicalin	*Scutellaria baicalensis* Georgi	PEGylated nanostructured lipid carriers	Anti-hypertensive	Chooi *et al*. (2022)
Ginkgo	*Ginkgo biloba*	Phytosome	Brain and vascular protection	Alharbi *et al*. (2021)
Roscugenin	*Ruscus aculeatus*	Phytosome	Anti-inflammatory	Alharbi *et al*. (2021)

3.2. Regenerative medicine and Phytomedicine

To replace or restore damaged organs or tissues, mesenchymal stem cells and tissue engineering is used but it is quite expensive and not that effective. There is a constant increase in the demand for safer and enhanced options to promote tissue engineering and cartilage joint repair in osteoarthritis. More than seventy thousand species of plants have been examined to check their therapeutic potential, inspired from the traditional plant-based medicines (Akhileshwar Jha *et al.*, 2024).

A great potential has been shown by herbal products in the differentiation and proliferation of human mesenchymal stem cells according to various studies. These herbal extracts are originated from Chinese folk medicine, Indian Ayurvedic medicine, and other traditional folk medicines. The antioxidant properties of *Tithonia diversifolia*, helps in treating the reduced antioxidant levels in obesity, leading to elevated adipogenesis (Joujeh and Joujeh, 2024). Few of the potential phytochemicals that affect stem cell activity are mentioned in Table - 2.

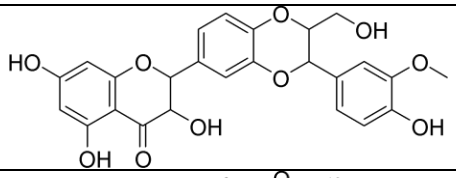
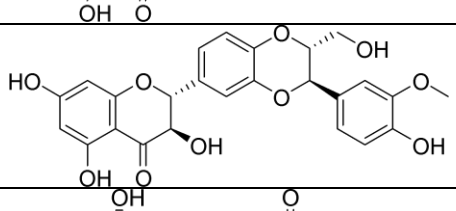
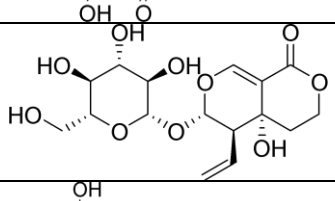
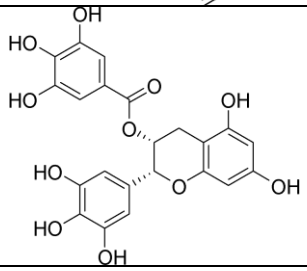
Table - 2: Potential Phytochemical that affect Stem cell activity

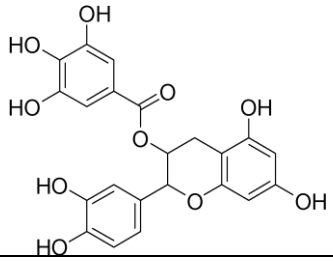
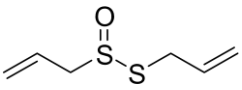
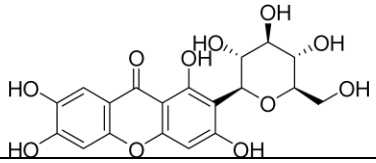
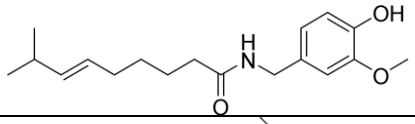
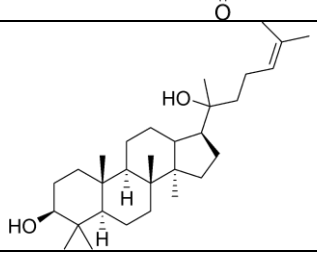
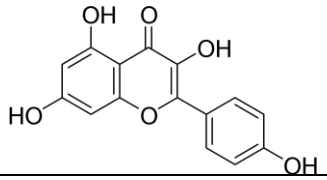
Phytochemicals	Plant	Stem cell type	Function	Reference
Curcumin	*Curcuma longa*	Bone marrow stem cell, mesenchymal stem cell, neural stem cell	Articular chondrocytes proliferation, Promote neurogenesis	Nath *et al*. (2023)
Epigallocatechin-3-gallate	*Camellia sinensis*	Bone marrow stem cell, neural stem cell	Promotes neurogenesis, Osteogenic differentiation, Osteoblastogenic differentiation	Nath *et al*. (2023)
Silibinin	*Silybum marianum*	Human bone marrow stem cell	Osteoblast differentiation	Dadashpour *et al*. (2017)
Icariin	*Epimedium brevicornum*	Rat bone marrow stem cell, Mouse bone marrow stem cell	Self-renewal	Dadashpour *et al*. (2017)
Naringin	Rutaceae plant	Bone marrow stem cell	Bone regeneration	Nath *et al*. (2024)
Acemannan	*Aloe vera*	Bone marrow stem cell	Bone regeneration	Boonyagul *et al*. (2014)
Berbeine	*Coptidis rhizome*	Bone marrow stem cell	Restores downregulation of the osteogenic gene expression and increases it as well as transcriptional activity	Sharifi *et al*. (2020)
Gastrodin	*Gastrodia elata, Galeola faberi*	Bone marrow stem cell	Prevents migration and maturation of osteoclast, prevents osteoclast formation and bone resorption	Sharifi *et al*. (2020)
Moringin	*Moringa oleifera*	Periodontal ligament stem cell	Bone regeneration, regulate osteogenic gene expression	Sharifi *et al*. (2020)

3.3. Bioinformatics and Computational Modelling

Bioinformatics is a combination of information technology, biology, computational algorithms, computer science and data integration to analyse data, interpret molecular mechanisms and speed up the process of drug discovery. In the recent years, bioinformatics has been an emerging field and has been offering a great outline for the study of herbal plants, providing tools and methods to learn about their complexity and utilize their therapeutic potential (Yoram Vodovotz *et al*, 2017). Bioinformatics opens up wide variety of approaches for identification and classification of herbal plants like DNA barcoding, Molecular phylogenetic, machine learning and pattern recognition, metabarcoding and metagenomics and database resources and repositories. Omic technologies like genomics, transpictomics, proteomics, metabolomics, pharmacogenomics and system biology provide understanding of the mechanisms for synthesis, interactions and therapeutic potential of the bioactive compounds extracted from the herbal plants (Zhang and Wang, 2023). Few phytochemical drugs available commercially and their medicinal properties are mentioned in Table - 3.

Table - 3: Phytochemical Drugs available Commercially and their Medicinal Properties (Hirakani *et al*., 2023)

Compounds	Structures	Plant	Medicinal properties
Silymarin		*Silybum marianum*	Type-2 diabetes Hepatoprotection Anti-oxidant
Silybin		*Silybum marianum*	Type-2 diabetes Hepatoprotection Anti-oxidant
Swertiamarin		*Enicostemma littorale*	Anti-cancer Anti-diabetic Anti-oxidant Anti-inflammatory
Epigallocatechin gallate		*Camellia sinensis L.*	Anti-oxidant Anti-cancer

Epicatechin gallate		*Camellia sinensis L.*	Anti-oxidant Anti-cancer
Allicin		*Allium sativum*	Anti-diabetic Anti-inflammatory Ant-microbial
Mangiferin		*Mangifera indica*	Anti-oxidant Anti-inflammatory Anti-cancer Anti-microbial
Capsaicin		*Capsicum frutescens*	Anti-cancer Anti-inflammatory
Ginsenosides		*Ginseng*	Anti-cancer Anti-inflammatory Anti-oxidant Anti-diabetic
Kaempferol		*Alium sepa*	Anti-oxidant Anti-inflammatory Anti-cancer Anti-obesity

4. Therapeutic Case Studies

The use of plant-based compounds for therapeutic applications has encouraged outcomes in a variety of clinical settings. Below are a few case studies demonstrating the therapeutic potential of phytomedicines in treating various health conditions in Table - 4:

Table - 4: Case studies for different Disease and Phytomedicine used

Disease	Phytomedicine	Key Finding	Reference
Alzheimer's disease	*Ginkgo biloba* extract	Improvement in cognitive function and routine activities with patients with mild Alzheimer's disease	Tan *et al.* (2015)
Type 2 diabetes	Berberine	Decreasing level in hbA1c levels, fasting blood sugar and postprandial blood glucose	Lan *et al.* (2015)
Osteoarthritis	*Boswellia serrate* extract	This extract reduces pain and enhanced physical function in knew of patients with osteoarthritis	Sengupta *et al.* (2008)
Prostate cancer	Green tea catechins	Due to advanced prostatic intraepithelial neoplasia	Bettuzzi *et al.* (2006)
Anxiety	Lavender oil (Silexan)	Decrease in the anxiety symptoms	Woelk and Schläfke (2010)
Irritable bowel syndrome	Peppermint oil	Improved symptoms and abdominal pain	Cash *et al.* (2016)
Chronic Fatigue syndrome	*Rhodiola rosea*	Reduced fatigue symptoms and enhanced cognitive function	Lekomtseva *et al.* (2017)
Migraine	Butterbur (*Petasites hybridus*)	Less migraine attacks	Lipton *et al.* (2004)
Ulcerative colitis	*Andrographis paniculata* extract	Improved clinical symptoms and compared to placebo, relapse rates were reduced	Tang *et al.* (2011)
Diabetic Neuropathy	Capsaicin	Reduction in pain intensity and life quality is improved for patients	Anand and Bley (2011)

These drugs exhibit diverse applications and effectiveness of herbal drugs for therapeutic treatment of various diseases. Yet, it is essential to note that even though these studies show positive results, large and long-term clinical trials are required to demonstrate the effectivity and safety of phytomedicines.

5. Future Prospects and Challenges

Phytomedicine has a great future aspect which includes personalized medicine, artificial intelligence, advanced drug delivery systems etc. Despite, the prospects this field faces certain challenges like regulatory hurdles, standardizing and stability of the drug, biopiracy etc. Safe and broadly accepted plant-based therapeutics in healthcare can be achieved by overcoming the challenges.

5.1. Artificial Intelligence

Artificial Intelligence, includes algorithms and computer systems to perform tasks using human intelligence for problems like problem-solving, decision making and pattern recognition. Artificial Intelligence has the potential to change many aspects like diagnosis, treatment plan for patient engaging and management making it a very powerful too (Ng *et al.*, 2024).

Artificial intelligence technologies like machine learning and natural language processing have demonstrated medical image analysis, predictive modelling and chatbots for interacting with the patients. Innovations like this have the potential to reduce errors in diagnosis, improve treatment outcomes, and improve the experience of the patients. However, as AI continues to develop, it is necessary to examine its role in supporting the principles of traditional, complementary and integrative medicine, which focuses on individual care and a holistic view of health (Ng *et al.*, 2024).

Incorporating Artificial Intelligence into traditional, complementary and integrative medicine is a unique opportunity, but it also presents a variety of unique challenges that must be considered. For example, due to the nature of empirical studies, many scientists doubt whether Artificial Intelligence algorithms can always provide the right answers. These, among other challenges, are linked to the principles of traditional, complementary and integrative medicine, and should not be left out (Ng *et al.*, 2024).

5.2. Personalized Medicine

Precision medicine is an emerging field in healthcare that aims to provide treatment suitable to person's molecular, genetic and clinical makeup. It can help enhance the prognosis, diagnosis, prevention and treatment for many diseases like cancer, diabetes, arthritis, autoimmune disorders, allergies and atherosclerosis. These problems, characterized by complex and different manifestations, include problems in the immune system, its main defence mechanism against external threats and different cellular functions. Precision based medicine can help distinguish

what triggers and how are the diseases related to resistance and find a way to prepare treatment strategies for each individual patient (Pillai and Antony, 2024).

One of the most potential application of Precision-based medicine is personalized medicine in immune-related disorders. As a source of personalized immunotherapy, natural products can be used for targeting genes, proteins and pathways engrossed in regulation of immunity and induce specific immune responses to death. This will play an important role in personalized immunotherapy, which provides a variety of compounds and medicinal products can help fight the diseases associated with the immunity. For example, Epigallatocatchin gallate from green tea inhibits certain immune checkpoint molecules, providing therapeutic benefits in cancer treatment (Pillai and Antony, 2024).

Natural products can also be used in the form of adjuvants, nutritional supplements, or delivery systems to improve the effectivity and safety of immunotherapy. It can increase the effectivity of immunotherapy when used in the form of adjunct or in combination with traditional treatments. Compounds such as quercetin, found in fruits and vegetables, show enhanced efficacy of immunotherapy by sensitizing cancer cells to destruction caused by immunity. Many natural products show low toxicity when compared to synthetic drugs, which make them potential candidates for immunotherapy. For example, compounds such as apigenin, found in parsley and chamomile, show good anti-inflammatory and immunomodulatory effects with minimal side effects (Pillai and Antony, 2024). Although, the combination of natural products with genomic insights have great promises for innovative drug discovery and advanced personalized medicines but still, it faces many challenges.

5.3. Challenges in the field of Phytomedicine

Phytomedicine has received major attention in the past years because of its potential to treat various diseases with natural and low side-effects. But, even this emerging field faces challenges.

a) *Formulation Development:* The application of western pharmaceuticals with traditional medicines shows diverse set of limitations. Formulation development is vital in research to formulate methods and on the basis of medical philosophies and practices to support the use of traditional folk medicine (HOSSAIN *et al.*, 2022).
b) *Stability of the Herbal Drug:* To control the product's Quality-Safety-Environment stability test is necessary. To check these parameters, it is difficult for manufactured drugs compared to the herbal medicines. Yet, difference in

the raw materials' biochemical properties, enzyme presence, chemical complexity and appropriate marker selection makes the testing challenging (Hossain *et al.*, 2022).

c) *Insufficient Regulatory Guidance:* For quality issues, agricultural, collection and storage practices, regulatory guidelines are insufficient in the herbal medicine industry. Most manufacturers are unaware of the 2009 GACP guidelines same as WHO. An elaborate explanation of the guidelines supported by herbal firms (Prabhakar and Mamoni, 2021).

d) *Quality Control and Assurance:* Quality control and quality assurance is a necessary department for every country that aims to regulate herbal drugs like for standardization and specifications national quality, for labelling, manufacturing, imports and marketing GMP (Hossain *et al.*, 2022).

e) *Biopiracy:* Conservation of traditional knowledge passed on from generations in every culture is necessary for development and biopiracy is a chief barrier in the field of phytomedicine (HOSSAIN *et al.*, 2022).

6. Conclusion

From ancient beginnings to modern uses, history proves that mankind has been constantly dependent on nature for well-being and treatment. All the ancient practices like Traditional Folk Medicine, Ayurveda have used plant-based therapies since years, and focus on health of whole-body. Combining modern techniques like nanotechnology, regenerative medicine, and bioinformatics has been bringing changes in the administration of plant-based ailments, their effectivity and precision, and thus creating new medicines from the bioactive compounds. The combination of the traditional medicine with modern technologies in phytomedicine, can provide a number of medicinal values and can be helpful to treat complex diseases like diabetes, cancer, Alzheimer's, and other neurodegenerative diseases. Technological advances like nanotechnology and artificial intelligence have been showing a tremendous improvement in the field of phytomedicine. Although, phytomedicine has a promising future, it faces challenges like consistency in quality, regulatory issues, ethical concerns, socio-economic conundrums, clinical validations etc. To maximize the potential of herbal medicines in global healthcare, these challenges are essential to address. Phytomedicine has the potential to revolutionize healthcare whilst respecting the cultural roots of herbal practices by combining traditional practices with modern advances. As research continues to reveal the therapeutic potential of plants, phytomedicine plays a critical role in tackling challenges like global health and therapeutic potential for patients in the upcoming years.

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Anacardium occidental (Cashew) as Phytomedicine

Chapter - 9

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Phytomedicine Innovations: The Future of Plant – Based Therapies
ISBN: 978-81-977907-4-4
First Edition
Chapter – 9, Page: 133 - 140

9

Anacardium occidental (CASHEW) AS PHYTOMEDICINE

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Abstract

The primary benefit of using plant derived medicine is that they are relatively safer than synthetic alternatives, offering profound therapeutic benefits and more affordable treatments. The search for better alternative anti-inflammatory and antimicrobial drugs from the bounties of our vegetation is thus a worthwhile venture. Cashew (*Anacardium occidentale*), is a evergreen shrub or tree of the family *(*Anacardiaceae*)*, cultivated for its characteristically curved edible seeds, which are commonly called cashew "nuts". This plant is a multipurpose tree whose leaves, stems and bark extracts are extensively used for the treatment of diarrhea, dysentery and Colonic pain. It has also been reported that, *Anacardium occidentale* possess antidiabetic, anti-inflammatory, antimicrobial, and anti-ulcerogenic properties. A number of secondary metabolites are present in its leaves, fruits, and other parts of the plant. Among the diverse Anacardium plants' bioactive effects, their antioxidant, antimicrobial, and anticancer activities comprise those that have gained more attention. Thus, the present article aims to review the Anacardium plants' biological effects. A special emphasis is also given to their pharmacological and clinical efficacy, which may trigger further studies on their therapeutic properties with clinical trials.

Keywords: *Anacardium occidentale,* Antimicrobial activity, Phytomedicine, Antioxidant activity and Antimicrobial activity.

1. Introduction

Cashew is an evergreen perennial plant belonging to the family Anacardiaceae. This family consists of 400-600 species. Among the eight species in the genus Anacardium, the only cashew is valuable due to its nutritious kernel. Cashew is a tropical tree present in South America and Brazil. Plant height varies from 5 to 14 m. The trunk is usually short and irregular, starting branches close to the ground. Leaves are green that are placed in a spiral pattern towards the end of the stem. Leaves become mature after 20-25 days. Flowering can occur at any time; individual flowers are short in size consisting of five yellowish-green sepals and five white to reddish petals. In 2011, about 4.7million tons of raw nuts were produced worldwide, which were distributed between Asia and Africa, where 1.8 million cashew apples were produced (Allen *et al.,*1977).

Cashew has been cultured essentially, and whole fruit is used for medicinal and food purposes, The Cashew nut has nutritious properties with a pleasant flavor. Cashew kernels have shown low density lipoprotein cholesterol levels and coronary risk diseases. Cashew part contains proteins and fats. The proteins include lysine, cysteine, arginine tyrosine, valine, and many vitamins like vitamin C, E, D (Cordeiro *et al.,*2003).

Anacardium occidentale, is one of the most commonly used herbs in the management of diarrhea in African Traditional Medicine, especially in Nigeria. Studies have reported the antidiarrheal properties of various parts of this plant, including the leaves, the gum, the stem bark and the kernel. The bark decoction is particularly used in the folkloric management of severe diarrhea. Although studies have revealed the potential of Ao stem bark extract as an alternative herbal remedy against diarrhea (Araujo *et al.,* 2015).

Cashew gum has been used widely for many health-related issues. These are less in saturated fatty acids and more in unsaturated fatty acids. Its health benefits have been used to decrease the risk of cardiovascular diseases, oxidative stress, inflammation, high cholesterol, and diabetes. Cashew nuts are used for several medicinal purposes and have great importance related to health, as evidenced by research. These are used for obesity, diabetes, heart disease, urinary disorders, digestive disorders, and many other clinical applications like bone relaxation, cold and flow, etc. It also has importance in Cancer, and protects from aging (Bes-Rastrollo *et al.,* 2003).

Cashew part that is less in soaked fat and more in monounsaturated fat lessens the general degrees of cholesterol and Low-density lipoproteins (LDL) - the claimed "bad cholesterol" that prompts coronary disease and builds High-density lipoproteins (HDL), hence assisting in making the heart more sound. The Cashew part contains fiber, carrying more fiber into the diet brings down the level of cholesterol and the danger of heart disease prominently, which is known as heart nibble. The fiber in the digestive tract lessens the assimilation of cholesterol from food consumption. Ordinary use of these nuts, as a feature of a low-soaked fat eating routine, can bring down the danger of coronary disease overall by advantageously influencing the cholesterol levels in blood and can reduce the risk of having a subsequent respiratory & cardiovascular failure (Cordeiro *et al.,*2014).

Daily utilization of food that is rapidly increasing the sugar level in the blood leads to developing heart diseases and diabetes as Cashew nuts contain high mono saturated fat that is beneficial for decreasing the blood glucose level and increase insulin production. Thus, diabetes can be managed by cashew pieces. They are essential for type 2 diabetes. They are lower in sugar and higher in fiber; when these factors are combined, they decreased the blood glucose level and prevent the development of type 2 diabetes (Dendena *et al.,*2014).

Selenium - rich cashew bits are helpful for lung, liver, skin, cerebrum, and gastrointestinal malignancy. Due to significant fiber content likewise assists with fighting malignancy. They act as an antioxidant and prevent the growth of cancer cells by removing the free radicals from the body. A class of flavonoids called Proanthocyanidins fight tumor cells and prevents them from further division. High copper content and proanthocyanidins in cashew nut fight copper content in cashew helping to prevent colon cancer (Fraser, 1994).

Sodium and Potassium is an essential element to protect the human renal system. As cashew contains sodium and potassium, it can be used to treat dehydration and essential minerals, which are suitable for the kidneys. 28.35gm of cashew portion gives 0.00015kg of potassium (Karthick *et al.,* 2018). Apart from the benefits of anacardium nuts, in-depth analysis of the literature highlights, leaf extract of Anacardium occidentale too. Research consistently demonstrates the antibacterial potential of Anacardium occidentale leaf extracts against various pathogens, including *Porphyromonas gingivalis, P. intermedia, Streptococcus mutans, Staphylococcus aureus, Escherichia coli,* and *Enterococcus faecalis*. A significant contribution of the study titled " Evaluation of Antibacterial Effects of Different Leaf Extracts of *Anacardium occidentale* (Cashew) Using Distilled Water and n-Hexane as Extracting Solvents " is its specific focus on the extraction methods and solvents utilized. By assessing the antibacterial

effects of n-hexane and aqueous leaf extracts, this research offers valuable insights into the effectiveness of different extraction techniques in harnessing the antibacterial properties of *Anacardium occidentale* (Cashew) leaves. This study sheds light on the comparative efficacy of two distinct extraction solvents, distilled water and n-hexane, providing crucial information for optimizing the extraction process to maximize the antibacterial potential of Cashew leaf extracts. Such insights are instrumental in guiding future research endeavours aimed at utilizing natural plant sources for developing antibacterial agents with potential applications in medicine, agriculture, and other relevant fields (Shobha *et al.,*2018).

In Brazil, the leaves of *Anacardium occidentale* are utilized for treating eczema, psoriasis, dyspepsia, scrofula, cough, bronchitis, intestinal colic, leishmaniasis, syphilis-related skin disorders, impotence, genital and venereal diseases. Its nut shell oil has anti-diabetic, analgesic and anti-inflammatory effects, and improves healing action on sore of leprosy (Aiswarya *et al.,*2011). The leaf of *Anacardium occidentale* was extracted with methanol and consecutively fractionated using hexane, ethyl acetate, butanol, and water. The methanol extract and fractions were quantitatively screened for phytochemical constituents and tested against selected microorganisms using standard procedures. Acute toxicity tests of the ethyl acetate and aqueous fractions were done on Wistar rats. The kidneys and livers of the rats were histologically examined. *Anacardium occidentale* methanol extract had the highest amount of phenolics (98.30 ± 0.15 gallic acid equivalent (GAE)/g) while the ethyl acetate fraction had the highest amount of anthraquinones and cardiac glycosides. The butanol fraction had highest saponin and tannin contents, while the aqueous fraction had highest steroids, terpenoids and carotenoids contents. The inhibitory activity of the ethyl acetate fraction against *Staphylococcus aureus, Bacillus cereus, Serratia marcescens, Klebsiella pneumoniae, Proteus vulgaris* and *Pseudomonas aeruginosa* ranged from 15.0 mm to 19.0 mm inhibitory zone diameter at 100 mg/mL. The ethyl acetate and aqueous fractions were not toxic to the rats at 2,900 mg/kg dose. Consequently, *Anacardium occidentale*, leaf extracts were rich in phytochemicals, had antimicrobial activity and safe for use.

The pharmacological applications of alkaloids are many including; antimalarials, anesthetics, analgesics and CNS stimulants. Although some plants containing alkaloids do not feature strongly in herbal medicine, because they are extremely toxic. However, they have always been important in homoepathy where the dose-rate is so low making them harmless and in allopathic systems where the dose is also strictly controlled. *Anacardium occidentale* leaf powder had the highest alkaloid content, followed by the methanol extract, aqueous fraction, ethyl acetate fraction, and hexane fraction, while the least alkaloids content was observed in the butanol fraction.

Interestingly, phenols have gained considerable attention as protecting factors against cancer and heart diseases because of their antioxidant potency. Phenolics was highest in the methanol extract of *Anacardium occidentale* followed by butanol fraction, hexane fraction, ethyl acetate fraction, and aqueous fraction but the leaf powder had the least phenolic content (Gordana *et al.,* 2007).

2. Antibacterial Properties

In antibacterial property of medicinal plants from Nigeria, *Anacardium occidentale* hydroethanolic extracts (leaf/bark) showed positive effects against *Escherichia coli, Staphylococcus aureus, Enterobacter species, Streptococcus pneumoniae, Corynebacterium pyogenes, Enterococcus faecalis*, multi resistant *S. aureus, Acinetobacter* species, *Pseudomonas aeruginosa*, and multi resistant *P. aeruginosa* during cavity diffusion tests with inhibition halos varying from 6 to 14 mm (Kudi *et al.,*1999).

Tyrosinase is a key component of the enzyme polyphenol oxidase, which plays an important role in the melanogenesis and enzymatic browning. Therefore, tyrosinase inhibitors can be attractive in cosmetical industries as depigmentation compounds, as well as in food industries as antibrowning agents. Phenolic and triterpenoid compounds obtained from plants are widely reported as tyrosinase inhibitors. For instance, phenolic compounds and other phytochemicals in the extracts of *Anacardium occidentale* fruits have been demonstrated to be effective in inhibiting the enzymatic capacity of tyrosinase (Araújo *et al.,* 2015).

Anacardium occidentale have been shown to have antidiabetic, antibacterial, anti-inflammatory, and antiulcerogenic properties. Ethanolic extracts of *Anacardium occidentale* stem bark and flowers contain flavones, phenolic compounds, triterpenes, xanthones, anacardic acids (AA) (e.g., 6-pentadecyl salicylic acid) and gallic acid. The antidiabetic potential of A. occidentale is also being explored using computational approaches. According to a ligand-based prediction model, 8 different hit compounds from the plant (kaempferol 3-O-β-D-Xyloside, myricetin, quercetin-3-O- β-Darabinofuranoside, delphinidin, gallic acid, quercetin-3-O-D-galactopyranoside, (+) catechin, protocatechuic acid, epigallocatechin, naringenin and (−) epicatechin) have potential action against glutamine-fructose-6-phosphate aminotransferase 1 (GFAT1) and dipeptidyl peptidase-4 (DPP-4), two promising therapeutic targets for DM management (Ukwenya *et al.,* 2021).

Repeated trauma, inadequate perfusion or oxygenation, excessive inflammation, infection, oxidative stress, and diabetes all contribute to impaired wound healing. In a clinical setting, delay in healing may result in severe complications such as gangrene, leading to extended hospitalization, amputation and even death of the patient. Slow wound healing and limitations of currently available synthetic medication, urges the need for a safe, affordable, patient-friendly, and multi-modal herbal wound care agent. *Anacardium occidentale* is reported to possess antidiabetic, antibacterial, antioxidant, anti-inflammatory and antiulcerogenic activities. The wound healing activity of gel containing the extract of *Anacardium occidentale* leaves in rats using incision, excision and dead space wound models. Increased wound contraction, breaking strength, hydroxyproline and hexosamine content, TGF-β level and decreased level of TNF-α indicated that the developed gel accelerated the wound healing process. Moreover, the docking studies indicated that the aqueous alcoholic extract exerted healing activity by inhibiting GSK3-β through β-catenin dependent Wnt signaling pathway. Thus, the *Anacardium occidentale* leaves extract can be a potential wound healing agent by acting on various phases of healing process. (Nehete *et al.,* 2018).

Anacardic acid (AA) is a bioactive phytochemical found in nutshell of *Anacardium occidentale*. Chemically, it is a mixture of several closely related organic compounds, each consisting of salicylic acid substituted with an alkyl chain. The traditional Ayurveda depicts nutshell oil as a medicinal remedy for alexeritic, amebicidal, gingivitis, malaria and syphilitic ulcers. However, the enduring research and emerging evidence suggests that AA could be a potent target molecule with bactericide, fungicide, insecticide, anti-termite and molluscicide properties and as a therapeutic agent in the treatment of the most serious pathophysiological disorders like cancer, oxidative damage, inflammation and obesity. Furthermore, AA was found to be a common inhibitor of several clinically targeted enzymes such as NFκB kinase, histone acetyltransferase (HATs), lipoxygenase (LOX-1), xanthine oxidase, tyrosinase and ureases (Newman *et al.,* 2000).

Anacardic acid with varied chain length induced cytotoxicity towards several human cancer cell lines in vitro. AA (C12:0) and (C15:1) exhibited nearly comparative cytotoxicity, suggesting the non-essentiality of unsaturation in the hydrophobic side chain. However, AA (C15:0) exhibited slightly more potent cytotoxicity with an IC50 of 0.008 mM than (C12:1) (fig. 1M). Indeed, AA (C15:0) had the higher molecular volume (Vm) of 341 cm3/mol than AA (C12:1), which had the Vm of 298 cm3/mol. Therefore, the molecular volume of the hydrophobic side chain is one of the main determinants of cytotoxicity. The anti-cancer activity exhibited by AAs could

be due to their ability to act as surfactants, although the possibility of chelating the essential metals cannot be denied. Further, studies need to be undertaken for a comprehensive perspective on the involvement of surfactant and chelating properties of AA and its derivatives in the induction cytotoxicity (Kubo *et al.,* 2006).

3. Conclusion

Anacardium occidentale plants have extensively been largely reported for its antioxidant, anti-inflammatory, anticancer, and antimicrobial effects. A number of *in vitro* studies have been reported with promising results. On the other hand, the anticancer potential of *Anacardium occidentale* secondary metabolites is also quite prominent. Thus, *Anacardium occidentale* plants should be further studied to better elucidate their therapeutic potential not only in the *in vitro* and *in vivo* studies, but also the clinical application.

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Innovation in Herbal Formulation

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Chapter - 10

Phytomedicine Innovations: The Future of Plant – Based Therapies
ISBN: 978-81-977907-4-4
First Edition
Chapter – 10, Page: 141 - 162

10

INNOVATION IN HERBAL FORMULATION

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Abstract

The rising global demand for natural health solutions has intensified interest in innovative herbal formulations, blending traditional knowledge with modern scientific approaches. This research explores the integration of biodiversity and phytochemistry to enhance the therapeutic potential of herbal products. Key methodologies, including advanced extraction techniques and bioactivity assessments, are examined to optimize the efficacy and safety of these formulations. Recent technological advancements, such as nanotechnology and biotechnology, have facilitated the development of novel delivery systems, improving the bioavailability of active compounds in herbs. This has led to the creation of synergistic formulations that combine multiple plant extracts to maximize health benefits. The importance of clinical trials is also emphasized, as they validate the efficacy of these innovations, bridging the gap between traditional practices and evidence-based medicine. By aligning innovation with sustainability, the herbal formulation industry can contribute to global health while minimizing environmental impact. The findings suggest that innovative herbal formulations can effectively address contemporary health challenges, including chronic diseases and rising resistance to synthetic drugs. As consumer preferences shift towards natural products, the research advocates for collaboration among herbalists, scientists, and regulatory bodies to establish standards ensuring quality and safety. This chapter highlights the potential of innovative herbal formulations, demonstrating how the synergy of tradition and modernity can lead to effective, sustainable health solutions that meet the needs of today's consumers.

Keywords: Herbal formulation, Innovation, Traditional medicine, Modern medicine and Ayurveda.

1. Introduction

The global resurgence of interest in natural and sustainable health solutions has placed herbal formulations at the forefront of contemporary medicine. Rooted in centuries of traditional use, these plant-based remedies are now undergoing a significant transformation driven by modern scientific advancements (Smith, 2020). The journey from traditional herbal practices to scientifically validated products highlight the evolution of herbal medicine, reflecting both a deep respect for ancient knowledge and a commitment to innovation (Jones and Brown, 2018).

Historically, herbal medicines have been the cornerstone of healthcare systems across the world. From the complex Ayurvedic formulations of India to the meticulously documented herbal compendiums of Traditional Chinese Medicine (TCM) (Lee, 2017), plants have played a central role in healing practices for thousands of years. These systems, based on empirical knowledge passed down through generations, laid the foundation for modern herbal medicine (Chen and Wang, 2016). However, as society progressed and scientific rigor became paramount, the need to validate these traditional remedies through systematic research became increasingly evident (Patel, 2019).

The modern era of herbal formulations began with the integration of traditional knowledge with contemporary scientific methods (Taylor, 2015). This convergence has led to a deeper understanding of the therapeutic potential of plants, resulting in the identification and isolation of active compounds that can be standardized and formulated into effective medicines (Anderson, 2021). Advances in technology have further facilitated this transformation, enabling the extraction, purification, and analysis of herbal compounds with unprecedented precision (Garcia, 2018).

One of the most significant challenges in the development of herbal formulations has been the variability in the composition of plant materials due to factors such as geographical location, cultivation practices, and harvesting techniques (Miller and Davis, 2017). To address this, innovative extraction and standardization techniques have been developed, ensuring that the active constituents in herbal formulations are consistent and reproducible (Johnson, 2020). These advancements have not only enhanced the efficacy of herbal products but also bolstered consumer confidence and regulatory acceptance (Williams, 2019).

Another critical area of innovation is the development of novel delivery systems for herbal formulations. Traditional methods of consumption, such as teas, tinctures, and powders, often suffer from limitations related to bioavailability and stability

(Kumar *et al.*, 2016). Modern pharmaceutical sciences have introduced advanced delivery systems such as nanoparticles, liposomes, and transdermal patches, which enhance the absorption and efficacy of herbal actives (Singh and Gupta, 2018). These innovations have opened new avenues for the application of herbal medicine, making it more effective and accessible to a broader population (Zhang, 2020).

The commercialization of herbal formulations also presents unique challenges, particularly in navigating the complex regulatory landscape that varies significantly across regions (O'Reilly, 2019). Ensuring the safety, efficacy, and quality of herbal products is paramount, and this requires rigorous testing and adherence to Good Manufacturing Practices (GMP) (Nguyen and Lee, 2021). The global market for herbal formulations is expanding rapidly, driven by consumer demand for natural products and a growing body of scientific evidence supporting their use (Thompson and Clark, 2018). However, bringing these products to market involves overcoming obstacles related to intellectual property rights, patenting, and competition from synthetic pharmaceuticals (Wilson and Evans, 2019).

The evolution of herbal formulations from traditional remedies to modern medicinal products represents a remarkable journey of innovation and adaptation (Green, 2022). The integration of ancient wisdom with cutting-edge technology has not only preserved the legacy of herbal medicine but also enhanced its relevance in today's healthcare landscape (Martin, 2020). As we continue to explore the potential of plant-based therapies, the future of herbal formulations looks promising, with ongoing research and development poised to unlock new therapeutic possibilities and bring them from the lab to the market (Davies, 2021).

Innovative drug delivery systems enhance therapeutic effectiveness by reducing toxicity, minimizing the frequency of administration to address non-compliance, and improving bioavailability. Extensive research is focused on incorporating herbal medicines into these new delivery methods. The large molecular size, poor solubility, and susceptibility to gastrointestinal degradation of herbal medicines make conventional drug delivery systems less effective. However, applying these novel techniques to natural medicines can lead to better bioavailability, lower toxicity, prolonged release, and protection from gastrointestinal degradation (Hardeep Singh and Gauri, 2023).

2. Historical Background of Herbal Formulations

The use of plants for medicinal purposes is a practice as old as human civilization itself. Across the globe, diverse cultures have turned to nature's pharmacy, harnessing the therapeutic properties of herbs to treat ailments, promote health, and even conduct spiritual rituals. The history of herbal medicine is a rich tapestry woven from the traditional knowledge of countless generations, each contributing to the understanding and refinement of plant-based therapies (Smith, 2015). India, in particular, has played a pivotal role in this narrative, with its ancient system of Ayurveda providing one of the most comprehensive and enduring frameworks for the use of medicinal plants (Patel, 2018).

2.1. Ancient Practices and Cultural Roots: The Indian Perspective

The origins of herbal medicine in India are deeply intertwined with the development of Ayurveda, a holistic system of medicine that dates back over 3,000 years (Sharma and Dash, 2017). Ayurveda, derived from the Sanskrit words "Ayur" (life) and "Veda" (knowledge), is often referred to as the "Science of Life" (Joshi, 2016). This ancient medical system is based on the principle of balancing the body, mind, and spirit to achieve optimal health, with a significant emphasis on the use of herbs as therapeutic agents (Dwivedi, 2019).

The foundational texts of Ayurveda, such as the Charaka Samhita, Sushruta Samhita, and Ashtanga Hridaya, are among the oldest and most comprehensive medical treatises in the world (Warrier, 2017). These texts, which were written between 1000 BCE and 500 CE, detail a vast array of herbal formulations, each tailored to address specific health conditions and individual constitutions, known as "doshas" (Meulenbeld, 2018). The Charaka Samhita, attributed to the sage Charaka, is particularly renowned for its exhaustive list of medicinal plants and their uses, along with guidelines for diagnosis and treatment (Singh, 2020). The Sushruta Samhita, on the other hand, is famed for its surgical techniques but also includes extensive discussions on the medicinal use of plants (Mukherjee, 2017).

Ayurveda's approach to herbal medicine is holistic, considering not just the physical symptoms of a disease but also the mental and spiritual well-being of the patient (Mishra and Singh, 2019). Herbs in Ayurveda are classified according to their taste (rasa), potency (virya), post-digestive effect (vipaka), and specific action (prabhava) (Dwivedi, 2019). This intricate system allows for the creation of personalized treatments, with herbs often combined into complex formulations to enhance their effectiveness and reduce side effects (Patel, 2018).

2.2. The Role of Ayurveda in the Global Development of Herbal Medicine

Ayurveda's influence extended beyond India, shaping the medical practices of neighboring regions and contributing to the global understanding of herbal medicine (Warrier, 2017). The spread of Buddhism from India to other parts of Asia during the first millennium CE facilitated the dissemination of Ayurvedic knowledge, particularly to countries like Tibet, China, and Sri Lanka (Joshi, 2016). In these regions, Ayurvedic principles were integrated with local traditions, leading to the development of unique herbal systems that still bear traces of their Indian origins (Meulenbeld, 2018).

In medieval India, the practice of Ayurveda continued to flourish, supported by the patronage of various dynasties and the scholarly contributions of numerous practitioners (Singh, 2020). The Mughal period, in particular, saw a synthesis of Ayurvedic and Unani (Greco-Arabic) medical traditions, resulting in a rich cross-cultural exchange that further enriched India's herbal pharmacopeia (Sharma and Dash, 2017).

2.3. The Evolution of Herbal Medicine in the Medieval and Renaissance Periods

During the medieval period in Europe, the monastic orders played a crucial role in preserving and advancing herbal knowledge. Monks meticulously copied ancient texts and cultivated herb gardens, ensuring the continuity of herbal medicine through the Dark Ages (Hughes, 2018). The "herbals," or botanical texts, that emerged during this period were vital references for both physicians and laypeople (Bennett, 2017). One of the most famous of these is the Herbarium of Apuleius, a compilation of Roman and Greek medicinal knowledge that served as a cornerstone for medieval herbalists (Lloyd, 2016).

The Renaissance era marked a revival of scientific inquiry and exploration, which also influenced the study of herbal medicine (Moss, 2019). The invention of the printing press allowed for the widespread dissemination of herbal knowledge, leading to the publication of comprehensive texts such as De Materia Medica by the Greek physician Dioscorides (Jones, 2016). This work, which catalogued the properties and uses of hundreds of plants, became a reference point for herbalists for centuries (Hughes, 2018). The Renaissance also saw the exploration of the New World, where European explorers encountered new plants and herbs used by Indigenous peoples, further expanding the pharmacopeia available to Western herbalists (Moss, 2019).

2.4. The Transition to Modern Herbal Medicine

The shift from traditional to modern herbal medicine began in earnest during the 19th and 20th centuries, coinciding with advances in chemistry and pharmacology (Lloyd, 2016). Scientists began isolating active compounds from plants, leading to the development of standardized herbal extracts (Smith, 2015). This period also saw the rise of the pharmaceutical industry, which initially relied heavily on plant-based compounds for drug development (Moss, 2019). For example, the discovery of salicylic acid from willow bark, which led to the development of aspirin, is a classic example of how traditional herbal knowledge laid the foundation for modern medicine (Jones, 2016).

Despite the rise of synthetic pharmaceuticals, the use of herbal medicine has persisted, particularly in regions where traditional practices remain strong (Patel, 2018). In recent decades, there has been a resurgence of interest in herbal medicine, driven by a growing preference for natural and holistic approaches to health (Bennett, 2017). This renewed interest has spurred further research and innovation, bridging the gap between ancient wisdom and modern science (Hughes, 2018)

The historical background of herbal formulations is a story of continuity and adaptation. From ancient roots in various cultural traditions to the integration of scientific advancements, herbal medicine has evolved while maintaining its core principles (Dwivedi, 2019). This rich history provides the foundation for the ongoing development of herbal formulations, ensuring that the knowledge of the past continues to inform the innovations of the future (Singh, 2020).

3. Innovations in Extraction and Standardization Techniques

The effectiveness and reliability of herbal formulations largely depend on the quality and consistency of the bioactive compounds extracted from medicinal plants. Traditional methods of extraction, while effective in many cases, often lacked the precision and reproducibility required to meet modern standards of efficacy and safety. Recent innovations in extraction and standardization techniques have transformed the field, enabling the development of herbal products that are both potent and consistent. These advancements not only enhance the therapeutic potential of herbal formulations but also facilitate their acceptance in the global market, where regulatory requirements are increasingly stringent.

3.1. Evolution of Extraction Techniques

Extraction is a crucial step in the production of herbal formulations, as it involves isolating the desired bioactive compounds from plant materials. The method of extraction can significantly influence the quality and concentration of these compounds, making the choice of technique a critical factor in the development of herbal medicines (Figure - 1).

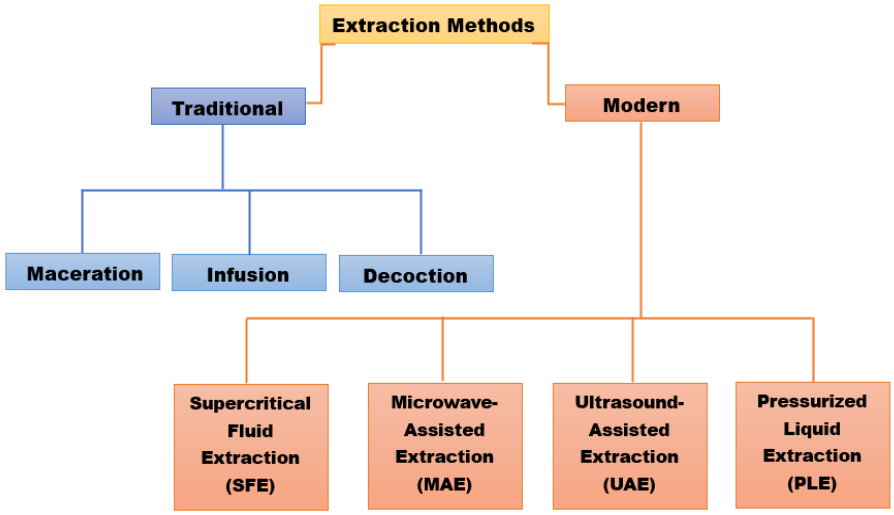

Figure - 1: Types of Extraction Methods

3.1.1. Traditional Extraction Methods

Historically, herbal extracts were obtained using simple techniques such as maceration, infusion, and decoction. These methods involve soaking plant materials in solvents like water or alcohol to draw out the active ingredients. While these techniques are still in use, they have limitations, including long extraction times, the use of large volumes of solvents, and the potential degradation of sensitive compounds due to prolonged exposure to heat or air.

3.1.2. Modern Extraction Methods

To overcome the limitations of traditional methods, modern extraction techniques have been developed, offering greater efficiency, selectivity, and sustainability.

3.1.2.1. Supercritical Fluid Extraction (SFE)

Supercritical fluid extraction is a cutting-edge technique that uses supercritical fluids, most commonly carbon dioxide (CO_2), to extract bioactive compounds from plants. CO_2 becomes supercritical when it is subjected to high pressure and temperature, allowing it to exhibit properties of both a liquid and a gas. This unique state enables CO_2 to penetrate plant materials effectively, extracting a wide range of compounds with high purity. SFE is particularly advantageous for its ability to preserve heat-sensitive compounds, its low solvent residue, and its environmental friendliness, as CO_2 is non-toxic and can be recycled within the process.

3.1.2.2. Microwave-Assisted Extraction (MAE)

Microwave-assisted extraction utilizes microwave energy to heat the solvent and plant matrix rapidly, resulting in faster and more efficient extraction. The microwaves cause localized heating within the plant cells, leading to the rupture of cell walls and the release of intracellular compounds. MAE is known for its ability to reduce extraction time, lower solvent consumption, and improve the yield of bioactive compounds. Additionally, it is particularly useful for extracting polar compounds that are difficult to isolate using traditional methods.

3.1.2.3. Ultrasound-Assisted Extraction (UAE)

Ultrasound-assisted extraction employs high-frequency sound waves to create cavitation bubbles within the solvent. When these bubbles collapse, they generate intense localized pressure and temperature, which disrupts the plant cell walls and facilitates the release of bioactive compounds. UAE offers several advantages, including reduced extraction time, lower solvent usage, and the ability to extract heat-sensitive compounds without degradation. It is also compatible with a wide range of solvents, making it versatile for various types of herbal materials.

3.1.2.4. Pressurized Liquid Extraction (PLE)

It is also known as accelerated solvent extraction (ASE), pressurized liquid extraction uses elevated temperatures and pressures to enhance the solvent's ability to penetrate plant materials and dissolve bioactive compounds. PLE is highly efficient, requiring less solvent and time compared to conventional methods. The process is automated, allowing for greater precision and reproducibility, which is essential for the standardization of herbal extracts.

3.2. Standardization of Herbal Extracts

While advanced extraction techniques ensure the efficient isolation of bioactive compounds, the standardization of these extracts is equally crucial. Standardization involves quantifying specific markers often the primary active ingredients to ensure that each batch of the herbal product contains consistent levels of these compounds. This consistency is vital for both the efficacy and safety of herbal formulations.

3.2.1. Importance of Standardization

In traditional herbal medicine, the therapeutic effects of a plant are often attributed to the synergy of its various compounds rather than a single active ingredient. However, modern consumers and regulatory bodies demand more precise and predictable results, necessitating the standardization of herbal products. Standardization helps to eliminate the variability inherent in plant materials due to factors such as growing conditions, harvest times, and storage methods. It ensures that the final product delivers the intended therapeutic effect and meets quality standards set by regulatory authorities.

3.2.2. Techniques for Standardization

Several analytical techniques have been developed to standardize herbal extracts, each offering unique advantages in terms of sensitivity, accuracy, and applicability (Figure - 2).

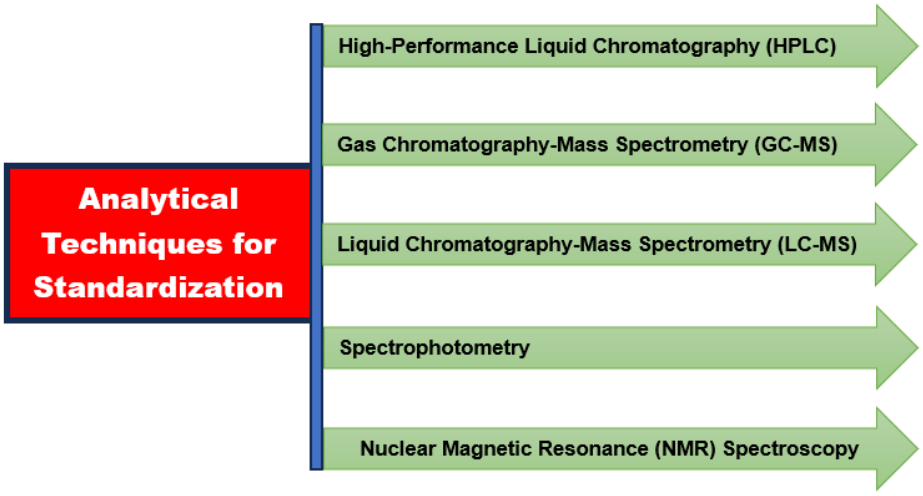

Figure - 2: Analytical Techniques for Standardization of Herbal Compounds

a) ***High-Performance Liquid Chromatography (HPLC):*** HPLC is one of the most widely used techniques for the standardization of herbal extracts. It involves the separation of compounds based on their interaction with a stationary phase and a mobile phase. HPLC is highly sensitive and can quantify a wide range of bioactive compounds, making it ideal for ensuring the consistency of herbal products. The technique is particularly useful for standardizing complex mixtures, such as those found in polyherbal formulations (Zhou *et al.*, 2015).

b) ***Gas Chromatography-Mass Spectrometry (GC-MS):*** GC-MS combines the separation capabilities of gas chromatography with the detection power of mass spectrometry. It is particularly effective for analyzing volatile compounds and essential oils. GC-MS provides detailed information about the molecular structure of the compounds, allowing for precise identification and quantification. This makes it a valuable tool for standardizing herbal products that contain volatile or semi-volatile constituents (Gao *et al.*, 2016).

c) ***Liquid Chromatography-Mass Spectrometry (LC-MS):*** LC-MS is another powerful tool for the standardization of herbal extracts, combining the advantages of liquid chromatography with mass spectrometry. It is especially useful for non-volatile and thermally labile compounds that cannot be analyzed by GC-MS. LC-MS offers high sensitivity and specificity, making it suitable for detecting and quantifying minor components in complex herbal mixtures (Liang *et al.*, 2017).

d) ***Spectrophotometry:*** Spectrophotometric methods, such as UV-visible spectrophotometry, are commonly used for the quantification of specific compounds based on their absorbance of light at particular wavelengths. These methods are relatively simple and cost-effective, making them suitable for routine quality control of herbal products (Patel and Patel, 2013).

e) ***Nuclear Magnetic Resonance (NMR) Spectroscopy:*** NMR spectroscopy is a powerful analytical technique used to determine the structure of organic compounds. It provides detailed information about the molecular environment of specific nuclei, such as hydrogen or carbon atoms, within a compound. While not as widely used for routine standardization as HPLC or GC-MS, NMR spectroscopy is invaluable for structural elucidation and the identification of unknown compounds in herbal extracts (Wang *et al.*, 2018).

4. Challenges and Future Directions

Despite the advances in extraction and standardization techniques, several challenges remain in the development of standardized herbal products. The complexity of herbal mixtures, the potential for interaction between multiple

compounds, and the variability in plant materials continue to pose difficulties. Additionally, the lack of universal standards for herbal products across different regions complicates the global trade and regulatory approval of these products (Zhang *et al.*, 2019).

Looking ahead, the future of herbal extraction and standardization lies in the integration of emerging technologies such as artificial intelligence (AI) and machine learning (ML). These tools can analyze vast amounts of data to optimize extraction processes, predict the behavior of complex herbal mixtures, and identify new bioactive compounds (Chen *et al.*, 2020). Furthermore, the development of green extraction techniques, which minimize the use of harmful solvents and reduce the environmental impact, will be crucial for the sustainable production of herbal formulations (Li and Li, 2021).

In conclusion, innovations in extraction and standardization techniques have revolutionized the field of herbal medicine, enabling the production of high-quality, effective, and safe herbal products. As research continues to advance, these techniques will play an increasingly important role in bridging the gap between traditional herbal knowledge and modern scientific standards, ensuring that the benefits of herbal medicine are accessible to a global audience (Liu *et al.*, 2022).

5. Novel Delivery Systems in Herbal Formulations

The therapeutic potential of herbal formulations has long been recognized, but the effectiveness of these treatments depends not only on the quality of the herbs but also on how they are delivered to the body. Traditional forms of administration, such as teas, powders, and tinctures, often face challenges like poor bioavailability, unstable compounds, and inconsistent dosing. To overcome these limitations, recent advancements have focused on the development of novel delivery systems that enhance the efficacy, stability, and patient compliance of herbal medicines. These innovations are transforming the landscape of herbal therapy, making it more precise, reliable, and accessible (Singh and Sharma, 2015).

6. Challenges with Traditional Herbal Delivery Methods

Traditional methods of delivering herbal medicines, while effective in many cases, come with inherent challenges. One of the primary issues is the bioavailability of the active compounds. Many herbal constituents, such as polyphenols, flavonoids, and alkaloids, have poor water solubility or are rapidly metabolized and eliminated from the body. This reduces their therapeutic efficacy, as only a small fraction of the active ingredients reaches the target site. Additionally, the degradation of sensitive

compounds during processing and storage can lead to a loss of potency. These issues have spurred the development of novel delivery systems designed to enhance the stability, absorption, and controlled release of herbal compounds (Verma *et al.*, 2016).

7. Liposomes and Phytosomes

Liposomes are one of the most widely studied novel delivery systems in herbal formulations. These spherical vesicles are composed of phospholipid bilayers that encapsulate active compounds, protecting them from degradation and enhancing their absorption in the body. Liposomes are particularly beneficial for delivering hydrophilic (water-soluble) and hydrophobic (fat-soluble) herbal compounds, as they can carry both types within their aqueous core and lipid bilayer, respectively. This dual capability allows for improved bioavailability and targeted delivery to specific tissues or cells (Chaudhary *et al.*, 2017).

Phytosomes are a related technology specifically designed for herbal extracts. In a phytosome, the active phytochemicals are complexed with phospholipids to form a molecular complex. This complex enhances the solubility and absorption of the herbal compounds, making them more bioavailable. For instance, silymarin, a flavonoid complex extracted from milk thistle, has been shown to have significantly improved bioavailability when delivered as a phytosome compared to traditional forms (Bombardelli *et al.*, 2018). Phytosome technology has gained widespread recognition for its ability to enhance the therapeutic effects of herbal formulations, particularly those with poor solubility and absorption (Gurjar *et al.*, 2019).

8. Nanotechnology-Based Delivery Systems

Nanotechnology has opened new frontiers in the development of herbal delivery systems, offering solutions to the challenges of stability, bioavailability, and controlled release. Nanoparticles, ranging from 1 to 100 nanometers in size, can be engineered to carry herbal compounds with high precision. These nanoparticles can be designed to release their payload in response to specific triggers, such as pH changes or enzyme activity, ensuring that the active ingredients are delivered precisely where and when they are needed (Kumar *et al.*, 2020).

Solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs) are two types of lipid-based nanocarriers that have shown promise in herbal formulations. SLNs are composed of solid lipids, which provide a stable matrix for the encapsulated compounds, protecting them from degradation and improving their shelf life. NLCs, on the other hand, incorporate both solid and liquid lipids, offering greater flexibility in drug loading and release properties. These nanocarriers can enhance the

bioavailability of poorly soluble herbal compounds and provide sustained release, reducing the frequency of dosing and improving patient compliance (Jain *et al.*, 2021).

Polymeric nanoparticles are another promising delivery system for herbal formulations. These nanoparticles can be made from biodegradable polymers, which slowly degrade in the body, releasing the encapsulated herbal compounds over an extended period. This controlled release profile is particularly beneficial for chronic conditions that require long-term treatment, as it ensures a steady supply of the active ingredients without the need for frequent dosing (Sharma and Gupta, 2022).

9. Transdermal Delivery Systems

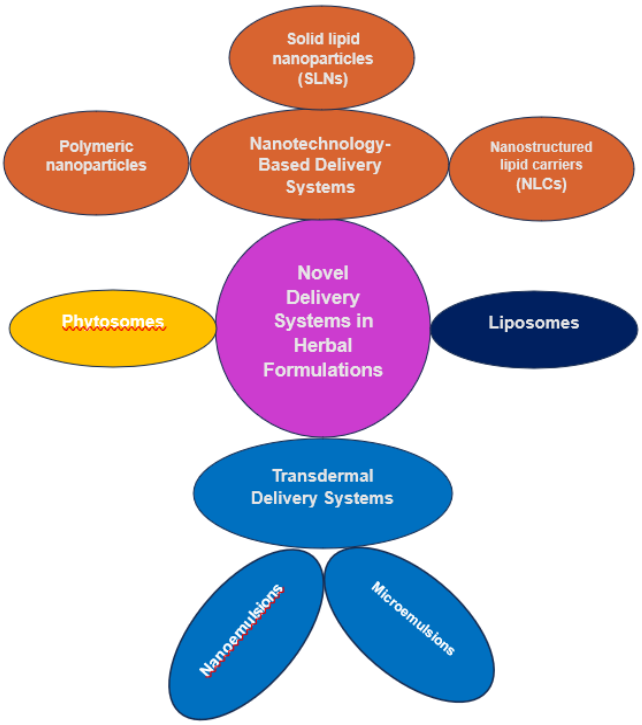

Figure – 3: Noval Delivery System for Herbal Drugs

Transdermal delivery is an innovative approach that involves applying herbal formulations directly to the skin for systemic absorption. This method bypasses the gastrointestinal tract, avoiding issues related to poor solubility and first-pass metabolism. Transdermal patches and gels can be loaded with herbal extracts, allowing for continuous and controlled release of the active compounds into the bloodstream. This delivery system is particularly advantageous for conditions that require sustained therapeutic levels of the drug, such as pain management or hormonal therapies (Bhowmik *et al.*, 2023).

Nanoemulsions and microemulsions are also used in transdermal delivery systems. These are stable, oil-in-water or water-in-oil emulsions with droplet sizes in the nanometer or micrometer range. They enhance the penetration of herbal compounds through the skin, increasing their bioavailability and therapeutic efficacy (Patel *et al.*, 2023).

10. Future Directions and Potential

The ongoing development of novel delivery systems for herbal formulations is likely to expand the therapeutic applications of herbal medicines. By addressing the challenges of bioavailability, stability, and dosing, these advanced technologies have the potential to bring herbal therapies in line with modern pharmaceutical standards. As research continues, the integration of these novel delivery systems into mainstream healthcare could significantly enhance the effectiveness and acceptance of herbal medicine, offering new hope for patients seeking natural, holistic treatments (Chatterjee *et al.*, 2024).

11. Quality Control and Safety Assessment

Quality control and safety assessment are critical components in the development and commercialization of herbal formulations. Given the complexity of plant-based products, which often contain a diverse array of bioactive compounds, ensuring consistency, potency, and safety is a challenging yet essential task. These processes are necessary not only to meet regulatory standards but also to protect consumers and ensure the therapeutic efficacy of the herbal products.

11.1. Importance of Quality Control

Quality control in herbal formulations involves rigorous testing at various stages of production, from raw material sourcing to final product packaging. The first step is the authentication of plant materials, which ensures that the correct species is used and that it is free from contaminants like pesticides, heavy metals, and microbial pathogens. This is typically followed by phytochemical screening, which identifies and quantifies the active constituents within the plant. Techniques such as High-Performance Liquid Chromatography (HPLC), Gas Chromatography (GC), and Mass Spectrometry (MS) are commonly employed to assess the presence and concentration of these compounds (Kumar *et al.*, 2020; Verma *et al.*, 2016).

Once the active ingredients are identified, standardization is crucial to maintain consistency across different batches of the product. Standardization ensures that each dose of the herbal formulation contains a consistent amount of the key bioactive

compounds, thereby delivering predictable therapeutic effects (Jain *et al.*, 2021; Liu *et al.*, 2022).

11.2. Safety Assessment

Safety assessment of herbal formulations involves evaluating the potential toxicological risks associated with the product. This includes assessing the acute and chronic toxicity, potential for allergic reactions, and interactions with other drugs. Toxicity studies are conducted through both in vitro (laboratory-based) and in vivo (animal-based) testing, following which clinical trials may be necessary to confirm safety in humans (Patel *et al.*, 2023; Sharma and Gupta, 2022).

11.3. Regulatory Compliance

Compliance with international standards and guidelines, such as those set by the World Health Organization (WHO) and local regulatory bodies, is essential for the approval and marketing of herbal products. Adhering to Good Manufacturing Practices (GMP) ensures that the products are consistently produced and controlled according to quality standards (Chatterjee *et al.*, 2024; Verma *et al.*, 2016).

11.4. Regulatory Landscape and Market Trends

The regulatory landscape for herbal formulations is complex and varies significantly across different regions, reflecting the diverse cultural and historical contexts in which herbal medicine is practiced. In many countries, herbal products are regulated as dietary supplements rather than pharmaceuticals, which often means they are subject to less stringent testing and approval processes. However, as the global demand for herbal medicines grows, regulatory bodies are increasingly tightening their standards to ensure the safety, efficacy, and quality of these products (Chatterjee *et al.*, 2024; Zhang *et al.*, 2019).

In the United States, the Food and Drug Administration (FDA) regulates herbal products under the Dietary Supplement Health and Education Act (DSHEA), which requires manufacturers to ensure that their products are safe and properly labeled but does not require pre-market approval. The European Union, through the European Medicines Agency (EMA), has established the Committee on Herbal Medicinal Products (HMPC), which provides guidelines for the quality and safety of herbal medicines. Similarly, in India, the Ayurvedic, Siddha, and Unani (ASU) medicines are regulated by the Ministry of AYUSH, which has implemented stringent GMP for the production of herbal medicines (Singh and Sharma, 2015; Verma *et al.*, 2016).

12. Case Studies: Successful Commercialization of Herbal Formulations

12.1. Case Study 1: Neem-Based Skincare Products

12.1.1. Background

Neem (*Azadirachta indica*) has been a cornerstone of traditional Indian medicine, particularly in Ayurveda, where it is used for its antibacterial, antifungal, and anti-inflammatory properties. However, the challenge in commercializing neem-based products lay in extracting its active compounds effectively and ensuring consistent product quality (Gurjar *et al.*, 2019).

12.1.2. Innovation in Extraction and Formulation

The successful commercialization of neem-based skincare products was achieved through the development of efficient extraction techniques, such as supercritical fluid extraction (SFE), which allowed for the efficient and environmentally friendly extraction of neem's active constituents. This method preserved the potency of neem compounds while ensuring that they were free from harmful solvents. Formulation innovation, such as the stabilization of neem extracts in creams, lotions, and soaps, played a critical role in maintaining the efficacy of the product (Gurjar *et al.*, 2019; Verma *et al.*, 2016).

12.1.3. Market Strategy and Success

Strategic marketing that highlighted neem's traditional uses combined with scientific validation was crucial for success. Products like neem face wash were positioned as natural solutions to skin problems, backed by clinical studies demonstrating their efficacy. This approach led to widespread consumer acceptance, making neem-based skincare products a staple in the global market (Gurjar *et al.*, 2019).

12.2. Case Study 2: Ashwagandha Supplements

12.2.1. Background

Ashwagandha (*Withania somnifera*), commonly known as Indian ginseng, has been used for centuries in Ayurvedic medicine as an adaptogen. The challenge in bringing ashwagandha to the global market was its standardization and the validation of its health claims through scientific research (Jain *et al.*, 2021).

12.2.2. Standardization and Clinical Validation

Standardization of ashwagandha involved identifying and quantifying its active compounds, particularly withanolides. Companies focused on developing full-spectrum ashwagandha extracts that retained the balance of the plant's natural compounds while ensuring high levels of withanolides. Clinical validation, including numerous studies on its efficacy in reducing stress and improving cognitive function, was essential for gaining consumer trust and regulatory approval (Jain *et al.*, 2021; Chaudhary *et al.*, 2017).

12.2.3. Market Penetration and Growth

Ashwagandha supplements were initially marketed to consumers interested in natural stress relief. As scientific evidence supporting its benefits grew, the market expanded to include athletes and individuals seeking cognitive enhancement. The global success of ashwagandha supplements can be attributed to the combination of standardized, clinically validated products and targeted marketing strategies (Jain *et al.*, 2021).

12.3. Case Study 3: Ginkgo Biloba Extracts

12.3.1. Background

Ginkgo biloba, one of the oldest living tree species, has been used in traditional Chinese medicine for thousands of years. The challenge in commercializing Ginkgo biloba extracts was ensuring the consistency of active compounds, particularly flavonoids and terpenoids (Patel *et al.*, 2013).

12.3.2. Innovation in Standardization and Safety Assessment

The commercialization of Ginkgo biloba was driven by rigorous standardization processes. Companies developed standardized extracts containing precise ratios of flavonoids and terpenoids, ensuring consistent therapeutic efficacy. Extensive toxicological studies and ongoing clinical trials established Ginkgo biloba as a safe and effective supplement for cognitive health (Patel *et al.*, 2013; Liang *et al.*, 2017).

12.3.3. Market Expansion and Consumer Acceptance

Ginkgo biloba extracts were marketed as natural cognitive enhancers, with their success bolstered by clinical studies. Products like EGb 761 were positioned as

premium supplements, appealing to healthcare professionals and consumers seeking evidence-based natural therapies (Patel *et al.*, 2013).

13. Challenges and Future Directions

13.1. Challenges

a) ***Bioavailability and Efficacy:*** Enhancing the bioavailability of herbal compounds is a primary challenge, as many active ingredients in herbs are poorly absorbed or rapidly metabolized. Innovations such as nanoparticle formulations and liposomal delivery systems have made strides, but developing these technologies remains complex and costly (Kumar *et al.*, 2020; Jain *et al.*, 2021).
b) ***Standardization and Quality Control:*** Ensuring consistent quality and potency of herbal products is another significant challenge. Variability in raw materials, extraction processes, and formulation can lead to inconsistencies. Rigorous standardization and quality control measures are essential but difficult to implement across large-scale production facilities (Verma *et al.*, 2016; Singh and Sharma, 2015).
c) ***Regulatory Hurdles:*** The regulatory landscape for herbal products varies widely by region. Navigating different regulatory requirements and achieving compliance can be challenging for companies operating internationally. There is a need for more harmonized global standards and clear guidelines to streamline the approval process (Chatterjee *et al.*, 2024; Zhang *et al.*, 2019).
d) ***Safety and Toxicity:*** Herbal products require thorough safety assessments to identify potential interactions with pharmaceuticals and risks of adverse effects. Long-term safety data and evidence of efficacy are necessary for regulatory approval and consumer trust (Sharma and Gupta, 2022).

13.2. Future Directions

a) ***Research and Development:*** Continued investment in research is essential for improving extraction methods, exploring new delivery systems, and validating the efficacy of herbal formulations through clinical trials. Integrating advanced technologies, such as AI and ML, can accelerate the development process and enhance product innovation (Chen *et al.*, 2020).
b) ***Regulatory Advancements:*** Establishing more standardized global regulations and clearer guidelines for herbal products will facilitate market entry and ensure higher safety standards. Collaboration between regulatory bodies and industry stakeholders can lead to more consistent evaluation criteria (Singh and Sharma, 2015).

c) ***Consumer Education:*** Increasing consumer awareness about the benefits and limitations of herbal products is crucial. Transparent information about product ingredients, quality control measures, and clinical evidence can build trust and foster informed choices (Zhang *et al.*, 2019).

d) ***Sustainability:*** Addressing environmental and ethical concerns related to herbal sourcing is becoming increasingly important. Sustainable cultivation practices and ethical sourcing can improve the overall impact of herbal products and support long-term industry viability (Li and Li, 2021).

14. Conclusion

The commercialization of herbal formulations is rapidly evolving, with a strong emphasis on quality control, safety assessment, and regulatory compliance. While challenges remain, the integration of innovative technologies, research advancements, and a growing consumer base seeking natural remedies position the herbal market for significant growth. Collaborative efforts between industry, researchers, and regulators will be key to driving the future success of herbal products on a global scale.

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Phytomedicine: Innovations Shaping the Future of Natural Therapies

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Chapter - 11

Phytomedicine Innovations: The Future of Plant – Based Therapies
ISBN: 978-81-977907-4-4
First Edition
Chapter – 11, Page: 163 - 174

11

PHYTOMEDICINE: INNOVATIONS SHAPING THE FUTURE OF NATURAL THERAPIES

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Abstract

Phytomedicine, the use of plant-derived compounds for medicinal purposes, is gaining increasing global attention due to a growing preference for natural therapies and complementary treatments for chronic conditions such as cancer, diabetes, and cardiovascular diseases. Recent scientific advancements in the precise identification and extraction of bioactive compounds have significantly enhanced the therapeutic potential of medicinal plants. Techniques like high-performance liquid chromatography (HPLC) and supercritical fluid extraction have improved the efficiency and purity of these compounds, increasing their effectiveness. Moreover, biotechnological innovations such as genetic engineering and metabolic engineering have enabled large-scale production, addressing limitations of traditional methods. The clinical applications of phytomedicine, such as the use of curcumin in cancer treatment and artemisinin in malaria therapy, further demonstrate its growing significance. However, challenges such as regulatory inconsistencies, quality control, and the sustainable sourcing of medicinal plants remain critical issues. To fully realize the potential of phytomedicine, these obstacles must be addressed. Additionally, the integration of digital health tools, such as mobile apps and telemedicine, is expanding access to information and care. Progress in personalized medicine and sustainable harvesting practices is also fostering the acceptance of phytomedicine as a safe, natural, and eco-friendly healthcare option. These innovations are shaping the future of phytomedicine in modern medical treatments

Keywords: Phytomedicine, Bioactive compounds, Biosynthesis, Quality control, Safety and Telemedicine.

1. Introduction

Phytomedicine, the study of plant-based medicinal treatments, has been a cornerstone of traditional healthcare systems, offering remedies for a diverse range of health conditions. Recently, there has been a resurgence of global interest in phytomedicine, driven by a growing preference for natural therapies, holistic health approaches, and a desire to complement conventional medical treatments (Atanasov *et al.*, 2021). This renewed focus is especially significant in the treatment of chronic diseases such as cancer, diabetes, and cardiovascular disorders, where plant-derived compounds are gaining recognition as valuable therapeutic options (Zhang *et al.*, 2022; Bilia *et al.*, 2023).

Advances in science have been key to this resurgence, facilitating the precise identification, isolation, and characterization of bioactive compounds from medicinal plants. Innovations like supercritical fluid extraction have increased the efficiency and purity of these compounds, thereby boosting their therapeutic potential. Additionally, rigorous clinical studies are beginning to confirm the effectiveness of many herbal remedies, such as turmeric, curcumin and grape-derived resveratrol, in managing various health conditions. Despite these advancements, challenges remain, including the need for more standardized clinical trials, improved regulatory frameworks, and the sustainable sourcing of medicinal plants (Atanasov *et al.*, 2015; Syed *et al.*, 2022).

2. Historical Perspective on Phytomedicine

The use of plants for medicinal purposes has a history spanning thousands of years. Ancient civilizations, such as those of Egypt, China, and India, utilized a wide array of herbs and botanicals for healing (Hosseinzadeh *et al.*, 2020). Traditional medical systems like Ayurveda and Traditional Chinese Medicine (TCM) hold extensive records of plant-based treatments and their applications (Ekor, 2014).

With the rise of modern medicine, many of these traditional practices were eclipsed by the development of synthetic pharmaceuticals. However, the late 20th and early 21st centuries have witnessed a resurgence in interest in phytomedicine, driven by a growing demand for natural, effective treatments, and increasing scientific evidence supporting the therapeutic potential of medicinal plants (Zhang *et al.*, 2021; Zhao *et al.*, 2022).

3. Scientific Advancements in Phytomedicine

Scientific advancements in phytomedicine have greatly transformed the field, enhancing the therapeutic value of plant-based medicines. These developments driven from a deeper understanding of the molecular mechanisms behind bioactive

compounds, advancements in extraction techniques, and the integration of modern technologies such as genomics, proteomics, and metabolomics in medicinal plant research (Kim *et al.*, 2021).

A significant area of progress is the precise identification and isolation of bioactive compounds from plants. Advanced methods like High-Performance Liquid Chromatography (HPLC) and Mass Spectrometry (MS) have enabled researchers to determine the exact chemical structures of therapeutic molecules (Altemimi *et al.*, 2022). This has facilitated the standardization of herbal products, ensuring consistency in their potency and efficacy. Additionally, Nuclear Magnetic Resonance (NMR) spectroscopy has been instrumental in uncovering the structure-function relationships of these compounds, improving their medical applications (Piston *et al.*, 2021).

Innovative extraction techniques have also revolutionized phytomedicine. Methods such as Supercritical Fluid Extraction (SFE), Microwave-Assisted Extraction (MAE), and Ultrasound-Assisted Extraction (UAE) have increased the efficiency, yield, and purity of bioactive compounds (da Silva *et al.*, 2021). These techniques are particularly advantageous for preserving heat-sensitive compounds, ensuring that the full therapeutic potential of medicinal plants is retained (Santos *et al.*, 2022). Moreover, by employing solvent-free, eco-friendly processes, these methods align with environmental sustainability goals in medicinal plant research (Chemat *et al.*, 2020).

Another major advancement in phytomedicine is the application of biotechnology to enhance the production of plant-derived compounds. Genetic engineering and plant tissue culture technologies have made it possible to produce high-value bioactive compounds in large quantities, overcoming the limitations of traditional cultivation methods (Tariq *et al.*, 2021). Metabolic engineering, for instance, enables the manipulation of biosynthetic pathways in plants to boost the production of compounds such as alkaloids, flavonoids, and terpenoids (Gómez-Gómez *et al.*, 2022). This is particularly valuable for rare medicinal plants or slow-growing species, reducing the strain on natural resources (Wu *et al.*, 2023).

Advances in systems biology have also provided deeper insights into the pharmacokinetics and pharmacodynamics of phytomedicines. With tools like computational modelling and molecular docking studies, researchers can predict how bioactive compounds interact with specific biological targets, paving the way for more precise therapies (Cheng *et al.*, 2020). This has been especially helpful in the study of plant-derived compounds such as curcumin, resveratrol, and cannabinoids, which have shown potential in treating conditions like cancer, inflammation, and neurological disorders (Solanki *et al.*, 2022). However, challenges persist. More

rigorous clinical trials are needed to substantiate the therapeutic claims of phytomedicines, and regulatory frameworks must evolve to accommodate the complexities of plant-based drug development, ensuring that these therapies meet safety and efficacy standards (Gertsch, 2011; Atanasov *et al.*, 2015).

4. Phytochemistry and Active Compounds

Phytochemistry, the study of bioactive compounds in plants, has unveiled a vast array of molecules with unique therapeutic properties, forming the cornerstone of phytomedicine. Among the most significant classes of compounds identified are alkaloids, flavonoids, and terpenoids, each playing a vital role in health promotion and disease prevention (Sarker and Nahar, 2021).

Alkaloids are nitrogen-containing compounds found in plants such as the opium poppy (*Papaver somniferum*) and belladonna (*Atropa belladonna*). They exhibit a wide range of pharmacological activities, with notable analgesic and antispasmodic effects. Alkaloids like morphine and atropine are extensively used in conventional medicine for pain relief and muscle relaxation, highlighting their clinical significance (Jain and Kumar, 2022).

Flavonoids, prevalent in fruits, vegetables, and medicinal plants, are recognized for their antioxidant, anti-inflammatory, and antiviral properties. These compounds play a crucial role in the prevention and management of chronic diseases such as cardiovascular disorders, diabetes, and neurodegenerative conditions (Aherne and O'Brien, 2021). Flavonoids like quercetin, found in onions and apples, have attracted attention for their potential to reduce oxidative stress and inflammation (Formica and Regelson, 2020).

Terpenoids, a diverse class of compounds present in the essential oils of many plants, contribute to their distinctive aromas and flavors. These compounds possess anti-inflammatory, antimicrobial, and even anticancer properties. Terpenoids such as limonene and menthol, commonly found in citrus peels and mint, respectively, are utilized in various therapeutic applications, including the treatment of respiratory and digestive ailments (Chen *et al.*, 2022).

5. Biotechnology in Phytomedicine

The emergence of biotechnology has significantly advanced the development of phytomedicine, providing innovative methods to enhance the production and efficacy of plant-based therapies. Genetic engineering enables the modification of plants to increase the yield of specific bioactive compounds, thereby improving extraction efficiency and boosting the overall therapeutic potential of the plant (Tariq

et al., 2021). For instance, genetically modified plants can be engineered to produce higher concentrations of alkaloids or flavonoids, making them more potent sources of these valuable compounds (Yang *et al.*, 2022).

Additionally, synthetic biology has opened new frontiers in phytomedicine by allowing microorganisms to be engineered for the production of complex plant-derived compounds. This approach addresses the challenges associated with traditional extraction methods, such as slow plant growth or the limited availability of certain species (Zhou *et al.*, 2022). Engineered bacteria or yeast can now biosynthesize high-value phytochemicals in controlled laboratory settings, ensuring a sustainable and scalable production of these compounds (Dixon and Strack, 2021).

Through these advancements, the collaboration between phytochemistry and biotechnology is shaping the future of phytomedicine, offering innovative strategies to harness the therapeutic power of plants for modern healthcare applications (Pandey *et al.*, 2023). For more insights on the biochemical diversity and applications of plant-derived compounds, see Wink (2015), and for information on biotechnological approaches, consult Kirby and Keasling (2009).

6. Innovative Extraction and Formulation Techniques

Advancements in extraction and formulation techniques have greatly enhanced the efficacy and delivery of phytomedicines. Modern extraction methods, such as supercritical CO_2 extraction and ultrasonic-assisted extraction, provide more efficient means of obtaining bioactive compounds from plants. For instance, supercritical CO_2 extraction utilizes CO_2 at high pressure and temperature to extract compounds without relying on harmful solvents, making it both environmentally friendly and effective in preserving the purity of the compounds (Sahena *et al.*, 2021). This method ensures that sensitive phytochemicals, including essential oils and flavonoids, are extracted without degradation. Similarly, ultrasonic-assisted extraction employs high-frequency sound waves to enhance the extraction process, increasing the yield while maintaining the integrity of the bioactive compounds (Chemat *et al.*, 2021). These advancements reduce dependence on toxic solvents and help preserve the medicinal properties of the plants, resulting in safer and more potent phytomedicinal products (Vaou *et al.*,2021)

In addition to extraction methods, innovations in formulation have revolutionized the delivery of phytomedicines. The development of nanoparticles and liposomal delivery systems has significantly improved the bioavailability of plant-based compounds. Nanoparticles are engineered to encapsulate bioactive molecules, shielding them from degradation and enhancing their absorption in the body (Sharma

et al., 2022). This targeted delivery system enables phytomedicines to reach specific tissues or organs, thereby increasing therapeutic efficacy while minimizing side effects. Liposomes, which are tiny vesicles composed of phospholipids, also play a vital role in enhancing the solubility and stability of phytomedicines, particularly those poorly soluble in water. These formulations improve the absorption of active compounds, allowing for more effective and sustained therapeutic effects (Kumari *et al.*,2022). Together, these innovations in extraction and formulation are paving the way for the future of phytomedicine, making plant-based therapies more potent, safe, and accessible for patients (Zhao *et al.*, 2023).

7. Clinical Applications and Case Studies

Phytomedicine has shown significant clinical applications across various fields, highlighting the therapeutic potential of plant-based compounds. In cancer treatment, phytochemicals like curcumin extracted from turmeric have attracted considerable attention for their anti-cancer properties. Curcumin has been demonstrated to inhibit cancer cell growth, reduce inflammation, and enhance the effectiveness of chemotherapy and radiation therapy when used as a complementary treatment (Aggarwal *et al.*, 2020). Its role in cancer therapies exemplifies how phytomedicines can complement conventional treatments and improve patient outcomes, with ongoing research aimed at exploring its full potential ((Tauchert, 2021).

In cardiovascular health, plant extracts such as garlic and hawthorn have shown promise in managing cholesterol levels and enhancing overall heart health. Garlic has been extensively studied for its ability to lower blood pressure and reduce cholesterol, while hawthorn is recognized for its vasodilatory effects and its use in treating heart failure and other cardiovascular conditions (Tauchert, 2021). These plant-based therapies provide alternative or adjunctive approaches for managing cardiovascular diseases, which remain leading causes of mortality worldwide.

A notable case study demonstrating the efficacy of phytomedicine is the use of artemisinin, derived from the sweet wormwood plant, in treating malaria. Discovered by Tu (2011) artemisinin revolutionized malaria treatment due to its rapid action against the malaria parasite. This ground breaking discovery earned the Nobel Prize in Physiology or Medicine in 2015 and stands as a landmark achievement in modern medicine, illustrating the powerful role phytomedicines can play in combating life-threatening diseases (Alter *et al.*, 2016). The success of artemisinin has inspired further exploration of plant-based compounds for treating infectious diseases and other complex health conditions. These examples underscore the growing significance of phytomedicine in modern healthcare, showcasing its versatility and effectiveness

across diverse medical fields. Research into plant-based therapies continues to expand, offering promising avenues for future clinical applications.

8. Challenges and Considerations

Despite the significant promise of phytomedicine, several challenges must be addressed to fully realize it's potential. One of the primary concerns is the regulatory framework governing phytomedicines, which varies widely across different regions. In many parts of the world, comprehensive guidelines for assessing the safety, efficacy, and quality of plant-based products are either inadequate or inconsistent. This fragmented regulatory landscape can lead to issues with product standardization, where differing formulations and preparation methods may impact therapeutic outcomes. Establishing universal regulatory standards is essential to ensure that phytomedicines meet the same rigorous criteria as conventional pharmaceuticals, ultimately enhancing patient safety and trust (Jiang *et al.*, 2022; Liu *et al.*, 2022).

Another significant challenge relates to quality control and safety. Given the natural variability of plant sources, there is a risk of contamination, adulteration, or inconsistencies in the active compounds of phytomedicines. Without stringent testing and standardized production methods, consumers may encounter products of uneven quality or efficacy (Smith *et al.*, 2022). Implementing robust quality control measures, such as Good Manufacturing Practices (GMP), is crucial to mitigate these risks. GMP protocols ensure that every stage of production, from sourcing plant materials to final packaging, adheres to high standards, thereby minimizing contamination and ensuring the potency and purity of the products (Zhou *et al.*, 2022). By addressing these challenges, phytomedicine can evolve into a more reliable and trusted component of healthcare, meeting the safety and efficacy standards necessary for broader acceptance and integration into mainstream medical practice (Shah *et al.*, 2022).

9. The Future of Phytomedicine

The future of phytomedicine appears promising, driven by several key trends shaping its evolution. One significant development is the potential for personalized medicine. By tailoring phytomedicinal treatments to individual genetic profiles, the effectiveness of plant-based therapies can be optimized. Understanding how specific plant compounds interact with genetic variations allows for more precise and targeted therapeutic approaches, potentially improving outcomes for patients with chronic conditions or those who respond differently to conventional treatments. Studies indicate that advancements in pharmacogenomics are paving the way for more personalized herbal medicine approaches, enhancing efficacy and minimizing adverse effects.

Moreover, the emphasis on sustainability and ethical sourcing in phytomedicine is gaining traction. As demand for medicinal plants increases, sustainable harvesting practices are crucial for preserving biodiversity and preventing the over-exploitation of natural resources. This is particularly vital for ensuring the availability of medicinal plants for future generations. Ethical bioprospecting is also an essential consideration, ensuring that indigenous communities, who often possess traditional knowledge of medicinal plants, receive fair compensation for their contributions. Sustainable practices and equitable benefit-sharing models are highlighted as critical components in bioprospecting. These approaches promote fair access to plant-based resources while ensuring that biodiversity and cultural heritage are respected and preserved as phytomedicine continues to advance.

10. Digital Health and Phytomedicine

Advancements in digital health, such as mobile applications and telemedicine, are revolutionizing the integration of phytomedicine into mainstream healthcare by enhancing access, patient education, and informed decision-making.

- ***Mobile applications*** provide functionalities like plant identification, access to extensive phytomedicinal databases, and personalized health tracking. They empower patients with reliable information about plant-based therapies, enabling users to monitor their health and make informed decisions about the safe use of phytomedicine. (Liu *et al.*, 2020).
- ***Telemedicine*** enhances access to expert guidance on phytomedicinal treatments, particularly in remote areas. Patients can consult practitioners online, receive personalized recommendations, and effectively manage chronic conditions through a combination of herbal and conventional therapies.

Together, these technologies promote the evidence-based use of phytomedicine, fostering patient empowerment and improving health outcomes, as emphasized in studies from BMC Complementary Medicine and the Journal of Medical Internet Research (Bae *et al.*, 2021; Furlong *et al.*, 2022).

11. Conclusion

Phytomedicine occupies a unique space where tradition meets innovation, providing promising solutions for modern health challenges. As scientific advancements progress, the potential of plant-based therapies to enhance health and well-being becomes ever more evident. Effective collaboration among researchers, healthcare practitioners, and regulatory bodies will be crucial to fully harness the benefits of phytomedicine while ensuring its safety, efficacy, and sustainability. The

path toward a future enriched by phytomedicine not only honors ancient wisdom but also serves as a beacon of hope for innovative therapeutic strategies.

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Molecular Docking and In silico Screening of Potentilla fulgens for Potential Antidiabetic Compounds

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Chapter - 12

Phytomedicine Innovations: The Future of Plant – Based Therapies
ISBN: 978-81-977907-4-4
First Edition
Chapter – 12, Page: 175 - 195

12

MOLECULAR DOCKING AND *In silico* SCREENING OF *Potentilla fulgens* FOR POTENTIAL ANTIDIABETIC COMPOUNDS

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Abstract

Diabetes, a chronic metabolic disorder that disrupts glucose levels in the body due to lack of insulin production or function. Bajradanti (*Potentilla fulgens*), grown in tropical and subtropical regions of North-East India has various traditional usage in Ayurvedic medicines like anti-inflammatory, analgesic, antipyretic, antimicrobial, antioxidant, and antidiabetic effects. Over expression of α-Glucosidase can cause excessive breakdown of complex carbohydrates to glucose, leading to type 2 diabetes. In this study, the antidiabetic effect of Bajradanti was evaluated using *in silico* study. Bajradanti has enormous bioactive compounds, which can be potentially responsible for its antidiabetic activities. 5 bioactive compounds such as Epicatechin, Potifulgene, Rutin, Epiafzelchin and Afzelchin were among the compounds shortlisted for the study. Various *in silico* methods such as selection of α-glucosidase protein from RCSB PDB, ADME (Absorption, Distribution, Metabolism, Excretion) study was done using SwissADME software, toxicity profiling with ProTox-3.0 software, protein preparation using Biovia DiscoveryStudio and Molecular docking using PyRx

software were executed methodically. This understanding opens a doorway in the futureto find more susceptible plant-based drug solutions against diabetes.

Keywords: α-glucosidase, Diabetes, Molecular docking and *Potentilla fulgens.*

1. Introduction

1.1. Diabetes

Diabetes is a metabolic disorder marked by elevated blood sugar levels, which arise from issues with insulin production or its effectiveness, or a combination of both. Typically, insulin, a hormone secreted by the β-cells in the pancreas's islet of Langerhans, maintains blood glucose levels within a narrow range by facilitating glucose uptake into cells. Insulin deficiency or receptor dysfunction is pivotal in all diabetes types. The earliest records of diabetes date back to ancient Egypt, where it was noted for symptoms such as weight loss and frequent urination. The term "diabetes mellitus," coined by the Greek physician Araetus, combines the Greek word for "to pass through" with the Latin word for "honey," referencing the sweetness of urine (Alberti and Zimmet, 1998; Ahmed, 2002). According to the World Health Organization (WHO), diabetes is a chronic condition defined by persistently high blood glucose levels, which over time can severely damage the heart, blood vessels, eyes, kidneys, and nerves. Type 2 diabetes is the most prevalent form, typically occurring in adults, and results from insulin resistance or inadequate insulin production. Over the last 30 years, the incidence of type 2 diabetes has significantly increased across all economic levels. Type 1 diabetes, formerly known as juvenile or insulin-dependent diabetes, is a lifelong condition where the pancreas produces little to no insulin. Access to affordable treatments, especially insulin, is essential for individuals with diabetes to manage their condition effectively. Prolonged high blood glucose can lead to serious complications, including vision loss, kidney failure, nerve damage, strokes, and limb amputations (Brownlee, 2001; Chawla *et al.*, 2016). Symptoms and related conditions may include hyperglycemia, hyperlipidemia, oxidative stress, increased urination, excessive hunger, increased thirst, kidney issues, nerve damage, and cardiovascular problems (Mayfield, 1998). These complications can be managed or reduced by keeping blood sugar levels near normal. Treatment strategies vary depending on the type and severity of diabetes. Both acute and chronic complications pose significant risks. Acute issues may involve extremely high or dangerously low blood sugar due to medications, while chronic complications can affect both small and large blood vessels, impacting the eyes, kidneys, nerves, and heart. Type 1 diabetes treatment focuses on insulin, exercise, and dietary management,

while Type 2 diabetes initially emphasizes weight loss, diet, and exercise. If blood sugar remains uncontrolled, oral medications may be prescribed, and insulin treatment may be introduced if necessary (Irons and Minze, 2014).

1.2. Types

Diabetes mellitus is commonly divided into two principal types, each distinct in etiologyand clinical presentation:

- ***Type 1 Diabetes*:** Type 1 diabetes is an autoimmune disorder in which the immune system mistakenly targets and destroys the insulin-producing beta cells in the pancreas, resulting in insufficient insulin production. Consequently, individuals with type 1 diabetes depend on insulin injections or pumps to manage their blood sugar levels. This condition can develop at any age but predominantly affects children (IDF Diabetes Atlas - Fifth Edition).
- ***Type 2 Diabetes*:** Type 2 diabetes, also referred to as non-insulin-dependent or adult-onset diabetes, is marked by insulin resistance, which means that tissues such as muscles and fat do not respond effectively to insulin. Initially, the pancreas compensates by producing more insulin, but eventually, it cannot sustain the necessary levels for adequate blood sugar control. This form of diabetes is often linked to lifestyle factors such as obesity and lack of physical activity. Management typically involves lifestyle changes, oral medications, and occasionally insulin therapy (Wang *et al*., 2012; Artanti *et al*., 2023).
- ***Gestational Diabetes*:** This type occurs in some women during pregnancy and usually resolves after giving birth. However, it does increase the risk of developing type 2 diabetes later in life.
- ***Other Specific Types*:** Other less common forms of diabetes result from specific genetic syndromes, surgery, drugs, malnutrition, infections, and other illnesses.

Each type of diabetes has its challenges and health implications, and managing the condition effectively involves understanding these distinct differences and tailoring treatment accordingly.

1.3. Global Burden

In 2019, approximately 463 million individuals worldwide were living with diabetes, a significant increase from 108 million in 1980 (Figure - 1). This rise

correlates with higher rates of risk factors like overweight and obesity. Over the last decade, diabetes prevalence has escalated more rapidly in low and middle-income countries compared to high-income nations. In 2012, diabetes was responsible for 1.5 million deaths, while an additional 2.2 million deaths were linked to elevated blood glucose levels, which raise the risk of cardiovascular and other diseases. Notably, 43 % of the 3.7 million diabetes-related deaths occurred in individuals under 70, with this rate being higher in low- and middle-income countries. According to the World Health Organization (WHO), diabetes is projected to become the leading cause of death globally by 2030. The growing number of diabetes cases is a pressing global issue, contributing to significant health complications and premature mortality, with nearly one death every 10 seconds, surpassing fatalities from HIV/AIDS. The condition has become a worldwide epidemic, driven by industrialization and rising obesity rates. Accurate prevalence measures are challenging due to differing data collection standards worldwide; however, recent forecasts suggest that adult diabetes prevalence will increase from 4 % in 1995 to 6.4 % by 2025 (King *et al.*, 1998). In developed countries, cases may rise by 42 %, while developing countries could see a staggering 170 % increase. The total number of adults with diabetes is expected to grow from 194 million in 2003 to nearly 380 million by 2025, with India, China, and the USA being the most affected. Alarmingly, nearly half of those with diabetes remain undiagnosed (WHO, 2016 global report).

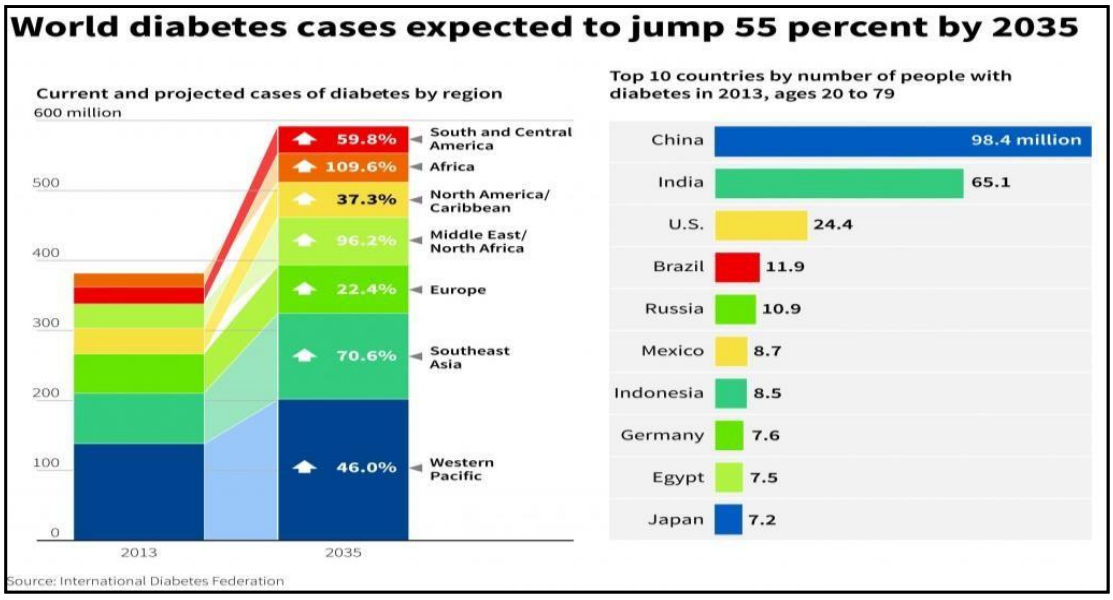

Figure - 1: Graphical representations of possible cases of diabetic population up to 2035 (Source: International Diabetes Federation)

1.4. Diabetes Outbreak in India

In India, approximately 77 million individuals over the age of 18 are living with type 2 diabetes, and nearly 25 million are classified as prediabetic, putting them at a higher risk of developing the condition. Alarmingly, over 50 % of those affected are unaware of their diabetes status, which can lead to serious health complications if not identified and treated promptly. Adults with diabetes face a two- to three-fold increased risk of heart attacks and strokes. Additionally, reduced blood flow combined with neuropathy (nerve damage) can heighten the risk of foot ulcers, infections, and potential limb amputations. Diabetic retinopathy, resulting from long-term damage to the small blood vessels in the retina, is a significant cause of blindness. Furthermore, diabetes is one of the leading causes of kidney failure in the country. India ranks second globally in terms of the number of diabetes patients. In the age group of 20 to 79 years, the diabetic population was 74.9 million in 2021, with projections indicating an increase to 124.9 million by 2045 (Federation, I. D. IDF Diabetes Atlas 10th Edition, Preprint 2021).

1.5. Risk Factors

1.5.1. Modifiable Risk Factors

- ***Obesity and Overweight*:** Excess body weight, especially in the abdominal area, is linked to insulin resistance and an increased risk of developing type 2 diabetes (Barrea *et al.*, 2023).
- ***Physical Inactivity*:** Inadequate physical activity can contribute to weight gain and insulin resistance, both of which are key risk factors for type 2 diabetes (Barrea *et al.*, 2023).
- ***Unhealthy Diet*:** The intake of high-calorie, ultra-processed foods and Western-style diets is associated with a higher risk of developing type 2 diabetes. In contrast, healthier dietary patterns are linked to a reduced risk of this condition (Barrea *et al.*, 2023).
- ***Smoking*:** Smoking may contribute to the onset of type 2 diabetes and exacerbate itscomplications by promoting inflammation and cellular damage (McEwen *et al.*, 2012).
- ***High Blood Pressure*:** Hypertension, or high blood pressure, is commonly seen in individuals with diabetes and can worsen diabetic complications (McEwen *et al.*, 2012).
- ***Abnormal Cholesterol Levels*:** An imbalance in cholesterol levels, with high

triglycerides and low HDL cholesterol, can lead to insulin resistance, a precursor to type 2 diabetes (McEwen *et al.*, 2012).

1.5.2. Non-Modifiable Risk Factors

- ***Age*:** The type 2 diabetes can increase with age, which could be attributed to changes in insulin sensitivity or beta-cell function over time (McEwen *et al.*, 2012).
- ***Genetic Predisposition and Family History*:** A family history of diabetes suggests a genetic component to the disease, indicating a higher risk for relatives of people with diabetes (McEwen *et al.*, 2012).
- ***Race or Ethnic Background*:** Some ethnic groups have a higher prevalence of type 2 diabetes due to a combination of genetic, environmental, and lifestyle factors (McEwen *et al.*, 2012).
- ***History of Gestational Diabetes*:** Women who have experienced gestational diabetes are at a higher risk of developing type 2 diabetes later in life (McEwen *et al.*, 2012).

1.6. Symptoms of Diabetes Mellitus

- ***Increased thirst and frequent urination*:** High blood sugar levels cause excess glucose to be filtered by the kidneys and excreted through urine. This leads to increased urine production, resulting in increased thirst and frequent urination (American Diabetes Association, 2021).
- ***Unexplained weight loss*:** Insufficient insulin production or insulin resistance can hinder glucose from entering cells for energy use. Consequently, the body starts to break down fat and muscle tissue for energy, resulting in unexplained weight loss (Brennan *et al.*, 1998; Castro, 2022).
- ***Increased hunger*:** When insulin is not properly regulating blood sugar levels, the body's cells may not receive enough glucose. This can trigger excessive hunger as the body tries to compensate for the lack of energy (American Diabetes Association, 2021).
- ***Fatigue*:** In diabetes, the cells are not able to efficiently use glucose for energy due to lack of insulin or insulin resistance. This can lead to feelings of fatigue and lack of energy throughout the day (Brennan *et al.*, 1998; Castro, 2022).

- ***Slow healing of wounds*:** High blood sugar levels can impair the body's ability to heal wounds. This happens because elevated glucose levels can damage small blood vessels and affect the delivery of nutrients and oxygen to injured tissues (American Diabetes Association, 2021).
- ***Blurred vision*:** Elevated blood sugar levels can draw fluid from the eye lenses, causing them to swell and change shape. This may lead to blurred vision or difficulties with focus (Brennan *et al*., 1998; Castro, 2022).
- ***Numbness or tingling in the hands or feet*:** Extended periods of high blood sugar can harm nerves, resulting in peripheral neuropathy. This condition may lead to sensations of numbness, tingling, or burning in the hands, feet, or other areas (American Diabetes Association, 2021).
- ***Recurrent infections*:** Excessive blood sugar levels can impair the immune system, increasing the likelihood of infections in individuals with diabetes. Common infections in this context include urinary tract infections, yeast infections, and skin infections (Brennan *et al*., 1998; Castro, 2022).
- ***Dry skin and itchiness*:** High blood sugar levels can cause skin to become dry and itchy. This happens because elevated glucose levels can disrupt the normal functioning of sweat glands and decrease skin moisture (American Diabetes Association, 2021).
- ***Erectile dysfunction*:** Diabetes can affect blood flow and damage blood vessels, leading to erectile dysfunction in men. High blood sugar levels can also cause nerve damage that contributes to this condition (Brennan *et al*., 1998; Castro, 2022).

1.7. Diagnosis of Diabetes Mellitus

The clinical diagnosis of diabetes is typically initiated by symptoms like excessive thirst, increased urination, frequent infections, unexplained weight loss, and in severe instances, drowsiness or coma. The World Health Organization outlines specific criteria for diagnosing diabetes mellitus as follows:

In patients presenting with classic symptoms of hyperglycemia or a hyperglycemic crisis, a random plasma glucose level of ≥200 mg/dl (11.1 mM/l) is indicative of diabetes.

Alternatively, a fasting plasma glucose level of ≥126 mg/dl (7.0 mM/l) is diagnostic, with fasting defined as no caloric intake for at least 8 hours.

Additionally, a plasma glucose level of >200 mg/dl (11.1 mM/l) two hours after an oral glucose tolerance test (OGTT) confirms diabetes. The OGTT should follow the World Health Organization's guidelines, using a glucose load of 75g of anhydrous glucose dissolved in water.

If symptoms are not clear, diagnostic tests should be repeated on a different day. In situations where resources are limited and blood glucose testing is unavailable, diagnosis may also be made through urine testing for glucose and ketones (American Diabetes Association, 2021).

1.8. Management of Diabetes

Diabetes mellitus is a chronic condition that currently has no known cure, except in rare cases. The focus of management is to maintain blood sugar levels as close to normal (Euglycemia) as possible while avoiding hypoglycemia. This is typically achieved through a healthy diet, regular exercise, and the appropriate use of medications. Additionally, it is important to address other health issues that can worsen the negative effects of diabetes, such as smoking, high cholesterol, obesity, hypertension, and insufficient physical activity.They should undergo self-monitoring and Insulin therapy (Chaudhury *et al.*, 2017).

Different types of drugs to treat and to attain a well-being state with the ability to lead a normal activity and to maintain normal blood biochemistry include:

- ***Oral Hypoglycaemic Drugs*:** These are suitable for most adult patients. The basic types of oral antihyperglycemic drugs are as follows-
    a) *Sulphonylurea* - Tolbutamide, Glibenclamide, Chlorpropamide, Gliclazide.
    b) *Biguanides* - Metformin, Phenformin.
    c) *Intestinal alpha-glucosidase inhibitors* - Miglitol, Acarbose, Voglibose.
    d) Sodium-glucose co-transporter inhibitors- Dapagliflozin, Canagliflozin, Sergliflozin, Ramogliflozin.
    e) Thiazolidinediones- Rosiglitazone, Pioglitazone
- ***Insulin Injection*:** Mostly used in serious cases of diabetes.

1.9. Alpha Glucosidase Inhibitors

It is well known that alpha-glucosidase catalyzes the final step of carbohydrate digestion within biological systems. This significance has led to numerous efforts aimed at developing effective inhibitors of alpha-glucosidase, known as alpha-glucosidase inhibitors. These agents are valuable for studying the enzyme's mechanisms at the molecular level and for creating therapeutic agents for conditions linked to carbohydrate metabolism, such as diabetes, cancer, HIV, hepatitis, certain types of hyperlipoproteinemia, and obesity (Truscheit *et al.*, 1981; McCulloch *et al.*, 1983). Over the past two decades, there has been a growing interest in discovering inhibitors that can further investigate the structure and function of alpha-glucosidase. Many effective inhibitors have been identified, including acarbose and voglibose derived from microorganisms, as well as 1-deoxynojirimycin, which is extracted from plants (Asano *et al.*, 1995; Gao *et al.*, 2007). Recently, flavones and their derivatives have garnered significant attention as a new category of alpha-glucosidase inhibitors due to their potent inhibitory properties (Gao *et al.*, 2007; Wang *et al.*, 2010).

1.10. Mechanism of Alpha-glucosidase Inhibitors

α-Glucosidase is an enzyme found in the brush border of the small intestine, where it catalyzes the hydrolysis of α-glycosidic bonds in oligosaccharides, releasing monosaccharide units that are then absorbed into the blood stream (Hostettmann and Miura, 1977). Inhibiting α-glucosidase effectively delays the absorption of dietary carbohydrates, helping to reduce postprandial hyperglycemia. This mechanism distinguishes acarbose and voglibose from other diabetes medications, such as biguanides and sulfonylureas. Acarbose and voglibose act as high-affinity, reversible inhibitors of intestinal α-glucosidase enzymes, specifically targeting pancreatic α-amylase and membrane-bound intestinal α-glucosidase (Figure - 2). Pancreatic α-amylase breaks down complex carbohydrates into oligosaccharides in the lumen of the small intestine, while intestinal glucosidase further hydrolyzes these oligosaccharides, disaccharides, and trisaccharides into glucose and other absorbable monosaccharides at the brush border of the small intestine.

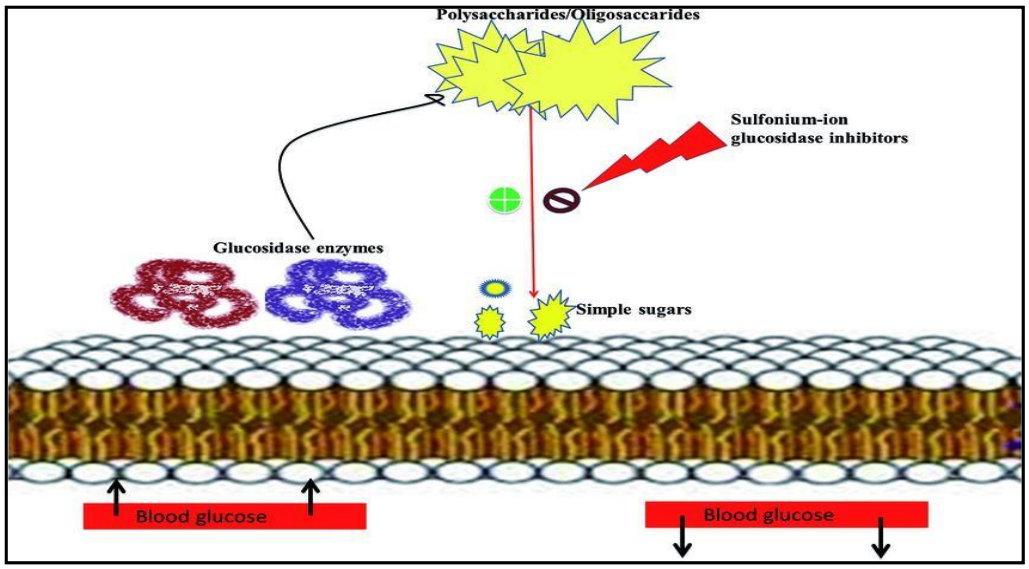

Figure - 2: Mechanism of Alpha-glucosidase Inhibitors (Source: Hostettmann and Miura, 1977)

Inhibiting these enzymes decreases the rate at which "absorbable sugar" is produced, leading to a delay in the increase of blood sugar levels after meals (postprandial). This effect can result in a reduction of postprandial plasma glucose by 30 – 35 %, as well as lower peaks in insulin, gastric inhibitory polypeptide, and triglycerides (Hostettmann and Miura, 1977).

2. Bajradanti (*Potentilla fulgens*)

Potentilla fulgens, commonly known as Himalayan Cinquefoil, is a perennial herb belongingto the Rosaceae family (Barua and Yasmin, 2018, Ardalani *et al.*, 2021; Kumari *et al.*, 2021). This plant is native to the Himalayan region,extending across India, Nepal, Bhutan, and other parts of South Asia (Figure - 3). It thrives in the high-altitude regions, often found growing on rocky slopes and meadows.

Figure 3: *Potentilla fulgens*

2.1. Botanical Characteristics

Potentilla fulgens exhibit a distinctive morphology characterized by its trifoliate leaves and bright yellow flowers (Barua and Yasmin, 2018; Pariyar *et al.*, 2020; Ardalani *et al.*, 2021). The plant's root system is robust, allowing it to anchor firmly in rocky terrains. The leaves are serrated, and the flowers, typically blooming from June to September, are five-petaled and vibrant, contributingto the plant's aesthetic appeal and ecological significance (Joshi *et al.*, 2016).

2.2. Traditional and Medicinal Uses

In traditional medicine, particularly Ayurveda and local indigenous practices, *Potentilla fulgens* is revered for its therapeutic properties (Roy *et al.*, 2010; Joshi *et al.*, 2016; Barua and Yasmin, 2018). The plant is commonlyknown as "Bajradanti" in India, a name that underscores its association with dental health— 'Bajra' meaning strong and 'Danti' referring to teeth. It has been traditionally used to treat dental problems such as toothaches and gum diseases. Additionally, it is utilized for its anti-inflammatory, astringent, and antimicrobial properties, making it a versatile remedy for various ailments including gastrointestinal issues, skin diseases, and fever (Jinarathne *et al.*, 2021).

2.3. Phytochemical Composition

The medicinal efficacy of *Potentilla fulgens* is attributed to its rich phytochemical composition.The plant contains several bioactive compounds, including flavonoids (such as epicatechin andrutin), tannins, and phenolic acids (Tomczyk and Latté, 2009; Pandey *et al.*, 2024). These compounds are known for their antioxidant properties, which contribute to the plant's ability to combat oxidative stress and inflammation (Jaitak *et al.*, 2010). Studies have also indicated the presence of specific compounds like afzelchin and epiafzelchin, which further enhance its medicinal value (Syiem *et al.*, 2003).

2.4. Research Significance

Research on *Potentilla fulgens* has gained momentum due to its potential health benefits and the growing interest in natural and plant-based remedies (Thabah *et al.*, 2023). Scientificinvestigations aim to isolate and characterize the active compounds in *Potentilla fulgens*, understanding their mechanisms of action, and validating traditional uses with modern pharmacological evidence (Roy *et al.*, 2010). This plant serves as a promising candidate for the development of new therapeutic agents, especially in the

context of dental care and the management of chronic diseases associated with oxidative stress and inflammation.

2.5. Conservation and Sustainable Use

Given its ecological niche in the fragile Himalayan ecosystem, conservation of *Potentilla fulgens* is crucial (Dhar *et al*., 2000). Sustainable harvesting practices are essential to ensure that valuable medicinal resource is not overexploited. Conservation efforts must balance the needs of local communities who depend on the plant for traditional medicine with the imperatives of biodiversity preservation. *Potentilla fulgens*, with its rich heritage in traditional medicine and promising pharmacologicalproperties, represents a valuable plant species both culturally and scientifically. Continued research and sustainable management are key to unlocking its full potential and ensuring its availability for future generations (Kaul *et al*., 2011).

3. *In silico* Study on *Potentilla fulgens* for Antidiabetic Properties

The virtual designing of the various components (Epicatechin, Potifulgene, Rutin, Epiafzelechin, Afzelchin) of Bajradanti was done using *in silico* process. Drawing of these designedcompounds along with conversion of 2D structure to 3D was done in ChemDraw Ultra 8.0software. Further molecular properties and toxicity was studied using Molinspiration Cheminformatics, Swiss ADME, and Pro Tox-3.0 software. For protein and ligand preparation and generation of bioactive binding poses of inhibitor molecular docking study will be carried out using BIOVIA Discovery Studio 2021 Client and PyRx software. *In silico* prediction studies focus on exploring the antidiabetic potential of bioactive compounds derived from *Potentilla fulgens* which discusses various computational methods utilized to predict the pharmacological activities of these compounds, providing insights into their molecular mechanisms of action and therapeutic potential in diabetes management (Şöhretoğl *et al*., 2017). Studies found exploring the role of *Potentilla fulgens* in mitigating oxidative stress and inflammation, both of which are implicated in the pathogenesis of diabetes using the computational methods to elucidate the antioxidant and anti-inflammatory properties of bioactive compounds from *Potentilla fulgens*. *In silico* studies investigating the pharmacokinetic properties of bioactive compounds from *Potentilla fulgens* using the computational methods can help predict Absorption, Distribution, Metabolism, and Excretion (ADME) properties, providing insights into their bioavailability and therapeutic potential.

3.1 Design and In silico study

- **CHEMDRAW ULTRA 8.0** for design of library of compounds.
- **MOLINSPIRATION CHEMINFORMATICS** for calculation of various molecular properties needed in QSAR, molecular modeling and drug design.
- **Pro Tox-3.0** for toxicity profile of the designed compounds.
- **BIOVIA DISCOVERY STUDIO** for protein preparation, ligand preparation and amino acid interactions.
- **PyRx** for calculation of binding energies of those designed compounds

3.1.1. Preparation of Ligands

Using Chemdraw Ultra 8.0, a library of compounds (ligands) was prepared. The designed compounds were saved in mol format (3D structure) for dockingstudies.

3.1.2. Study of various parameters using Molinspiration Cheminformatics which are mentioned below

- Milog P value
- TPSA value
- Number of atoms (N-atoms)
- Molecular weight (MW)
- Number of H-bonds acceptors
- Number of H-bonds donors
- Number of violations (nviolations)
- Number of rotable bonds (nrtable)

3.1.3. Toxicity Profile Studies using Pro Tox-3.0

- Mutagenecity
- Carcinogenecity
- Cytotoxicity
- Hepatotoxicity

3.1.4. Preparation of Protein

The 3D structure of the protein was obtained from the RCSB PDB (Research Collaboratory for Structural Bioinformatics Protein Data Bank), with the selected protein having the PDB ID 7JTY. It was downloaded in PDB text file format.

3.1.5. Protein-Ligand Docking Study

The aim of the molecular docking study is to identify the orientation and interaction between the protein and ligand. Input files for docking were generated using BIOVIA DISCOVERY STUDIO. The grid region was defined around the active site to facilitate binding. This grid was selected based on the amino acid residues that indicate the most favorable area for interaction.

3.1.6. Binding Energy Calculation

Binding Site analysis is a quick detection tool for "the identification and monitoring of potential binding sites" and "the distribution of surrounding residues in the active sites". After docking the binding energy is calculated ofthe binding interactions (i.e. binding energy in kcal/mol) between protein andligand by using PyRx software.

3.2. Molecular property determination using Swiss ADME Software

Molecular Property of the selected chemical compounds was determined usingMolinspiration property calculator and Swiss ADME software (Table - 1).

Table - 1: Molecular Property Determination using Swiss ADME Software

Chemical Compound	Lipinski's Parameters							Drug Likeness		Synthetic Accessibility
	MW (g/mol)	LogP	nHBA	nHBD	TPSA(Å²)	N. violation	nrotb	Aqueous Solubility Class	GI Absorption	
Epicatechin	290.27	0.24	6	5	110.38	0	1	Soluble	High	3.50
Potifulgene	528.55	2.46	8	5	128.84	1	4	Poorly soluble	Low	5.19
Rutin	610.52	- 3.89	16	10	269.43	3	6	Soluble	Low	6.52
Epiafzelechin	274.27	0.79	5	4	90.15	0	1	Soluble	High	3.39
Afzelchin	562.52	0.23	11	9	200.53	3	3	Moderately soluble	Low	5.27

Lipinski's Rule of Five is a set of guidelines to evaluate the drug-likeness of a compound, specifically its potential as an orally active drug in humans. According to these rules, a compound is more likely to be absorbed well if:

a) Molecular Weight (MW): Less than 500 g/mol.
b) Lipophilicity (Log P): Less than 5.
c) Hydrogen Bond Acceptors (nHBA): 10 or fewer.
d) Hydrogen Bond Donors (nHBD): 5 or fewer.

3.3. Toxicity study using Pro Tox-3.0 Software

All the studied compounds (Epicatechin, Potifulgene, Rutin, Epiafzelechin, Afzelchin) were found to be inactive for mutagenicity, carcinogenicity, cytotoxicity, and hepatotoxicity according to Pro Tox-3.0 software, with varying probability scores indicating the confidence level of these predictions (Table - 2).

Table - 2: Evaluation of Toxicity using Pro Tox-3.0 software

Component Name	Mutagenicity	Carcinogenicity	Cytotoxicity	Hepatotoxicity
Epicatechin	Inactive	Inactive	Inactive	Inactive
Potifulgene	Inactive	Inactive	Inactive	Inactive
Rutin	Inactive	Inactive	Inactive	Inactive
Epiafzelechin	Inactive	Inactive	Inactive	Inactive
Afzelchin	Inactive	Inactive	Inactive	Inactive

3.4. Molecular Docking Study

Molecular docking is typically employed to identify how proteins and ligands interact and orient themselves (Li *et al.*, 2019). The PyRx software was used to generate the input files for docking. The grid area was defined around the active site to facilitate binding. This grid was chosen based on the amino acid residues associated with the binding site of Acarbose, a standard drug obtained from the PDB entry 7JTY, which was deemed the optimal active region for favorable interactions (Figure - 4). Molecular docking and virtual screening analyses to identify potential α-glucosidase inhibitors from *Potentilla fulgens*. The study identified several bioactive compounds with high binding affinity to the target enzyme, suggesting their potential as therapeutic agents for controlling postprandial hyperglycemia in diabetes. Computational exploration of phytochemicals from *Potentilla fulgens* helps to evaluate their potential as α-amylase inhibitors using molecular docking studies, identification of several compounds with promising inhibitory activity against the target enzyme, suggesting their utility in controlling starch digestion and postprandial blood glucose levels. Molecular docking simulations plays a key role to investigate the interaction between bioactive compounds from *Potentilla fulgens* and key enzymes involved in glucose metabolism, including α-glucosidase and α-amylase which can suggest the potential of these compounds as dual inhibitors for managing postprandial hyperglycemia. Docking

studies can also help to evaluate the inhibitory activity of bioactive compounds from *Potentilla fulgens* against aldose reductase, an enzyme involved in the polyol pathway associated with diabetic complications which can potentially lead us to the compounds for further experimental validation as aldose reductase inhibitors (Agarwal and Mehrotra, 2016). Molecular docking studies can help understand the interaction between bioactive compounds from *Potentilla fulgens* and key enzymes involved in glucose metabolism, including glycogen synthase kinase-3β (GSK-3β) which can identify potential GSK-3β inhibitors, suggesting their utility in regulating glycogen synthesis and glucose metabolism in diabetes. Molecular dynamics simulations can help us to study the dynamic behavior of bioactive compounds from *Potentilla fulgens* when bound to their target proteins, such as peroxisome proliferator-activated receptor gamma (PPAR-γ) elucidating the conformational changes and stability of the ligand-protein complexes, providing insights into their therapeutic potential in diabetes.

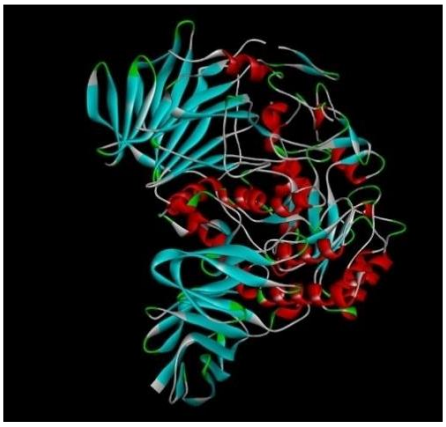

Figure - 4: 3D Structure of Prepared Co-crystal structure of Alpha Glucosidase (7JTY)

Therefore, through molecular docking studies we can sort all the compounds into standard antidiabetic drugs (Acarbose):

- Afzelchin < Acarbose
- Potifulgene < Acarbose
- Rutin < Acarbose
- Epicatechin < Acarbose
- Epiafzelechin < Acarbose

We can find all the compounds of Bajradanti to show a profound docking score with respect to the standard antidiabetic drug (Acarbose). Afzelchin, Potigulgene and Rutin have shown the best possible binding affinity among the selected compounds of Bajradanti.

4. Conclusion and Future Prospect

Bajradanti demonstrates promise as a treatment for diabetes due to its diverse mechanisms of action. Historically used for various health applications, including oral and skincare, it has also proven effective for its antidiabetic properties. Our research aimed to explore the potential of specific compounds within Bajradanti, employing *in silico* studies to enhance laboratory experiments. This computational approach is invaluable for conserving time, costs, and resources, allowing us to predict the efficacy of selected compounds against diabetes. The molecular docking analysis indicated that the compounds could significantly inhibit the overexpression of α-Glucosidase, a key enzyme in diabetes. Among the five compounds studied, Afzelchin, Potifulgene, and Rutin exhibited the highest binding affinities. Interestingly, these compounds showed more violations of Lipinski's parameters compared to Epicatechin and Epiafzelchin, despite their superior docking scores with our target protein (7JTY). This finding highlights the complexities of compound compatibility and their potential applications in various health contexts. Looking ahead, the promising results pave the way for several research avenues in diabetes treatment. Future studies should focus on in vivo testing to validate the efficacy and safety of these compounds in clinical settings. Additionally, insights from the molecular docking studies can guide the design of more potent derivatives, exploring structural modifications to enhance binding affinity while minimizing violations of drug-like properties. Integrating *in silico* approaches with laboratory experiments will streamline the drug discovery process, facilitating the identification of lead candidates. Collaborative efforts among chemists, biologists, and pharmacologists will be essential for advancing this research. Finally, the phytochemical diversity of Bajradanti invites exploration of its other therapeutic applications, potentially unlocking new treatment strategies for various ailments beyond diabetes and solidifying its role in modern medicine.

Acknowledgement

The authors are thankful to the Department of Biotechnology, Haldia Institute of Technology for providing necessary facilities to carry out the experiments of this work. The authors acknowledge Dr. Ruma Satra for upgrading the efficacy of the English language used in the manuscript.

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Phytoremedies: Plant Materials as Drugs for Illness

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Chapter - 13

Phytomedicine Innovations: The Future of Plant – Based Therapies
ISBN: 978-81-977907-4-4
First Edition
Chapter – 13, Page: 196 - 202

13

PHYTOREMEDIES: PLANT MATERIALS AS DRUGS FOR ILLNESS

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Abstract

Plants and plant-derived materials have been used for centuries as effective remedies for various ailments, forming the foundation of traditional medical systems such as Ayurveda and Traditional Chinese Medicine. Known as phytomedicines, these plant-based treatments contain a wide array of bioactive compounds, including flavonoids, carotenoids, polyphenols, and phytosterols, which exhibit significant biological activities such as anti-inflammatory, antioxidant, antimicrobial, and anti-cancer effects. Modern pharmaceuticals continue to benefit from these natural sources, with an estimated 25–50% of medications derived from plant materials or their synthetic analogs. Phytomedicine offers numerous advantages, including affordability, reduced side effects, and environmental sustainability, making it a valuable option for preventive care, chronic disease management, and symptomatic treatment. However, challenges such as variability in plant composition, potential interactions with conventional drugs, regulatory inconsistencies, and limited clinical validation highlight the need for rigorous research and standardized practices. With ongoing scientific advances and a growing emphasis on natural and sustainable healthcare solutions, phytomedicines hold promising potential for future pharmaceutical and therapeutic applications.

Keywords: Plants, Phytoremedies, Phytochemicals, Drugs, Plant materials and Human illness.

1. Introduction

Plants and plant materials were used as medicines for centuries for different ailments due presence of many compounds present within them. The plant based medicines are called as phytomedicnes, phytopharmaceuticals, herbal medicines or botanicals (Astin, 1998; Sam, 2019). Most of the modern medicines have been derived from plant materials which are used as medicines to cure different ailments or diseases or infections. The plant materials such as leaves, root, stem, bark, resins, oil, seeds, flowers, fruits were used as herbal remedies in traditional medicines and in modern days (Avery and Hains, 2017). Plants materials consist of various bioactive compounds like carotenoids, flavonoids, carnitine, choline, coenzyme Q, dithiolthiones, phytosterols, phytoestrogens, polyphenols and taurine (Cushnie *et al.*, 2008; Dar *et al.*, 2023). These compounds posses various biological and functional activities such anti-inflammatory, anti-oxidant, anti-diabetic, anti-cancer and anti-microbial properties (Singh *et al.*, 2008; Grover *et al.*, 2002)

2. Benefits of Phytomedicine

The common benefits of medicinal plants is used to boost the immune system, digestive issues, anti-inflammatory and effectiveness of herbal remedies depends on the dosage, method of preparation and health condition of the individual (Petrovska, 2012; Jamshidi-Kia *et al.*, 2017; Martin *et al.*, 2020). Some of the plants may induce the side effects vary from mild to severe (Balunas and Kinghorn, 2005). Currently researchers are involved in exploring the traditional knowledge information's can be applied in the modern medicine. Nutraceutical and drug research now considers systematic searching for useful bioactive compounds from medicinal plants to be a rational approach (Puri *et al.*, 2022, Silna *et al.*, 2023).

There are major benefits of using herbal medicines are cost effective, natural healing and mitigating risk of side effects. The major benefits of plant based medicines are it produces less carbon, reduces the amount of waste sent to landfill, and doesn't produce any toxins when broken down. More than hundreds of drugs have been formulated from the medicinal plants to cure diseases and infection in humans and animals. There are different key aspects of plant based medicines such as presence of active ingredients, herbal extracts, essential oils, whole herbs are used as preventive medicine, chronic diseases and symptomatic treatment. Many clinical trials are necessary to determine whether the combined effect of multiple compounds can be more effective due to the increase in phytomedicines (Hamilton, 2004; Yazarlu *et al.*, 2021).

3. Folklore of Phytomedicine

There are many uses for phytomedicine, or the use of compounds derived from plants for medical purposes:

A) Traditional Medicine: Herbal treatments have been used for ages to treat a wide range of diseases in many cultures. Ayurveda and traditional Chinese medicine are two examples.

B) Symptom Relief: Phytomedicines are frequently used to treat symptoms like pain and digestive problems, such as indigestion and headaches (e.g., willow bark).

C) Chronic Illnesses: A few herbs, including the following, are used to treat chronic illnesses:

i. Bitter melon and fenugreek: diabetic diet.
ii. Garlic and hawthorn for heart health.
iii. Inflammation: Turmeric and ginger.

D) Mental Health: Some phytomedicines, such as ashwagandha and St. John's wort, are used to treat stress and mood problems.

E) Immune Support: It's well known that echinacea and elderberries boost immunity and shorten cold duration.

F) Skin Care: *Aloe vera* and calendula are two herbs that are applied topically to treat skin problems and wounds (Shedoeva *et al.*, 2019).

G) Antibacterial Properties: Several herbs, like the oils of tea tree and oregano, are used to treat illnesses because of their proven antibacterial properties.

H) Nutraceuticals: Supplements designed to improve general health and well-being contains plant extracts.

I) Cosmetics: Due to their advantageous qualities, including moisturizing and anti-aging benefits, herbal components are found in many cosmetic products.

Although phytomedicine has many advantages, it's crucial that users speak with medical professionals, particularly when it comes to appropriate usage and possible interactions with prescription drugs. Plant materials contain diverse bioactive chemicals that can have therapeutic effects through multiple mechanisms such as antioxidant activity, reducing inflammation, fighting diseases brought on by bacteria, viruses, or fungi are known as antimicrobial properties and hormonal modulation (Abbaszadeh *et al.*, 2018; Sile *et al.*, 2020).

Around 25 % to 50 % of current medications are believed to come from plants, involves both pure isolated compounds and synthetic drugs modeled after natural substances (Tungmunnithum *et al.*, 2018). Hundreds of pharmaceutical agents derived from plant materials have been approved for use and more than 120 authorized medications sourced from the opium poppy. Conventional medicines are not the only option; there are numerous traditional herbal treatments being utilized worldwide, with many of them recorded in pharmacopoeias and herbal medicine guides. Continuous research is ongoing to find new plant-based compounds in the field of Research and Development. An instance is the recognition by the World Health Organization (WHO) of over 1,500 medicinal plants employed in traditional medicine systems globally (Gry *et al.*, 2007; Olvera-Aguirre *et al.*, 2023).

4. Challenges and Considerations

The use of compounds obtained from plants for medicinal purposes, or phytomedicine, comes with a number of difficulties. Variability in plant composition can have an impact on potency and efficacy. These factors include growth circumstances, harvest time, and processing techniques. Because of impurities and adulterants can jeopardize safety, it can be challenging to ensure the purity and quality of phytomedicinal products (Wagner, 2005). The approval and usage of herbal medicines are subject to differing rules in different nations, which affect their quality and accessibility. There may be unanticipated adverse effects or diminished efficacy when using phytomedicines in conjunction with prescription drugs. Public Perception: The use of herbal treatments may be hampered by misconceptions and differing degrees of acceptance among the general public and healthcare professionals. Excessive collection of therapeutic plants may pose a risk to biodiversity and cause ecological imbalances. It can be difficult to incorporate phytomedicines into traditional healthcare because there are frequently insufficiently strong clinical trials to confirm the safety and effectiveness of many of them. Because bioactive components vary widely, it can be challenging to determine appropriate dosages for phytomedicines (Yau *et al.*, 2015; Muthukaviya *et al.*, 2024; Huang *et al.*, 2024).

a) ***Standardizing Potency and Purity:*** It is challenging because of the natural variation in plant materials.
b) ***Interactions between Drugs:*** Numerous compounds derived from plants may interact with standard medications, resulting in possible side effects.
c) ***Research and Development:*** Despite the fact that numerous medications are obtained from plants, in-depth research is required to completely comprehend their impacts and enhance their utilization.

5. Conclusion

There is great potential for innovation and growth in the future of pharmaceuticals derived from plant materials. Taking advantage of advances in science and technology, as well as honoring traditional wisdom and advocating for sustainability, plant-based medicines are likely to play a prominent and influential role in healthcare.

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Recent Developments and Potential Avenues of Herbal Medicine for Well-being and Health

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Chapter - 14

Phytomedicine Innovations: The Future of Plant – Based Therapies
ISBN: 978-81-977907-4-4
First Edition
Chapter – 14, Page: 203 - 230

14

RECENT DEVELOPMENTS AND POTENTIAL AVENUES OF HERBAL MEDICINE FOR WELL-BEING AND HEALTH

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Abstract

For decades, the developed world has been in high demand for phytomedicine derived from botanical sources. Many infectious diseases have long been treated using plant-based folk herbal remedies, and the natural compounds found in plants have served as an inspiration for the creation, research, and manufacturing of novel pharmaceuticals. These plant-based medications make a significant contribution to contemporary medicine. Drug development from medicinal plants continues to be a significant source of new therapeutic leads, but there are still a number of obstacles to overcome, such as finding and using appropriate high-throughput screening bio-assays, increasing the availability of bio-active compounds, and obtaining plant materials. Because they are safe and have fewer adverse effects, they have demonstrated their effectiveness for primary healthcare. They also provide treatments for age-related illnesses such immune system problems, cognitive loss, and osteoporosis. The development of phytomedicine for healthcare system should be done to minimize risks to the traditional and modern healthcare systems and to bring about harmony between them. It requires multidisciplinary, national, and international collaborations in design, synthesis, discovery, and drug development methodologies to investigate these natural resources. This review examines recent developments as well as potential avenues for future research into natural products, such as

therapies that promote well-being and health. In order to facilitate upcoming plant-based medicine discoveries, it also provides an overview of global plans for standardizing the therapeutic application of natural compounds produced from plants.

Keywords: Phytomedicine, Bio-active compounds, Bio assay, Medications and Drug discovery.

1. Introduction

For thousands of years, herbs have been used as traditional medicines in Eastern countries (Gaire, 2018). In these countries, knowledge on certain herbs with healing properties, has been in experimentation through trial and error for hundreds of years, has been passed from generation to generation (Parveen *et al.,* 2020). The use of such natural products is of great importance in Ayurveda, Kampo, Siddha, Traditional Korean Medicine (TKM), Traditional Chinese Medicine (TCM), Unani, and others (Yang and Luan, 2020). Some of these products are incorporated into modern medicine and have gradually entered the Western medical market as complementary and alternative therapies (Matole *et al.,* 2021). Nature is a source of new medicines to facilitate suffering and cure for various diseases. According to the WHO, almost 80 % of the global population relies on herbal species for health care needs (Kumar *et al.,* 2021). Moreover, 122 medicinal compounds have been isolated from 94 plant species (Yuan *et al.,* 2016).

Unfortunately, with the increased global utilization of herbs and herbal products, many plant species are already on the edge of extinction (Sen *et al.,* 2011). The overuse of such medicinal plants threatens their survival. The conservation and protection of such plants are essential to ensure the future supply of beneficial herbal compounds and secure livelihoods (Das and Rajasekharan, 2020).

Medicinal and aromatic plants, especially those with ethnopharmacological uses, have been utilized as a natural source of remedies and healthcare for millennia (Okigbo *et al.,* 2009; Chaachouay *et al.,* 2023; Ansari *et al.,* 2023). Initially, these popular medications were primitive formulations such as powders, tinctures, macerations, teas, infusions, percolation products, poultices, decoctions, tinctures, inhalations, and other herbal preparations (Chaachouay *et al.,* 2020; Orch *et al.,* 2021; Benkhnigue *et al.,* 2022). The precise dose of the plant and the mode of administration for specific diseases have been transmitted by oral tradition from one generation to another (Chaachouay *et al.,* 2020; Avery *et al.,* 2017; d'Avigdor *et al.,* 2014). Multiple fields of study and various investigation methods have been included in drug discovery from medicinal plants. Botanists, ethnobotanists, ethnopharmacologists, and plant ecologists often gather and identify the plants of interest (Balunas *et al.,* 2005). New

technological developments enable plants to be transformed into "factories" that create natural medical compounds for use in the production of biotech pharmaceuticals, medications, and treatments (Paul *et al.,* 2011). The application of plants as drugs has recently required the separation of active ingredients, starting with the early-19th-century isolation of morphine from *Papaver somniferum* (Brook *et al.,* 2017; Yuan *et al.,* 2016). The identification of early pharmaceuticals, such as digitoxin, cocaine, pilocarpine, codeine, and quinine, that are derived from medicinal plants marked a remarkable achievement in the field of medicine (Kong *et al.,* 2003). These compounds have been separated and analyzed for their medicinal characteristics and are still acknowledged for their therapeutic uses in the present day. Furthermore, apart from these initial findings, several additional molecules originating from plants have been identified in more recent times. These compounds have undergone extensive research and development and have subsequently been commercialized as pharmaceutical medications (Ernest *et al.,* 2010). Scientists' investigation of medicinal plants has been crucial in uncovering early drugs, each possessing distinct pharmacological characteristics.

In addition, scientists' continuous endeavors to separate and describe pharmacologically active substances from medicinal plants have resulted in the identification of supplementary compounds with therapeutic promise. The procedure includes a thorough study to comprehend the chemical structures, modes of action, and possible medicinal uses of these substances. This continuous investigation highlights the significance of nature as a significant source of bioactive compounds that continue to aid in the creation of new medications and treatments in modern medicine. To date, drug development approaches have been used to standardize herbal remedies to identify analytical marker biomolecules (Chin *et al.,* 2006). Plant-made pharmaceuticals result from the creative application of biotechnology to plants to make drugs derived from natural products that the medical profession can employ to fight life-threatening ailments, such as asthma, influenza, cancer, tuberculosis, diabetes mellitus, coronary artery disease, and diarrhea (Mohr, 2015). Developing drugs using plant-based pharmaceutical techniques offers an efficient, cost-effective, and safe alternative to conventional procedures using animal cell cultures or microbial fermentation. Therefore, drugs derived from natural compounds in plants can offer patients greater and quicker access to medications (Subramoniam, 2014; Veeresham, 2012).

2. Types of Traditional Medicine Systems

In order to treat, diagnose, and prevent illnesses or maintain well-being, traditional medicine refers to health practices, approaches, knowledge, and beliefs that include manual techniques and exercises, spiritual therapies, and medicines derived from plants, animals, and minerals. These practices can be used alone or in combination (Fokunang *et al.,* 2011). Some of the best-known traditional medicine systems include Traditional Chinese Herbal Medicine, Traditional Indian (Ayurveda) Herbal Medicine, and Traditional Arabic (Unani) Herbal Medicine.

2.1. Traditional Chinese Herbal Medicines

Ethnic herbal and folk medicines are included in Chinese herbal medicines (Lin and Lian, 2018). It includes roughly 1500 animal/animal parts and insects, over 11,000 medicinal plants, 80 mineral treatments, 50 processed remedies, and 5,000 herbal formulae with clinical approval (El Sheikha, 2017; Saad *et al.,* 2017). Every herbal prescription is a mixture of several herbs customized for a specific patient. People living in different parts of China have distinct cultures, customs, lifestyles, and illness spectrums because of variations in climate and geography (Lu *et al.,* 2020). Due to these developments, a wide range of conventional medical procedures have emerged. China is home to 56 distinct ethnic groups, each with their own languages, customs, and traditional herbal remedies (Shu *et al.,* 2018). Cloves, pinellia, angelica, tianma, fritillaria, eucommia, licorice, turmeric, frankincense, rhubarb, wolfberry, berberine, and panax are among the more than 7000 varieties of medicinal and related herbal products that China exports annually to more than 130 countries worldwide (Pan *et al.,* 2014; Nwafor *et al.,* 2021). China's herbal medicine exports are valued at USD 1.567 billion (Shi and Zhang, 2020).

2.2. Traditional Indian Herbal Medicine

About 8 % of the world's biodiversity is thought to reside in India, which is home to about 126,000 species (315 of the 400 families of flowering plants) (Ramesh and Valan, 2021). The Indian subcontinent is home to about 45,000 species, or about 20 % of all species worldwide. Of these, about 3500 have medicinal value, with 500 of them being employed in the Ayurvedic field (Qadir and Raja, 2021). According to Barata *et al.* (2016), almost 80 % of therapeutic plants are harvested from the wild. According to Rathore and Mathur (2018), of the herbal goods that India exports, 10 % are Ayurvedic medicines, 30 % are crude herbal extracts, and 60 % are processed herbal extracts. Mehdi leaves, menthol, isabgol, sandalwood oil, cinchona alkaloids,

jasmine oil, agarwood oil, and opium alkaloids are a some of the important pharmaceuticals that India exports that are made from plant components (Shaheen *et al.,* 2019).

2.3. Traditional Arabic Herbal Medicine

More than 700 of the 2600 plant species found in the Middle East are used as botanical pesticides or have therapeutic benefits (Ibrahim *et al.,* 2017). Nonetheless, only about 200 – 250 plants, along with 29 inorganic chemicals and 30 animal species, are still utilized to cure a variety of ailments (Tahri, 2020). Of the 48 families of plants, 230 species have been documented ranging from Egypt to the Mediterranean coast and Alexandria. Totally, 89 % of these species have a reputation for having therapeutic qualities (Azaizeh *et al.,* 2010). According to Said *et al.* (2002), 129 medicinal plants are utilized in Israel to treat a wide range of medical conditions, such as obesity, high cholesterol, digestive system disorders, skin conditions, and several cancer kinds.

3. Methods for Discovery

The process of discovering and developing therapies from naturally occurring molecules found in plants is complex and multifaceted, involving multiple crucial steps, all of which are necessary to convert the potential of botanical chemicals into effective pharmaceuticals. Here is a detailed breakdown of these essential exploratory approaches Figure - 1.

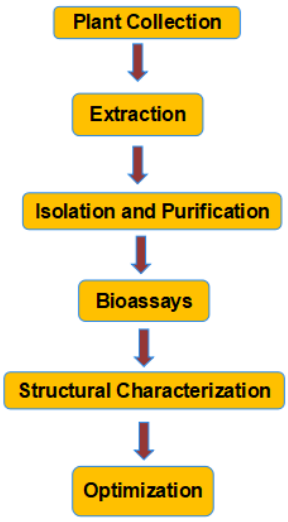

Figure – 1: Various Stages of the Drug Discovery Process from Natural Products

4. Historical Significance of Herbal Medicine

The historical significance of herbal medicine exemplifies the enduring relationship between humans and the natural world in the pursuit of health and well-being. Throughout history, several cultures from across the globe have acknowledged and used the therapeutic qualities of plants. Herbal treatments have been used since ancient times, as shown by archeological findings that suggest the usage of medicinal herbs as early as the Paleolithic era, some 60,000 years ago (Aboelsoud, 2010; Sam, 2019). The Sumerians, who kept lists of plants, left written records of herbal treatments that may be traced back over 5000 years (Yaniv, 2014). Subsequently, the use of herbs has seen fluctuations in popularity within the medical domain; there were several instances when ancient societies such as the Egyptians, Greeks, and Romans heavily relied on herbal medicines for medicinal purposes (Sendker and Sheridan, 2017). These traditions have not only endured throughout time but also have significantly shaped the advancement of contemporary pharmacology and healthcare practices (Msomi and Simelane, 2018). Exploring significant milestones in the historical use of plant-based treatments offers a comprehensive viewpoint on this long-lasting connection:

5. Ancient Healing Practices

The innovative utilization of therapeutic herbs by the ancient Egyptians is a source of great respect. Herbal medicines are well documented in the written records of their civilization, which date back to 1500 BCE (Aboelsoud, 2010). These documents offer a comprehensive picture of the wide variety of plants they employ medicinally. Many modern herbal remedies and medical procedures are based on their knowledge and techniques (Forshaw, 2014). Numerous details about herbal remedies and other medical treatments can be found in the Ebers Papyrus, an ancient Egyptian medical text. It is one of the oldest medical manuscripts known to exist, with an estimated genesis date of 1550 BCE. More than 700 bewitching incantations and traditional remedies can be found in the papyrus, many of them are derived from plant sources and herbal extracts. Many people consider the manuscript to be among the best-preserved and most complete records of ancient Egyptian medicine that are now available (Forshaw, 2014).

6. Chinese Herbal Medicine

Herbal medicine has a long history in China and has been used with diligence for thousands of years. The principles of traditional Chinese medicine (TCM), an empathic system that employs herbal treatments to restore balance and promote overall well-being, are the basis of this practice. (Tang *et al.,* 2008). TCM practitioners employ herbal and botanical compositions to support optimal health and increase organ function. Understanding the basic properties of various herbal ingredients enables the TCM practitioner to provide a therapeutic effect that goes beyond the physical and chemical characteristics of the herbs. Chinese herbal formulas, some of which date back more than 2200 years, are made up of ingredients chosen for their complimentary roles. TCM typically uses a combination of botanicals to create a synergistic effect, in contrast to the individualistic approach that is common in Western medicine (Fan *et al.,* 2012; He, 2013).

7. Plant-Derived Products in the Traditional Pharmacopeias

Organic compounds produced by plants that are not directly involved in the basic processes of growth, development, or reproduction are known as secondary metabolites (Thirumurugan *et al.,* 2018). Nonetheless, these compounds frequently carry out ecological functions, such luring pollinators, serving as a defensive mechanism against herbivores, or competing with other plants (Pagare *et al.,* 2015; Chaachouay and Zidane, 2023). A number of secondary metabolites are crucial components of conventional pharmacopeias and have been employed for their medicinal properties. Alkaloids, for instance, are a class of nitrogen-containing chemicals that are present in many different species and have a wide range of pharmacological actions. Examples include quinine from the cinchona tree, caffeine from coffee beans, and morphine from the opium poppy (Alamgir, 2018). For ages, traditional medicine has utilized these substances due to their unique analgesic, antimalarial, and stimulant characteristics (Ravina, 2011). Because of these substances' stimulant, antimalarial, and pain-relieving properties, traditional medicine has been using them for many centuries (Gurib-Fakim, 2006; Chaachouay *et al.,* 2023).

Plant-based materials that are high in secondary metabolites are frequently the basis of traditional pharmacopeias, which are based on the knowledge and practices of indigenous societies (Kennedy, 2014). Through millennia of transmission, herbal remedies and formulations based on traditional knowledge continue to play a significant role in healthcare practices throughout numerous cultures (Ahmed *et al.,* 2014; Chaachouay *et al.,* 2023). These concoctions are thought to have cultural as well

as therapeutic value. Herbs with secondary metabolites, such as flavonoids, terpenoids, and saponins, are among the many plant-based medications used in traditional Chinese medicine (Tang *et al.,* 2008). Likewise, plant-based medicines, including secondary metabolites like polyphenols and alkaloids, are the mainstay of India's traditional medical system, Ayurveda (Alamgir *et al.,* 2017). The addition of plant-derived secondary metabolites to conventional pharmacopeias emphasizes the value of biodiversity in enhancing human health as well as the usefulness of natural resources in the research and development of pharmaceuticals.

8. Quinine - Quinine

Malaria, a highly fatal disease caused by the Plasmodium parasite, has plagued humankind for generations. The native people of South America used the bark of the cinchona tree (*Cinchona officinalis*) as a fever treatment (Packard, 2021). In the seventeenth century, quinine, a bioactive substance present in cinchona bark, was identified as a particularly effective treatment for malaria (Capasso, 2003). This discovery was a major breakthrough in the treatment of the illness; quinine remained a vital anti-malarial drug for generations until more modern treatments were developed (Dagen, 2020). The longstanding knowledge of past civilizations in recognizing the healing potential of the natural environment is demonstrated by the historical significance of plant-based medicine (Rogers, 2012). First techniques accepted for the evolution of current pharmacology and its role in the progress of healthcare have been played (David *et al.,* 2015).

9. Aspirin – Acetyl Salicyclic Acid

Aspirin, an analgesic extensively used worldwide scale, serves as a salient example of this phenomenon. Aspirin was first extracted from the bark of the *Salix alba* species, often known as the willow tree (Ugurlucan *et al.,* 2012). Several process underwent for the synthesis of the active compound acetylsalicylic acid. Finally, it was well accepted and is used worldwide as a fundamental component in pain management (Ugurlucan *et al.,* 2012). The willow bark was used by the Greeks and Egyptians as an analgesic. During the 19th century, scientists effectively extracted the active ingredient, acetylsalicylic acid, which brought about a significant transformation in the treatment of pain and control of inflammation (Levesque and Lafont, 2000).

10. Requirement for Production of Plant-Based Drugs

Natural products have always attracted the pharmaceutical industry, with interest in plant-derived drugs and alternative therapies for many reasons. Though synthetic medicines provide quick relief, many adverse effects accompany them. Synthetic medicine is costly due to its manufacturing process and may be inaccessible to a large section of the world's population. On the other hand, traditional medicines are by and large harmless, more effective with minimum side effects, and easily metabolized and absorbed in the body. Due to the cultural and social belief of the people, they are widely accepted, affordable and easily accessible to the people. Increased scientific studies and clinical trials by researchers and pharmaceutical companies have provided evidence-based medicines (Wangchuk, 2018). Furthermore, the purification and standardization of a single compound is more convenient, thereby facilitating its use in the modern drug delivery system Table - 1.

Table - 1 Plant-Based Drugs and Its Applications

Compounds Isolated	Plants Species	Applications	References
Aristolochic acid	*Aristolochia* spp.	To induce weight loss, liver disease, arthritis, headache, edema	Yang *et al.,* 2018
Flavonoid (Sciadopitysin)	*Taxus celebica*	Diabetes, vascular diseases	Yang *et al.,* 2018
Flavonoid	*Cupressus funebris*	Vascular diseases, used instead of "yew"	Yang *et al.,* 2018
Ephedrine, Norephedrine, Pseudoephedrine	*Ephedra sinica*	Cough, to induce weight loss, to cause sexual arousal	Yang *et al.,* 2018
Glycyrrhetinic acid, Glycyrrhizic acid	*Glycyrrhiza glabra*	Cough, sore throat, arthritis, to induce weight loss	Yang *et al.,* 2018
Anthraquinones, Oxalic acid	*Rhizoma rhei*	Laxative, antiinflammatory	Yang *et al.,* 2018
Active moiety triptolide	*Tripterygium wilfordii*	Arthritis, antiinflammatory, immunosuppressant	Yang *et al.,* 2018
Oxidative degradation products	*Aloe capensis*	Constipation, insect bites	Yang *et al.,* 2018
Colchicine	*Colchicum autumnale*	Gout	Yang *et al.,* 2018
Atropine	*Atropa belladonna* L.	Anticholinergic	Rajput, 2013
Berberine	*Berberis vulgaris* L.	Bacillary dysentery	Imanshahidi and Hosseinzadeh, 2008

Caffeine	*Camellia sinensis* (L.) Kuntze	Neuroprotection	López and Calvo, 2011
Camptothecin	*Camptotheca acuminata* Decne.	Anticancer	Zhao *et al.,* 2017
Colchicine	*Colchicum autumnale* L.	Antigout, antitumor	Singh *et al.,* 2009
Convallatoxin	*Convallaria majalis* L.	Cardiotonic	Morimoto *et al.,* 2021
Digitoxin	*Digitalis purpurea* L.	Cardiotonic	Pérez-Alonso *et al.,* 2009
Digoxin	*Digitalis lanata* Ehrh.	Cardiotonic	Bhusare *et al.,* 2018
Ephedrine	*Ephedra sinica* Stapf	Sympathomimetic	Limberger *et al.,* 2013
Quinine	*Cinchona officinalis* L.	Antimalarial	Yeka *et al.,* 2009
Reserpine	*Rauvolfia serpentina* (L.) Benth.	Antihypertensive	Kumari *et al.,* 2013
Scopolamine	*Datura metel* L.	Sedative	Malami *et al.,* 2014
Taxol	*Taxus brevifolia* Nutt.	Anticancer	Sze *et al.,* 2008
Thymol	*Thymus vulgaris* L.	Topical antifungal	Sokovi´c, 2008
Vinblastine	*Catharanthus roseus* L.	Anticancer	Rai *et al.,* 2014
Vincristine	*Catharanthus roseus* L.	Anticancer	Rai *et al.,* 2014
Yuanhuacine	*Daphne genkwa* Siebold & Zucc.	Abortifacient	Bailly *et al.,* 2022

11. Challenges in Production of Phytopharmaceutical Drugs

Despite several advantages, there exist a few challenges associated with the production of PPD. Plant-derived products sometimes lack quality and are ineffective due to India's poor regulation of natural products. As a result, there is a decline in trade and reluctance in prescribing PPDs. Other hurdles include (i) low yield of the plant material used, (ii) solubility level of plant extracts in water and other solvents, (iii) presence of cytotoxic components in the extract, (iv) limited bio-availability of the sample, (v) inappropriate use of available phytomedicines leading to toxic accidents, (vi) error in botanical identification of plants and their use, (vii) unauthorized usage of popular remedies, (viii) domestic accidents due to consumption of decorative plants having cardiotonic components, (ix) haemorrhagic accidents and hypertensive accidents due to coumarin derivatives present in some plants, (x) presence of oestrogenic components in plants, (xi) use of plants causing allergic reactions due to pollens or volatile components (Nooreen *et al.,* 2018).

12. Herbal Medicine: Definition and its Prospects

Traditional medicine plants have good knowledge and beliefs for medicines, spiritual therapies, and physical therapy for the combination to treat, diagnose, and prevent illnesses or maintain well-being. Traditional medicine are called complementary and alternative medicine in developed countries (Gunjan *et al.*, 2015). Herbal medicine or phytomedicine is used for curing of diseases and improve human health. World Health Organization (WHO) has defined that medicinal plant parts contain an active ingredients (WHO, 2008; Parveen *et al.,* 2015). Herbal medicines are classified as (1) herbal drugs with proven efficacies (2) herbal drugs with expected efficacies (3) herbal drugs with uncertain efficacies (Parveen *et al.,* 2015). Plants are commonly used as raw material in traditional medicine and they have rich dietary sources of biomolecules, vitamins and minerals for maintaining the healthy body (Shakya, 2016).

13. Approaches for Phytopharmaceutical Drug Development

For drug development herbal plants are used for the development of herbal medicine and end-products are used as a herbal medicine with various formulations.

13.1. Ethnopharmacology

In ethnopharmacology the most important step is selecting the plant for pharmacological study. We used plants with a good history of traditional medicines being used in different ethnic groups are choosed and this approach is known as ethnobotany or ethnopharmacology (Süntar, 2020). Various extraction methods are used for the preparation of herbal formulations. They provide detailed explanation on how the drug is consumed and the amount we want to used. Whereas, proper screening of the herbal drug is needed with various health concepts and healthcare systems (Wangchuk, 2018). Biologically active compounds with good pharmaceutical properties are extracted from the plants during the drug development process. Plant extracts have high concentrations of bioactive compounds and they are responsible for overall quality. Fractionation technique is needed to isolate and identify bioactive compounds from plants. Various bioactive molecules standardized and also have been reported (Cui, *et al.,* 2020).

13.2. Reverse Pharmacology

Conventional drug development process can be inefficient and expensive for drug discovery. Reverse pharmacology has recently emerged, and is cost-effective with less time and toxicity levels when compared to the other conventional method and this method is called Reverse Pharmacology (RP) (Patwardhan *et al.,* 2008). Reverse pharmacology is documented based on the experimental validation of the findings and identifying effective drugs. Identified drugs can be documented, clinical studies done for herbal formulations, followed by studies on drug dose, drug tolerance, and in vitro and in vivo analysis of the formulation for drug target activity. Reverse pharmacology has replaced the common route of "laboratory-to-clinic" with the "clinic-to-laboratories" pathway (Surh, 2011). Reverse pharmacology based drug discovery starts and ends with humans, thereby assuring their safety and efficacy (Arulsamy *et al.,* 2016).

13.3. High Throughput Screening

For drug delivery programs decades before they screen the natural products and identify the potential drugs. Whereas, High Throughput Screening (HTS) is one of the latest approaches for drug delivery programs. HTS incorporates high-quality components and assays used to explore the biological activity of many samples. The identified bioactive compounds along with their derivatives have anti-cancer, anti-diabetic, as well as anti-inflammatory activities, however, more than hundred natural compounds are under clinical screening. For identifying, isolating, and purifying natural products, are easy with the availability of advanced analytical screening with the HTS (Lautie *et al*., 2020).

13.4. Fragment-Based Drug Discovery

The Fragment-Based Drug Discovery (FBDD) approach is an alternative technique to HTS in the pharma industry. This approach is mainly used for the identification of structure-based drug design and to identify potent drug molecules. FBDD can identify very small molecules with low-molecular-weight (~150 Da), which bind to macromolecules or drug leads (Erlanson, 2011).

13.5. Polypharmacology

Numerous bioactive compounds such as alkaloids, bacosides, phyllanthins, curcumin, piperidines from medicinal plants have been successfully treated many human diseases. Whereas, complicated diseases such as cancer, heart diseases,

multiple sclerosis, and diabetes require a multi-targeted approach (Fang *et al.,* 2018). Fang *et al*. (Fang *et al.,* 2018) demonstrated the polypharmacological profile of five natural compounds namely, curcumin, epigallocatechin gallate, quercetin, resveratrol and berberine. Databases constrution as well as evolution of new bioinformatics tools will speed up and change polypharmacology-based studies (Wagner *et al.,* 2016, Wang *et al.,* 2015).

13.6. Network Pharmacology

In system biology, the idea of 'one-disease one-target drug' in treating diseases is becoming less popular. The idea of network pharmacology is based on systems biology, pleiotropy, connectivity, redundancy, and network analysis (Li *et al.,* 2014). Whereas, network pharmacology is the next model in drug discovery due to its cost-effective nature and efficiency of network theory and systems biology (Wan *et al.,* 2019). The network pharmacology is used to study different biological systems, diseases, drugs, and "compound-proteins/genes-disease" pathways based on network biology (Zhang *et al.,* 2019).

14. Modern Approaches in the Field of Drug Discovery

Modern pharmaceutical research is increasingly moving towards the consideration of compounds produced by plants due to their medicinal applications. Biotechnology and synthetic biology techniques play major role to create such compounds in various domain (Ausländer *et al.,* 2017). Moreover, metabolic engineering as well as pathway engineering techniques may be utilized to alter the genetic composition of these organisms, and enhancing their efficiency in producing specific substances (Deparis *et al.,* 2017). Sustainability and uniformity can be improved and also guarantee the uniformity and excellence of the obtained plant-derived compounds. At the same time, high-throughput screening, computer modeling, and bioinformatics are deeply transforming the discovery process. High-throughput screening is used to check the quality of plant extract against specified biological targets, whereas this will help for the quick discovery of active compounds (Ismail *et al.,* 2018). Computational modeling techniques, such as molecular modeling and virtual screening, are used to predict the interactions between compounds originating from plants and biological targets. Molecular modeling is a computational method we uses computer simulations to forecast the behavior of molecules and their interactions with other molecules (Dhoundiyal *et al.,* 2023). It is used for the examination of the arrangement and operation of proteins, DNA, and other biological

substances, as well as for the development of novel medications and therapeutic agents (Bischoff and Hoffmann, 2002).

Bioinformatics provides extensive data on the genetic, metabolic, and pharmacological characteristics of these molecules, facilitating the identification of novel compounds and offering valuable knowledge on their biosynthesis processes (Xia, 2017). Technology integration enhances the identification and improvement of plant-based molecules, leading to a more efficient and successful age in drug development. These modern approaches embody a potent combination that not only addresses environmental issues but also expedites the discovery and development of novel pharmaceuticals. Biotechnology and synthetic biology enable the precise manufacture of plant derived molecules, reducing the impact on the environment and the amount of reliance on natural plant resources (Cravens *et al.,* 2019; Pereira, 2019). Simultaneously, high-throughput screening and computational tools provide a rapid and systematic approach to finding prospective therapeutic compounds, reducing time and resource consumption (Sharma and Sarkar, 2013). Bioinformatics enhances our comprehension of the chemicals, aiding the identification of new pharmaceuticals (Wishart, 2005). In general, the combination of biotechnology and powerful computational tools drives the pharmaceutical sector towards a more environmentally friendly and faster medication development process Table - 2.

Table – 2: Therapeutic Effects and Applications of Compounds developed from Herbal Sources (Perumal and Gopalakrishnakone, 2007)

Plant	Plant part used	Use
Exporting Plants		
Acorus calamus	Rhizome	Aphrodisiac, Sedative
Argemone mexicana	Fruit	Sedative, Antimalarial
Curcuma amada	Rhizome	Alzheimer's disease, Cancer, Arthritis
Curcuma aromatica	Rhizome	Remove cell accumulations such as a Tumors
Cassia lanceolata	Leaves	Purgative. Sedative
Glycyrrhiza glabra	Root	Chronic viral hepatitis
Withania somnifera	Vegetable rennet	Aphrodisiac, sedative, rejuvenative and life prolonging properties
Myrica nagi	Leaf	Anti arthritic, antiseptic, aromatic, astringent, carminative, ophthalmic and stimulant.
Piper longum	Fruit	Nerve depressant, analgesic, tonic, stimulant and carminative properties.
Rubia cordifolia	Madder root	Antidysenteric, antiseptic, and deobstruent
Symplocos racemosa	Bark	leucorrhea, menstrual disorders, hemorrhage, tumors
Swertia chirata	Whole plant	Anthelmintic, dyspepsia and diarrhoea.
Terminalia chebula	Bark and seed	Rejuvenative and appetizer

Zingiber officinale	Rhizome	Gastrointestinal benefits and carminative and anti-inflammatory properties.
Importing Plants		
Aloe vera	Dried leaf	Wound and burn healing, minor skin infections
Adhatoda vasica	Whole plant	Antispasmodic bronchodilator, and mucolytic agent in asthma
Cinnamomum iners	Bark and leaf	Fever
Curcuma aromatica	Rhizome	Preventing and curing cancer
Garcinia indica	Fruit	Curing allergies
Gloriosa superba	Tuber and seed	Anthemirtic, laxative, alexiteric, abortifacient,
Juniperus communis	Fruit	Cystitis, flatulence and colic.
Myrica nagi	Bark	Anti arthritic, antiseptic, aromatic, astringent, carminative, ophthalmic and stimulant Bark
Strycnos nux-vomica	Bark and seed	Atonic dyspepsia. pruritis and as a local anodyne in inflammations of the external ear.
Phyllanthus amarus	Fruit	Anti-viral, hepatoprotective, hypoglycemic
Ricinus communis	Seed	Laxative purgative
Rauvolfia serpentina	Root	Insomnia and insanity
Ocimum sanctum	Leaf and essential oil	Anthelmintic, Anti-amnesic and nootropic
Tylophora purpuria	Root	Laxative, expectorant, diaphoretic and purgative
Vinca rosea	Leaf, seed and stem	Sedative, hypotensive, tranquilizer and anti-cancerous

15. Natural Products Derived from Plant Sources

Numerous natural compounds with a spectrum of medicinal qualities can be found in plants, and these resources are constantly being investigated to create new medications (Singh *et al.,* 2012). These natural materials have long been used by traditional medicine to treat a wide range of illnesses. Nowadays, these natural ingredients are used to make the majority of pharmaceutical drugs. Numerous bioactive chemicals make up natural goods. These bioactive substances have biological activity against certain pathogens. Plants have yielded a multitude of secondary metabolites with varying structures and pharmacological characteristics to date (Gad *et al.,* 2013, Singh *et al.,* 2012). The knowledge upheld by the traditional medical system has made it possible to continue researching medicinal plants for use in the production of pharmaceuticals (Mushtaq *et al.,* 2018). Over 85 – 90 % of people worldwide rely on traditional medicine to treat a variety of illnesses Table - 3 (Wangchuk, 2018).

Table - 3 Plant-Derived Natural Products and their Medicinal Applications

Plant name	Compounds Identified	Uses	References
Hyperian perfotum	Hypericin	Immunogenic cell death inducer	Krysko *et al.,* 2012
Lithospermum erythrorhizon	Shikonin	Immunogenic cell death inducer	Yin *et al.,* 2016
Scutellaria baicalensis	Wogonine	Immunogenic cell death inducer	Li *et al.,* 2018
Piper nigrum	Piperine	Nanotheranostic agent for cancer treatment	Chelora *et al.,* 2019
Berberis vulgaris L	Berberine, Jatrorrhizine, Palmatine, Ceptisine	Antidiabetic, Anticancer, Antibacterial, Analgesic, Antiinfammatory, and Cardiovascular	Singh *et al.,* 2021
Cinchona spp	Quinine	Antimalarial drugs	Mohammadi *et al.,* 2020
Artemisia annua	Artemisinin	Type I diabetes and cancer	Lai *et al.,* 2013
Salvia divinorum	Salvinorin A	Neuro-psychopharmacothera peutic plant-based drugs	Listos *et al.,* 2011
Cleome	Pinocembrin, Kaempferol, Kaempferitrin	Anti-cancer	Chand *et al.,* 2022
Silybum marianum	Silymarin	Hepatoprotective activities	Flora *et al.,* 1998
Taxus brevifolia	Taxol	Lung, ovarian and breast cancer	Mamadalieva and Mamedov, 2020
Coleus forskohlii	Forskolin	Antiglaucoma drug	Wagh *et al.,* 2012
Curcuma longa L. (Turmeric)	Curcumin	Antioxidant, anti-infammatory, arthritis, metabolic syndrome and pain	Hewlings *et al.,* 2017
Galanthus nivalis	Galantamine	Alzheimer	Coyle *et al.,* 2001
Capsicum annuum	Capsaicin	Pain relievers	Pasierski *et al.,* 2022
Artemisia glabella	Arglabin	Anti-tumor	Lone *et al.,* 2015
Genista tinctoria L.	Genistein	Anticancer, Alzheimer's disease	Tuli *et al.,* 2019
Vitis vinifera L.	Resveratrol	Chemotherapeutic, antidiabetic, antioxidant	Ferraz da Costa *et al.,* 2020
Azadirachta indica A. Juss (Neem)	Azadirachtin	Insecticidal and antimicrobial	Tembe-Fokunang *et al.,* 2019
Trigonella foenum-graceum L.	Trigonelline, Diaszhenin	Antidiabetic, Anti-conception	Bahmani e*t al.,* 2016
Capsicum annuum	Capsaicin	Antilithogenic effect, Anti-inflammatory	Srinivasan, 2016

16. Conclusion

Apart from its traditional virtues, phytomedicine is highly sought after by the global medical community and public for its ability to provide innovative lead chemicals for drug development or nutraceuticals. The development of herbal remedies not only opened up new avenues for study but also had a direct impact on human health care. The development of phytomedicine's integration into the healthcare system should be done so as to minimize risks to the traditional and modern healthcare systems and to bring about harmony between them. Medicinal herbs have gained a substantial place in the global health system for both humans and animals, not only in the treatment of sickness but also as a potential resource for preserving good health. Lack of knowledge about the potential social and financial advantages of using medicinal plants for industrial purposes has been a major barrier to the growth of enterprises based on these plants in poor nations. There hasn't been much information on these plants market potential or trading opportunities, aside from its application for local medical purposes. Because of this, neither governments nor business people have fully utilized the potential of these plants.

17. References

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Chapter - 15

Phytomedicine Innovations: The Future of Plant – Based Therapies
ISBN: 978-81-977907-4-4
First Edition
Chapter – 15, Page: 231 - 251

15

ETHNOBOTANICAL AND ETHNOMEDICINAL SURVEY OF PILLUR BEAT, KARAMADAI RANGE, WESTERN GHATS, TAMIL NADU, INDIA

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Abstract

The present investigation deals with the ethnomedicinal plants of Pillur Beat, Karamadai Range, Western Ghats, Tamil Nadu. Traditional medicine and ethnobotanical information play an important role in scientific research, particularly when the literature and field work data have been properly evaluated. There is no documentation of this ethnomedicinal knowledge. It is thus important to document and understand the medical heritage of a changing culture before it is lost entirely to future generations. The study was carried out in the villages of Pillur Beat concerns for the medicinal plants used for the treatment of various diseases by local inhabited. 114 plant species belonging 15 families are used for treating various diseases. The information on correct botanical identities, family, local, name, plant parts used & uses of each plant. This study presents the results of a field survey of the plants used medically by the rural people of Pillur Beat, Karamadai Range in Coimbatore district.

Keywords: Ethnobotany, medicinal plants, Remedies, Pillur Beat and Karamadai Range.

1. Introduction

Nature always stands as a golden mark to exemplify the outstanding phenomenon of symbiosis. The plants are indispensable to man for his life. Nature has provided a complete store-house of remedies to cure all ailments. The knowledge of drugs has accumulated over thousands of years as a result of man's inquisitive nature so that today we possess many effective means of ensuring health-care. In the past, almost all the medicines used were from the plants, the plant being man's only chemist for ages. A study of WHO depicts that over 80 % of world's population directly depends on the natural diversity and its associated traditional system of medicine for their primary healthcare demands (WHO, 2000). Today, a vast store of knowledge concerning therapeutic properties of different plants has accumulated (Evans *et al.*, 2002).

The history of herbal medicines is as old as human civilization. The documents, many of which are of great antiquity, revealed that plants were used medicinally in China, India, Egypt and Greece long before the beginning of the Christian era. In China, many medicinal plants had been in use since 5000 B.C. Drug plants were extensively described by Aristotle and Theophrastus as early in 77 B.C. Indians also, worked meticulously to examine and classify the herbs which they came across, into groups called Gunas. India holds a global credibility of having diverse social, cultural and regional convention of indigenous medical heritage with an unbroken tradition coming down across millennia. Though, medical heritage of such a kind is quite a few centuries old, several million people in rural/remote places in this subcontinent still depend on traditional system of medicine to satisfy their healthcare demands (Jain, 1967).

Western Ghats is endowed with several medicinal plants with a plethora of historical information for their use in the management of many disease conditions (Lawal *et al.*, 2014). Several scientific reports have also justified the biological activities that are traditionally stipulated for these medicinal plants (Mensah *et al.*, 2011; Agyare *et al.*, 2012; Kyei *et al.*, 2012; Fleischer *et al.*, 2013). Tribals dwelling in remote places depend on the forest that includes rich diversity of flora and fauna to meet their livelihood and healthcare needs (Chopra *et al.*, 1986). Herbal medicines have been used by them since antiquity in treating diseases. However, valid scientific data on the usage of ethnomedicinal plants is rather obscure. In India, a tropical country with rich biological and cultural diversity, there are about 67.37 million tribal people belonging to 573 tribal groups living in different geographic locations with various subsistence

patterns (Murugesan *et al.,* 2005). These tribal groups living in biodiversity rich areas possess a wealth of knowledge on the utilization and conservation of medicinal plants. This knowledge has been passed on from one generation to another without any written document, and also it has helped them to have sense of responsibility in judicious utilization and conservation of the plant resources (Ragupathy *et al.*, 2008; Ragupathy and Newmaster, 2009). The state of Tamil Nadu having 36 scheduled tribes; the different ethnic groups settled throughout this state have their own way of life style even in using the plant resources. The present survey was under taken to investigate the traditional medicinal plants in villages of Pillur Beat (Pillur slope RF and Nellithurai RF), Karamadai Range, Coimbatore District, Western Ghats, Tamil Nadu, India.

2. Materials and Methods

2.1. Study Area

In the present study an attempt has been made to enumerate the diversity of medicinal plants distributed in Pillur beat (Pillur slope RF and Nellithurai RF), Karamadai Range, Western Ghats, Coimbatore District, Tamil Nadu, India. The study area Pillur beat encompasses 12 Tribal villages namely Gethaikkadu, Poochamaruthur, Nellimarathur, Korappathi, Veerakkal, Baralikadu, Neeradi, Melpillur, Situkunni, Kadaman kombai, Veppamarathur and Sundappatti. The hill range is situated at about 250 to 900 meters above the sea level and it is noted for its natural flora and fauna. The hill group has rare medicinal plants in its lush green forests (Plate – 1 & 2).

2.2. Climatology

Climatic data such as total rain fall, minimum and maximum temperatures and type of soil were collected from District Forest Officer, Coimbatore Circle, Tamil Nadu, India.

2.3. Soil

The Southern Western Ghats is a part of the South Indian Precambrian terrain dominated by low-grade metamorphic and gneissic rocks. There are three types of rocks found in this region such as charnokites, khodalites and granites, in which granites are restricted in low lying areas and a fewer foot hill regions. The soil is showed appreciable differences linked to the effect of rocks (khondalites and charnokites). The variations are also due to climatic gradients. Almost all the Ghat

areas are mainly composed on highly developed humiferous soils except exposed Savannah lands and foot hills. Deciduous forest zone area has less developed humiferous soil but also have considerable humitropets.

a - Upper view of the Study Hill

b - Panoramic View of Pillur Beat

c- Slope View of the Study Hill

PLATE – 1

a- Tribals hamlets

b- Tribal family

c - Temple of the tribes

d - Cattle rearing by the tribals

e - Cultivation in the forest

f - Animal watch hut

PLATE – 2

2.4. Plant Collection, Identification and Preservation of Medicinal Plants

Field trips were made in every three months in the beginning and for every six months later to obtain a thorough collection of ephemerals. Field investigations were conducted in the top, middle and foot hill around the study area. The Tribals in the settlements were approached through mediators who had good relationships with the tribals such as forest officials and tribal chief. Resource persons (informants or tribal practitioners or traditional healers) with the knowledge of medicinal preparations were selected to gather the information. The ethnobotanical data (mode of preparation, Medicinal uses) were collected through interviews and discussion among the tribal practitioners in and around the study area. Data were also collected through questionnaires in their local language. In addition to the botanical names and medicinal uses, detailed information about mode of preparation (i.e., decoction, paste, powder and juice) was also collected. The collected specimens were pressed properly. Succulent plants and Orchids were collected and preserved individually. After drying the specimens were poisoned with 0.1 % $HgCl_2$ dissolved in absolute alcohol and mounted with glue on standard herbarium sheet (42 × 28 cm) following the method of Jain and Rao (1970). Field data with collection number, locality, short description, vernacular name and collector's name were transferred from the field note book to the right hand corner of the herbarium sheet for ready identification.

The mounted specimens were identified with the help of regional floras *viz*., Flora of Tamil Nadu Vol. II (Henry *et al*., 1987), The Flora of the Tamil Nadu Carnatic (Matthew, 1982) and The Flora of Presidency of Madras (Gamble, 1915; Gamble and Fischer, 1928). The voucher herbarium specimens were later identified authentically in comparison with specimens available in the herbarium of Botanical Survey of India, Southern Circle, TNAU Campus, Coimbatore, Tamil Nadu. All the collected plants were preserved in the form of herbarium and were deposited at Post Graduate and Research Department of Botany, Vellalar College for Women, Erode, Tamil Nadu. The medicinal properties of the plants were checked by the earlier reports (Warrier *et al*., 1996; Nudrat *et al*., 2005). Secondary information were collected by reviewing numerous research papers, reports, records, documents, articles, books and journals related to the present study.

2.5. Enumeration of Medicinal Plants

During the study, daily activities of the local inhabitants were closely observed and interpersonal contacts were established by participating in their functions.

Interviewees were chosen without distinction of gender after seeking the consent from each respondent. All verbal information on the medicinal plants were obtained and recorded from the elderly local people from all age groups, except people who were below 37 years and were interviewed on their knowledge about the uses of plants in this region. There were 11 informants within the age group of 37 to 68 among them two were Nattu Vaidhiars. Informants were asked to name the plants they knew, and to reveal the uses of the respective species. In cases of illiterate informants, photographs and fresh plant specimens from the field were presented to them and questionnaire were filled from their responses. Ethnobotanical data were collected according to the methodology suggested by Jain and Goel (1995) and were record through a modified schedule based on Schultes (1960). The species mentioned by the informants were taxonomically identified and the data were meticulously entered in to a field notebook. The information of the collected plants were documented and recorded alphabetically with the local name, parts of plants used, binomial, family and uses. Taxonomical studies of the plant were carried out and the systematic position of the plant has been assigned as per the angiosperm taxonomic classification of Bentham and Hooker's (1862-1883).

3. Results

The forests in Karamadai Range are verdant and virgin forests of approximately 150 million years old. Of the total area of 11,233.93 hectares, Pillur beat occupies an area of 2742.22 hectares which comes under reserve forest. Pillur beat forest division exhibits luxuriant tropical forest in the top level, deciduous forest types in the middle level and scrub jungle in the foot hills. This variation in flora is due to the diversity of climate, altitude and soil conditions of the hill. The study area harbours a high number of medicinal and other economically important plants in their understories, despite the existence of adequate soil moisture at all times during the year.

3.1. Ethnomedicinal Plants

The survey on ethnomedicinal plants revealed that 114 plants species have been used by Irulas to treat different ailments. These plants are used to treat minor ailments like fever, dysentery, rheumatism, skin diseases, ulcers, cough, wounds, diarrhoea and major ailments like asthma, bronchitis, diabetes, inflammation, snake bite, jaundice and tumors. The plants are used both externally as well as given internally. The medications are prepared in the form of decoction, juice, extraction, paste, tonic, powder and infusion. The complete data are given in Table – 1.

Table -1: Enumeration of Ethnomedicinal Plants used by Irulas in Pillur beat

Botanical Name	Local Name	Parts used	Therapeutic uses	Mode of Preparation
Abutilon indicum G. Don.	Thuthi	Leaves	Anti-inflammation, skin eruptions and ulcer	Extraction
Acacia nilotica (Linn.) Del.	Karuvel	Leaves and fruits	Diabetes, skin disease, cancer and antidiarrhoeal	Infusion
Acalypha fruticosa Forsk.	Ceerasedi	Roots, leaves and stem	Whooping cough	Extraction
Acalypha indica Linn.	Kuppaimeni	Leaves and roots	Skin diseases and ulcers	Extraction
Acalypha paniculata Miq.	-	Leaves, stem and fruit	Bronchitis, asthma, rheumatism and skin diseases	Decoction
Achyranthes aspera Linn.	Nayuruvi	Whole plant	Dysentery	Extraction
Adhatoda vasica Nees.	Adathodai	Leaves and roots	Asthma	Juice
Aegle marmelos Corr.	Vilvam	Root, bark and fruit	Diarrhoea and dysentery	Decoction
Agave americana Linn.	Kantala	Leaves	Antiseptic, diarrhoea, diuretic, dysentery, flatulence, gonorrhoea, hydrophobia, jaundice, snake bites, stomachic, toothache, venereal disease and wounds	Decoction
Aglaia elaeagnoidea (A. Juss.) Benth.	Chokla	Fruits and seeds	Astrigent, antidiarrhoeal and skin diseases	Tonic and Paste
Ailanthus excelsa Roxb.	Peru	Bark	Skin diseases, jaundice, and bronchoitis	Paste
Allophylus serratus Radlk.	Siruvalli	Leaves, seed, flower and root	Anti-inflammatory, carminative drug, oedema, fractured bone, wound healing, ulcer, diarrhoea, dyspepsia and gastrointestional disorder	Juice, Paste and Decoction
Aloe vera Linn.	Katthazhai	Whole plant	Jaundice and skin diseases	Extraction
Alysicarpus monilifer DC.	Kasukkoti	Leaves, stem and root	Inflammation, skin diseases, jaundice and fever	Paste and Decoction
Alysicarpus rugosus DC.	-	Whole plant, root and seed	Worms, diarrhoea, cough and dysentery	Extraction, Decoction, powder and paste
Anagallis arvensis Linn.	Culliver	Flower	Fever, skin diseases and wound healing	Infusion
Anaphalis beddomei	Pearl	Whole plant	Fever, cough and diarrhea	Juice
Andrographis paniculata Nees.	Siriyanangai	Whole plant	Snake bites, fever and skin diseases	Infusion
Anisomeles indica O. Kze.	Gobura	Leaves	Ulcers, fever and cough	Tonic and Decoction
Anodendron paniculatum A. DC.	Sarakkodi	Leaves and fruits	Jaundice	Powder
Anogeissus latifolia Wall.	Namai	Flowers and fruits	Diabetes, diarrhoea and dysentery	Decoction and juice
Anona muricata Linn.	Mul seetha	Seeds and leaves	Tumor and diabetes	Decoction

Anona reticulata Linn.	Ramachita	Root, bark and seed	Diarrhea and dysentery	Decoction and juice
Argemone mexicana L.	Birammathandu	Root	Fever and rheumatism	Decoction
Aristolochia bracteata Retz	Esvaraveru	Whole plant	Anti-inflammation and Anthelmintic	Dry powder
Artocarpus hirsuta L.	Aiyinipila	Seed and fruit	Asthma and skin diseases	Powder
Asparagus racemosus Willd.	Neervekkaea	Tuber	Tumors, cough and bronchitis	Decoction
Azadirachta indica A. Juss.	Vembu	Whole plant	Anti-inflammatory and skin diseases	Extraction
Azima tetracantha L.	Sangliai	Leaves	Cold and cough	Juice
Blepharis boerhaaviaefolia Pers.	-	Leaves, root, fruit and seeds	Wound healing, ulcers, nasal, hemorrhage, asthma, throat inflammation, ascitis, spleen disorders, dysmenorrhoea, urinary disorder, kidney stone, nervous system disorders and aphrodisiac	Decoction
Boerhaavia verticillata Poir.	-	Whole plant	Fever, dysentery, skin diseases, poisonous bites, wound healing and rheumatism	Paste
Bridelia stipularis Bl.	-	Bark, root, leaves and fruit	Skin diseases, cough, fever, asthma, sores in mouth, jaundice, reducing inflammation, anti diarrhoea, vomiting and anti toxic	Decoction, Powder and Juice
Buchanania axillaris (Desr.) Ramam.	Kolamaavu	Leaves, seeds and flowers	Diarrhoea, ulcer, reduce fever and skin diseases	Juice and Paste
Calamus rotang Linn.	Pirambu	Fruit and leaves	Astringent, antidiarrhoeal, anti-inflammatory, chronic fevers, piles, abdominal tumours, strangury, antibilious, spasmolytic	Decoction
Canthium coromandelicum (Burm. F.) Alston.	Bellakarai	Bark and root	Fever and diarrhoea.	Decoction
Capparis zeylanica Linn.	Adhandai	Root	Dysentery and diarrhea	Extraction
Caralluma adscendens R.Br.	Kullee mooliyan	Stem, root and flower	Cough, cold and diarrhea	Decoction and Paste
Caralluma pauciflora N. E.Br.	Puliyanprinadai	Leaves and whole plant	Ulcer, rheumatism, diabetes and inflammation	Decoction and paste
Cardiospermum halicacabum Linn.	Mudakkattan	Leaves	Rheumatism, fevers, skin diseases and poisonous bite	Extraction
Carissa carandas Linn.	Kallakai	Root bark	Wound healing and diabetes	Decoction
Carmona retusa Vahl.	Malaiverrilai	Leaves, root and stem	Dysentery and cough	Decoction
Cassia auriculata Linn.	Aavaram	Leaves and flower	Diabetes and joint and muscle pain (rheumatism)	Paste and Juice
Cassia montana Heyne.	Malaikkondrai	Stem, root, and leaves	Ring worm and skin diseases	Tonic and Paste
Cassia obtusa Roxb.	Nilavaagai	Leaves, stem and fruit	Fever, cough and cold	Decoction

Cassia occidentalis Linn.	Peyaverai	Seeds, leaves root, fruit and whole plant	Cutaneous diseases, cough, aphrodisiac, alexeteric, asthma, sweetish, bitter, stomachic, fevers, good for sore throat, diuretic, whooping cough, elephantiasis, snake bite, ascites, purgative, febrifuge, sore eyes and skin diseases	Extraction
Cassia tora Linn.	Tagarai	Whole plant	Skin diseases and snake bite	Decoction
Cissus vitiginea Linn.	Cemperandai	Whole plant	Anti-inflammation	Juice
Citrullus colocynthis (L.) Schrader	Pey-komatti	Whole plant	Skin diseases, used in sciatica and joint disorders	Decoction
Cleome felina Linn.	Taivelai	Leaves	Cough, asthma and skin diseases	Paste
Cleome gynandra Linn.	Taivelai	Leaves and root	Fever, cough, asthma and skin diseases	Decoction
Cleome monophylla Linn.	Ellukku	Leaves, seeds, root, fruit and stem	Ulcers, boils, wounds cough, headache, swellings caused by plague, hasten maturation, treatment for swellings, treatment of ear discharges, treatment of fevers, vesicant anthelmintic and rubefacient	Juice, Paste and Decoction
Cleome viscosa Linn.	Naikkaduku	Seeds and leaves	Wounds and ulcers	Juice and Paste
Coccinia grandis Voigt.	Kovakai	Fruit	Fever, asthma, bronchitis and jaundice	Juice
Combretum albidum G.Don.	Vennangukodi	Leaves, fruit and stem bark	Peptic ulcer, diarrhoea, dysentery, jaundice and skin diseases	Paste, Decoction and Juice
Cymbopogon coloratus Stapf.	Elumiccaippul	Leaves and root	Fever, cough and cold	Decoction and Tonic
Decalepis hamiltonii Wight & Arn.	Magalie	Tuber	Wound healing, fever and asthma.	Tonic
Dioscorea tomentosa J. Konig ex Spreng.	Noorai	Tuber	Fever, cough, cold and body swelling	Juice
Ehretia cymosa Thonn.	Kalvirasu	Leaves	Fevers and wound healing	Infusion
Euphorbia antiquorum Linn.	Chatura Kalli	Stem, root and latex	Anasrea,anodyne,bronchiti, deafness, dropsy, dysentery, dyspepsia, emetic, gout, nervine, phthisis, purgative, rheumatism, rubifacient, ulcers, tumor,vesicant, whitlow, asthma, constipation, skin diseases, ascites and stomach distention	Tonic
Euphorbia elegans Spr.	-	Leaves and root	Fever, cough and anti – inflammation	Paste and Tonic
Euphorbia hirta Linn.	Chittarap	Whole plant	Female disorder, respiratory ailments, cough, coryza, bronchitis, asthma, worm infection, dysentery jaundice, gonorrhoea, digestive problems and tumors	Decoction

Ficus bengalensis Linn.	Aal	Bark and latex	Rheumatism, dysentery and Diabetes	Juice
Ficus microcarpa Wight.	Kallichchi	Whole plant	Rheumatism and fever	Infusion
Gloriosa superba Linn	Kanthal malar	Whole plant	Skin diseases and anti cancerous	Decoction
Grewia bracteata W. & A.	Pantripidukku	Leaves, root and seed	Anti-inflammation and anti cancerous	Decoction
Grewia orbiculata Rottl.	Ney-c-citti	Bark and root	Skin diseases and wound healing	Paste and Juice
Gymnema montanum Hook. f.	-	Leaves and stem	Diabetes, cough, snake bites and digestive disorders	Decoction, Tonic and Paste
Gymnema Sylvestre Linn.	Cherukurinja	Leaves	Snake bite and Diabetes	Decoction
Hemidesmus indicus (Linn.) R. Br	Nannari	Root	Ulcer and wound healing	Juice
Heteropogon contortus Beauv.	-	Leaves, stem and root	Rheumatism and wound healing	Decoction
Ichnocarpus frutescens R.Br.	Udarkkoti	Whole plant	Cough, dysentery and glandular tumors	Extraction and Decoction
Indigofera trita Linn. f.	Punal-murunkai	Leaves and root	Stomach cancer	Decoction
Ipomaea obscura K-Gawl.	Siruthaali	Seed, root and leaves	Anthelmintic, diuretic and laxative	Decoction
Jatropha curcas Linn.	Kattamanakku	Leaves, stem and seeds	Liver, detoxifier, anticancerous, diuretic, laxative, bitter tonic, antispasmodic, infective hepatitis, restores normal color to urine epilepsy, gastritis, wounds, purgative, poisoning, anthelmintic, rheumatism and skin diseases	Decoction
Justicia glauca Rottl.	Thavasimurungai	Leaves, root and flower	Anti-inflammatory	Paste and Decoction
Leonotis nepetaefolia R.Br.	-	Whole plant, leaves and seeds	Anti cancer, rheumatic pains, skin diseases and fever	Paste
Leptadenia reticulata (Retz.) Wight	Palaikkodi and Paalaikeerai	Leaves and root	Skin disease and asthma	Juice, Paste and Decoction
Leucas aspera Spr.	Thumbai	Whole plant and leaves	Snake bites, cough and fever	Decoction and Paste
Lindernia caespitosa (Blume) G. Panigrahi	Panigrahi	Whole plant	Fever, cough, cold and anti - inflammatory	Decoction
Mecardonia procumbens (Mill.) Small.	-	Leaves and root	Fever, cough and wound healing	Infusion
Micrococca mercurialis (Linn.) Benth.	Kunukkuth thukki	Leaves	Curing sores, rheumatic pain, constipation, fever, purgative, skin diseases, instilled in to the nose, eyes or ears to treat headache, filariasis of the eye or otitis	Juice
Moringa concanensis Nimmo	Karimurungai	Leaves, bark, flower, fruit, seed and root	Joint pain, asthma, cancer and diabetes	Decoction and Paste
Moringa tinctoria Roxb.	Mannanunai	Leaves	Diarrhoea and ulcer	Paste

Opuntia dillenii Haw.	Sappattukkalli	Whole plant	Purning sensations, asthma, whooping cough, hepatitis, poison, fever, constipation, conjunctivitis, boils, ulcers, edema, diuretic, purgative menorrhagia and liver complaints	Decoction
Oxystelma esculentum R. Br.	Oosippalai	Leaves	Cough and joint pain	Juice
Pandanus odoratissimus Roxb.	*Thazhampoo*	Leaves	Antipyretic, expectorant, diuretic, cardiotonic, purgative, leprosy, mallpox, scabies, heart and brain diseases	Juice
Phyllanthus debilis Hook. f.	Arulundi	Root, leaves and whole plant	Fever, jaundice, asthma and wound healing	Paste and Decoction
Randia dumetorum Lam.	Karamul	Whole plant	Cough, skin diseases, ulcers and asthma	Decoction
Sanseviera roxburghiana Schult.	Marul	Leaves	Snake bite	Tonic
Santalum album Linn.	Sandhanam	Leaves and stem	Dysentery and skin diseases	Paste
Sarcostemma brevistigma W. & A.	Kondapala and kodikalli	Whole plant	Asthma, rheumatism, joints pain, ear ache, dog bite, chronic ulcer, lactating mother, wounds, cuts, digestive disorder, fever, cough, cold, menstrual disorder, bone fracture, emetic, snake bite bronchitis, tumor and skin diseases	Decoction
Solanum nigrum Linn.	Manatakkali	Leaves, root and fruit	skin diseases, rheumatism, ear and eye diseases	Juice
Solanum trilobatum Linn.	Thoodhuvalai	Fruits and leaves	Chest colds, cough, sore throat, and throat inflammation.	Juice and Decoction
Solanum erianthum D. Don.	Anai-c-cuntai	Leaves , root, root bark and fruits	Dysentery, fever, wound healing and skin diseases	Decoction
Solena amplexicaulis (Lamk.) Gandhi.	Pulivanchi	Root and leaves	Anti inflammation and diabetes	Decoction and juice
Streblus asper Lour.	Kurripila	Stem,bark and root bark	Dysentery, diarrhoea, fever, skin diseases, snake bites and disinfecting wounds	Decoction, powder and Paste
Strychnos nux-vomica Linn.	Yetti	Stem and bark	Dysentery, fever and cold	Decoction
Syzigium cumini (L.) Skeels.	Naval	Seeds	Diabetes and reduce the level of sugar in the blood	Decoction
Tephrosia villosa W. & A.	-	Leaves	Leprosy, ulcers, asthma, tumors, liver damage, spleen, heart, blood, dyspepsia, diarrhoea, rheumatism and urinary disorders.	Decoction
Terminalia arjuna W. & A.	Marutham	Bark	Snake bite, fever and diarrhoea	Paste

Terminalia chebula Retz.	Kadukkai	Leaves and stem	Skin diseases and relieves inflammation	Extraction and Juice
Toddalia aculeata (SM.) pers.	Kattumilaku	Whole plant	Anti inflammatory, fever, cough, asthma and cold	Decoction
Tribulus terrestris Linn.	Nerunchi	Whole plant and flower	Fever and head ache	Decoction, Juice and Paste
Trichodesma indicum R. Br.	Kallutaitumapi	Roots, leaves and fruits	Snake bites and cough	Decoction
Trichodesma zeylanicum	Kalutaikkali	Leaves	Fever, cough and cold	Tonic
Tylophora asthmatica	Naypalai	Leaves	Bronchial and tuberculosis	Decoction
Vallaris solanacea	-	Root and bark	Anti diarrhoeal and dysentery	Tonic and Paste
Vitex altissima Linn.	Mayilainochi	Leaves and root	Inflammation, wounds and ulcer	Paste and Decoction
Vitex peduncularis Wall.	Mayilei	Leaves	Anti inflammation	Extraction
Wrightia tinctoria R.Br.	Veppalai	Bark, fruit and leaves	Fever, skin disease and anti inflammation	Paste and Tonic
Zizyphus glabrata W.	Karakodamaram	Fruits	Fever, cough and rheumatism	Extraction
Zizyphus mauritiana L.	Illandai	Fruits	Ulcer, cuts, asthma and fever	Decoction
Zizyphus nummularia	Jhar beri	Leaves	skin diseases	Decoction
Zizyphus oenoplia Mill.	Churipala chedi	Fruit and bark	Diarrhoea, diabetes and anti cancerous	Decoction

3.2. Enumeration of Parts used for Medicinal Purposes across different Taxa

The study showed that quite a number of plant parts from the 114 species especially the leaves, roots and whole plant have been found to be efficient in the management of various diseases. The various plant parts mentioned include bulb, fruit, leaves, rhizome, root, seed, stem bark and whole plants. It was observed that leaves formed the most frequently used part (53.5 %), followed by roots (34.21 %), whole plant (21.05 %), fruits (18.4 %), stem (14.9 %), seeds (14.0 %), bark (9.64 %), flowers (7.01 %), tuber (2.6 %) and latex (1.7 %). The plant leaves are important ingredient in traditional treatment of various diseases as it features as a component in many herbal preparations (Table – 2).

Table -2. Number of Plant Parts used for Medicinal Purpose

S.No	Plant parts	Total Number of Species	Percentage (%)
1.	Leaves	61	53.5
2.	Roots	39	34.21
3.	Whole plants	24	21.05
4.	Fruits	21	18.4
5.	Stems	17	14.9
6.	Seeds	16	14.0
7.	Barks	11	9.64
8.	Flowers	8	7.01
9.	Tubers	3	2.6
10.	Latex	2	1.7

3.3. Mode of Preparation of Medicine

The mode of preparation of medicines was documented during the study and it is shown in Table - 3. The mode of preparation used for medicinal purposes were decoction (51.7 %), paste (28.9 %), juice (21.05 %), extraction (12.3 %), tonic (11.4 %), infusion (5.3 %) and dry powder (4.4 %).

Table - 3. Mode of Preparation of Medicines in the Study Area

S.No	Mode of Preparation	Total Number of Species	Percentage (%)
1.	Decoction	59	51.7
2.	Paste	33	28.9
3.	Juice	24	21.05
4.	Extraction	14	12.3
5.	Tonic	13	11.4
6.	Infusion	6	5.3
7.	Dry powder	5	4.4

3.4. List of Ailments Treated by the Tribals

The tribal of Pillur beat used plants to cure ailments such as, anaemia, aphrodisiac, cancer, spasm, arthritis, body ache, bronchitis, asthma, cold, cough, diabetes, digestion, diarrhoea, dysentery, eye infection, epilepsy, elephantiasis, fever, headache, jaundice, joint pain, leprosy, liver and spleen disorders, menstrual problem, mouth ulcer, nervous disorders, piles, hiccups, rheumatic pains, muscular pain, ring worm, skin disease, styptic, scald burns, snake, spider, scorpion and other poison bites, swelling, stomach ulcer, throat inflammation, whooping cough, wound, etc. The medicines were administered topically, orally, by inhalation and as steam baths. The oral route was the most frequently used route of administration, while inhalation was the least (Plate - 3).

a-Fauna of study hill

b - Investigator with Tribal people of Pillur Beat (gathering information on ethnomedicinal plants)

c – Observation and collection of plants by the investigator

PLATE - 3

3.5. Percentage of Species used to Treat different Ailments

Out of the large variety of species available in the study area 35.1 % was used for the treatment of asthma, followed by skin diseases (31.6 %), fever (28.1 %), diarrhoea/dysentery (20.2 %), wound healing (16.7 %), ulcer (15.8 %), inflammation and rheumatism (13.2 %), snake bite (10.5 %), cancer (8.8 %), diabetes (7.1 %) and jaundice (6.2 %) and the same has been represented in Table – 4.

Table - 4. Percentage of Species used to Treat different Categories of Ailment

S.No	Name of the Diseases	Percentage (%)
1.	Asthma	35.1
2.	Skin disease	31.6
3.	Fever	28.1
4.	Diarrhea/dysentery	20.2
5.	Wound healing	16.7
6.	Ulcer	15.8
7.	Rheumatism	13.2
8.	Anti inflammatory	13.2
9.	Snake bite	10.5
10.	Cancer	8.8
11.	Diabetes	7.1
12.	Jaundice	6.2

3.6. List of Plants Used to Treat Maximum Number of Diseases

An attempt was made to list out the plants used to treat maximum number of ailments and the same was depicted in Table - 5. From the surveyed species *Sarcostemma brevistigma* was used to cure maximum number of diseases such as asthma, rheumatisum, arthritis, joints pain, ear ache, dog bite, chronic ulcer, wounds, digestive disorder, fever, cough, cold, menstural disorder, bone fracture, anti-inflammation, emetic and hypodermic diseases, snake bite, anasrea, anodyne, deafness, dropsy, dysentery, dyspepsia, gout, nervous disorders, phthisis, bronchitis, leprosy, tumor, vesicant, whitlow, constipation, skin diseases, ascites and stomach distention. The species *Cassia occidentalis* (27), *Euphorbia antiquorum* (23), *Jatropha curcas* (17), *Opuntia dillenii* (17), *Blepharis boerhaaviaefolia* (14), *Agave americana* and *Tephrosia villosa* (13) hold a very high value for the treatment of different forms of ailments. The plants like *Azadirachta indica*, *Acalypha fruticosa, Albizzia lebbeck, Asparagus racemosus, Boerhaavia diffusa, Cassia auriculata, Cissampelos pareira, Dichrostachys cinerea*, *Clitoria ternatea*, *Leonotis nepetaefolia, Nicandra physaloides, Randia dumetorum and Zizyphus jujuba* are found to be curing agents for many major ailments such as cough, asthma, diabetes, jaundice, ulcer, fever and cancer.

The plant species like *Gmelina asiatica*, *Sapindus emarginatus*, *Moringa concanensis*, *Tamarindus indica* and *Santalum album* with higher economic values have poor ecological perpetuation in the studied habitat. In course of time, these species may lose their ecological importance, further may become rare elements due to some intrinsic and extrinsic factors. Hence, it is suggested that in addition to habitat protection, priorities must be given for these species so as to protect the genetic stock and species as well.

Table – 5: List of Plants Used to Treat Maximum Number of Diseases

S. No	Name of the Plants	Family	Number of Diseases
1.	*Sarcostemma brevistigma*	Asclepiadaceae	41
2.	*Cassia occidentalis*	Caesalpiniaceae	27
3.	*Euphorbia antiquorum*	Euphorbiaceae	23
4.	*Jatropha curcas*	Euphorbiaceae	17
5.	*Opuntia dillenii*	Cactaceae	17
6.	*Blepharis boerhaaviaefolia*	Acanthaceae	14
7.	*Agave americana*	Agavaceae	13
8.	*Tephrosia villosa*	Fabaceae	13
9.	*Cleome monophylla*	Capparidaceae	12
10.	*Calamus rotang*	Arecaceae	11
11.	*Euphorbia hirta*	Euphorbiaceae	11
12.	*Bridelia stipularis*	Euphorbiaceae	10
13.	*Pandanus odoratissimus*	Pandanaceae	10
14.	*Phyllanthus debilis*	Euphorbiaceae	10
15.	*Allophylus serratus*	Sapindaceae	10
16.	*Micrococca mercurialis*	Euphorbiaceae	10

4. Discussion

In the last few decades eco-friendly, bio-friendly, cost-effective and relatively safe herbal medicines have moved from the fringe to the mainstream with increased research in the field of traditional medicine. Medicinal plants are an integral component of alternative medical care. For millennia, Indian people traditionally played an important role in the management of biological resources and were custodians of related knowledge that they acquired through trial and error over centuries. India has a rich wealth of medicinal plants and the potential to accept the challenge to meet the global demand for them. Ayurveda, Naturopathy, Unani, Siddha and folk medicine are the major healthcare systems in Indian society, which fully depend upon natural resources (Jena and Satapathy, 2015; Mishra e*t al.*, 2015).

The present communication is undertaken to ascertain the detailed information on the traditional healing potential of plant species used by Irula tribals who inhabit the forest areas in Pillur Beat (Pillur slope RF and Nellithurai RF), Karamadai range, Western Ghats, Tamil Nadu, India. The study area Pillur beat encompasses 12 Tribal villages namely Gethaikkadu, Poochamaruthur, Nellimarathur, Korappathi, Veerakkal, Baralikadu, Neeradi, Melpillur, Situkunni, Kadaman kombai, Veppamarathur and Sundappatti. Several hamlets, each of approximately 3-53 families, dot the roads within the reserve forest. Total number of peoples in these 12 villages exceeds above 800 (approximately 829). The tribals of Pillur beat are Irulas.

The villagers are economically very poor. Most of the elder people in this area possess immense knowledge on forest plants. They use a wide variety of plant species for their daily sustenance and livelihood. They are the ultimate jungle folk and their knowledge of plants and animals is a data bank of immense value (Dhivya and Kalaichelvi, 2015; 2016e).

The traditional knowledge systems of the folk, oral tradition, published and unpublished literature are the important sources for locating the potential of bioresources. The old people even now utilized their traditional knowledge for treating ailments which had been developed by their forefathers through trial and error methods and passed on them through an oral tradition from one generation to another. Most of the traditional knowledge about medicinal plants and their use survived only by words of mouth from generation to generation and are slowly lost. Moreover, the herbal healers had the strong tendency to keep their knowledge secret without any documentation (Vethanarayanan *et al*., 2011; Dhivya and Kalaichelvi, 2016e).

In the present study, an intensive survey was made in 12 villages of Pillur Beat to know the indigenous knowledge of the village tribals and the herbal medicine practitioners. The information on native plants used for medicinal purposes were collected through questionnaire, personal interviews and discussions among the informants in their local language during field trips. Questionnaire and discussion method is commonly followed by the earlier researchers (Anusha and Samant, 2012; Mahbubur Rahman *et al*., 2013; Datta *et al*., 2014; Shosan *et al*., 2014; Dhivya and Kalaichelvi, 2016e).

The present study explored 114 plants were used by the tribals and medicinal healers in Pillur Beat for treating a wide range of human ailments. Similarly Anusha and Samant (2012) studied the plants used in folk medicines in Pachamalai hills, Tamil Nadu, India. Sharmila *et al.* (2014) explored 57 medicinal plants in Thiashola, Nilgiri South division, Western Ghats, Tamil Nadu, India. Ampitan (2013) carried out studies on medicinal plants of Borno state Nigeria. Shosan *et al*., (2014) conducted ethno botanical study in Ogun state, Nigeria to record the native uses of medicinal herbs. Birhanu *et al*. (2015) reported the availability of higher number of plant species with ethnomedicinal values in the Gondar town, North-Western, Ethiopia.

5. Conclusion

This study shows that knowledge and usage of herbal medicine for the treatment of various ailments among Irulas is still in practice. It may be surprised to observe that the modern systems of medicine are only modification of these old formulations. In conclusion, there is an obvious need for documentation and conservation of wild medicinal plants is the only way to preserve the knowledge on the plant resources. The information given in the present study will be helpful for the pharmacognosist, botanist and pharmacologist for the collection and identification of the plant for their research work. The survey may create awareness on the importance and conservation of medicinal plants among young budding botanists.

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Chapter - 16

Phytomedicine Innovations: The Future of Plant – Based Therapies
ISBN: 978-81-977907-4-4
First Edition
Chapter – 16, Page: 252 - 272

16

AYURVEDA BASED PHYTOMEDICINES: A NEW AVENUE FOR FUTURE THERAPIES

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Abstract

Plant secondary metabolites (PSM) are compounds that are not required for a cell (organism) to live, but play a role in protection of plant against biotic or abiotic stresses. In the present chapter, we enlist the various secondary metabolites found in the *Terminalia* genus of *Combretaceae*, family. The pharmacological activities of these PSM were also elaborated. Genus *Terminalia* is commonly found in the India and has tremendous medicinal importance. These pharmacological properties are due to its secondary metabolite composition. The chapter further focuses on the different secondary metabolites, their classification, their biosynthesis and secondary metabolites like Triterpenoids - Arjugenin, Arjunic acid, Arjungenin, Terminic acid, Arjunolic acid, Arjunetin, Arjunoside I & II, Arjunolone, Arjunolitin, and Terminoside-A present in *Terminalia arjuna*. Gallic acid, Tannins, Chebulic acid, Ellagic acid, chebulagic acid, Neo chebulic acid, corilagin, Flavanol, and aglycones is present in *Terminalia Chebula*. The above mensioned PSm showed various pharmacological activities in different disease conditions like antioxidant and antimicrobial activity, antidiabetic potential, antihepatic and antimalarial properties, anticancer activity, anti-inflammatory activity, immunomodular activity, hypolipidemic activity, cardioprotective activities and its effects on central nervous system.

Keywords: Ayurveda, Phytomedicines, *Terminalia arjuna*, *Terminalia chebula*, Secondary metabolites and Pharmacological activities

1. Introduction

Ayurveda, originated in India more than 3000 years ago, is based on a belief that health and wellness depend upon a balance between the body mind and spirit. Ayurveda is based on phytomedicines which are plant-derived substances to be used as therapeutic or medicinal agents. The pharmacological properties of various herbs, roots and leaves are utilized in formulating these remedies and the same have been systematically divided in terms of their energetic qualities known as 'Gunas'. The Gunas emphasized on the effect of these phytomedicines on the body. One of the foundational concepts in Ayurveda is the idea of "doshas," which are biological energies that govern physiological and psychological processes. The three doshas - Vata, Pitta, and Kapha - represent different combinations of the five elements: earth, water, fire, air, and ether. Phytomedicines are selected based on their ability to balance these doshas, thus addressing individual health needs. For example, herbs like Ashwagandha are often recommended for their adaptogenic properties, helping to balance Vata and support stress management. Vata is a combination of air and ether, Pitta of fire and little water, Kapha of earth and water. These phytomedicines are administered in accordance to type of doshas torpid in the body, thereby catering all sorts of aspects.

Phytomedicines also embody a holistic approach to healing. Unlike conventional pharmaceuticals that often target specific symptoms, Ayurvedic treatments aim to restore overall balance and promote wellness. This is achieved through formulations that may include single herbs or complex mixtures, known as "churna" (powders) or "kashayam" (decoctions). Turmeric, with its active compound curcumin, is a notable example; it is revered for its anti-inflammatory and antioxidant properties and is commonly used to support digestive health and boost immunity. These phytopharmaceuticals are prepared and used in compliance with certain standards to ensure their effectiveness and safety. It recognizes the significance of seasonality, individual body type, and external factors in defining the appropriate herbal treatment. In addition to reducing the adverse effects of medications, this personalized paradigm enhances therapeutic efficacy for many patients seeking holistic health solutions. Research into Ayurveda-based phytomedicines has only recently piqued the interest of researchers across the globe wherein a plethora of traditional claims by various herbal preparations has been validated. Gradually, the biochemical pathways through which herbal preparations show their effects are being revealed by modern science, thereby bridging the gap between ancient wisdom and contemporary medicine. For example, the anti-diabetic properties of Fenugreek and

cardio-protective benefits of Arjuna have been experimentally tested and have high prospects of being true. However, Ayurvedic phyto-medicines should be approached critically, demanding standardization, quality control, and strict clinical testing. The global boom of the market of herbal medicines raises a problem of purity and authenticity of the Ayurvedic products. Thus, the initiatives of certifying and regulating these remedies should be considered primarily to guarantee patients' safety and treatment efficacy.

In conclusion, Ayurveda-based phytomedicines offer a rich and holistic approach to health, rooted in centuries of tradition. By integrating the wisdom of ancient practices with modern scientific research, these natural remedies hold great potential in promoting wellness and preventing disease, making Ayurveda an invaluable component of contemporary healthcare. As interest in holistic health continues to grow, the role of Ayurvedic phytomedicines is poised to expand, fostering a deeper appreciation for the power of nature in healing.

2. Plant Secondary Metabolites

Plant secondary metabolites (PSM) are compounds that are not necessary for a cell (organism) to live, but play a role in the interaction of the cell (organism) with its environment. These secondary metabolites are frequently involved in protection of plant against biotic or abiotic stresses (Pagare *et al.,* 2015). Plant kingdom is reported to have over fifty thousand different secondary metabolites. Medicinal herbs and many modern medicines rely on secondary plant metabolites for their actions.

Various products are produced by plants naturally which has variety of chemical natures. These chemicals are used for the growth and development of plants. Primary metabolites provide the supplies requires for processes, such as photosynthesis, translocation and respiration. Products derived from primary metabolites, not directly involved in growth and development, are considered as secondary metabolites. Secondary metabolites are the product of primary metabolites and are produced from biosynthesis modifications, including methylation, glycosylation and hydroxylation. Secondary metabolites are certainly more complex in structural composition and side chains compared to primary metabolites; they are interesting for various diverse reasons as their structural diversity and their potency as a drug candidate and/or antioxidants (Twaij *et al.,* 2022). PSM have tremendous potential to treat health disorders, infections, and illness. Since last few decades, they are slowly replaced by other synthetic drugs. Many of these higher plants and their

products are major sources of useful in different industries such as pharmaceutical, agrochemical, flavor and other aroma industries (Umashankar, 2020).

3. Classification of Secondary Metabolites

Plant secondary metabolites are classified into different groups (Figure - 1) depending on their biosynthesis pathway, chemical structure, composition, solubility in organic solvents or water and metabolic processes. The plant secondary metabolites are classified into various classes based on functional groups and chemical structure. These classes include polysaccharides, phenolic compounds, phytoalexins (sulfur-containing compounds), terpenes (including volatile compounds, sterols, and carotenoids), flavonoids, alkaloids (nitrogen-containing compounds), and hydrocarbons. Almost all of these metabolites contribute significantly to defense against stressful situations.

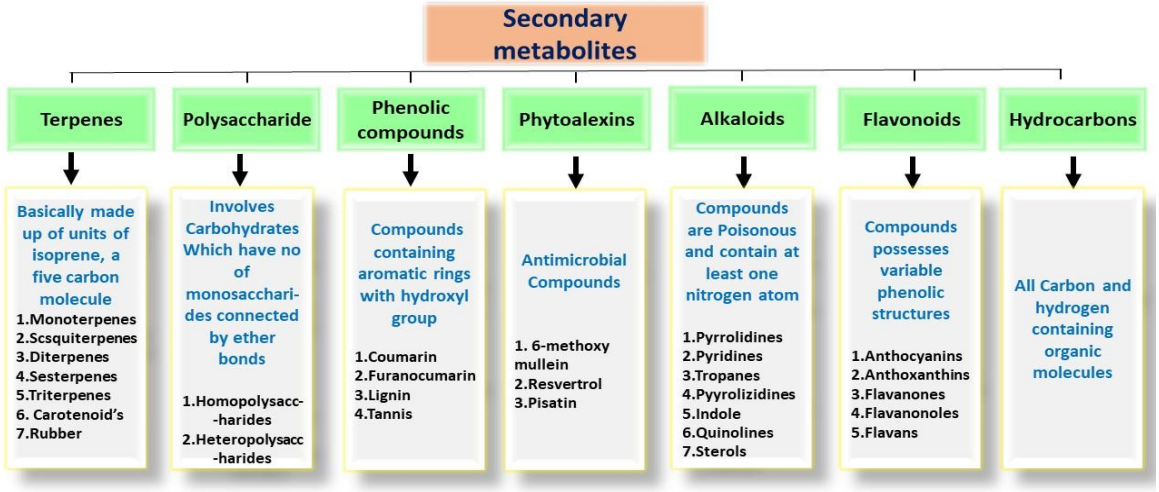

Figure - 1: Classification of Secondary metabolites

Basically, terpenes consist of isoprene molecules a five carbon volatile compound, called as a fundamental building block of this class. Polysaccharides are polymeric carbohydrates composed of monosaccharides connected with ether bonds. Phenolic compounds contains the aromatic ring with one or more hydroxyl group in their structures. Phytoalexins are mostly antimicrobial compounds or sometimes also antioxidant, mainly play role in defense mechanism. Alkaloids contain at least one nitrogen in their structure and mainly poisonous Flavonoids are very abundant in plants and possess variable phenolic structures. Hydrocarbons involve all the hydrogen

containing organic molecules. The pictorial representation of the plant secondary metabolites is given in the Figure - 2.

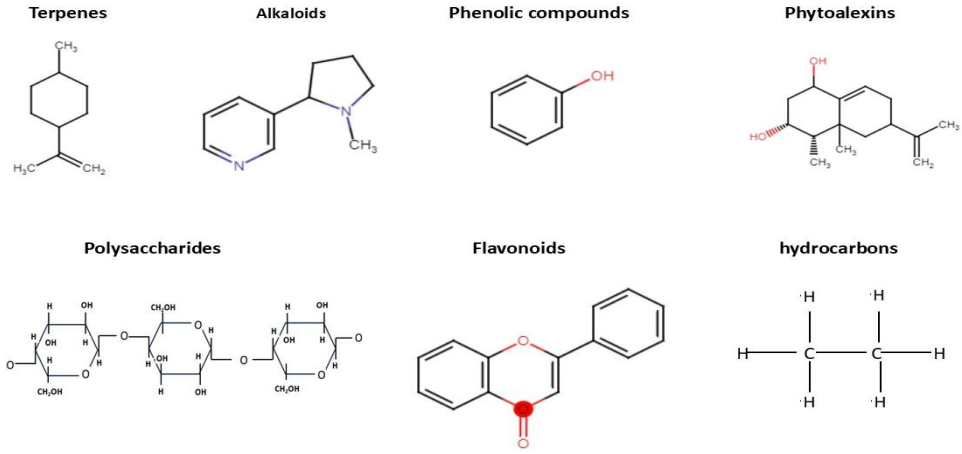

Figure - 2: Major classes of Secondary metabolites and their representative structures

4. Synthesis Pathways for Plant Secondary Metabolites

Plants produce Secondary metabolites through several metabolic pathways that effectively respond to stress conditions. These pathways are initiated from primary metabolite pathways, which produce the ultimate precursors of Secondary metabolites. The precursors of metabolites are essentially produced in the Krebs cycle and shikimate pathway. Primary metabolites are the critical precursors of Secondary metabolites. Biosynthesis of secondary metabolites mainly involves three major pathways

- *Shikimic acid Pathway:* The shikimic acid pathway produces phenolic compounds mainly. And also the nitrogen containing compounds like alkaloids in association with other pathways.
- *Acetate-mevalonate pathway:* The mevalonate pathway produces a variety of secondary metabolites, including monoterpenoids, sesquiterpenoids, diterpenoids, carotenoids, polyprenols, isoprenoids, sterols, ubiquinone, and dolichols.
- *Acetate malonate pathway:* This pathway produces vast range of products in fatty acid metabolism, and also the compounds like glycosides.

These biosynthesis pathways are inter connected with each other at different steps. Primary metabolites are utilized to form secondary metabolites. Erythrose-4-Phosphate from Pentose phosphate pathway is utilized with Phosphoenol puruvate as a substrate for synthesis of Phenylalanine, which is utilized to synthesize flavones, chalcones, anthocyanines, condensed tannins. Phenylalanine from shikimic acid pathway can be utilized to produce nitrogen containing secondary metabolotes Biosynthesis of anthocyanins is carried out by shikimic acid pathway. In Shikimic acid pathway, Malonyl-co A from Mevalonic acid pathway is utilized. This Malonyl CoA is combined with p-Coumaroyl Co-A to form chalcones and these chalcones are modified to form anthocyanin. Acetyl Co-A a connecting metabolite between glycolysis and Crebs cycle is utilized in Malonic pathway to form Malonyl CoA. This Malonyl Co A is utilized in synthesis of phenolic compounds and also in synthesis of Nitrogen containing secondary metabolites. Malonic acid formed in the Malonic pathway is utilized in biosynthesis of fatty acids. Acetyl Co A is also utilized in Mevalonic pathway to produce sesquterpenes, diterpenes, steroids etc.

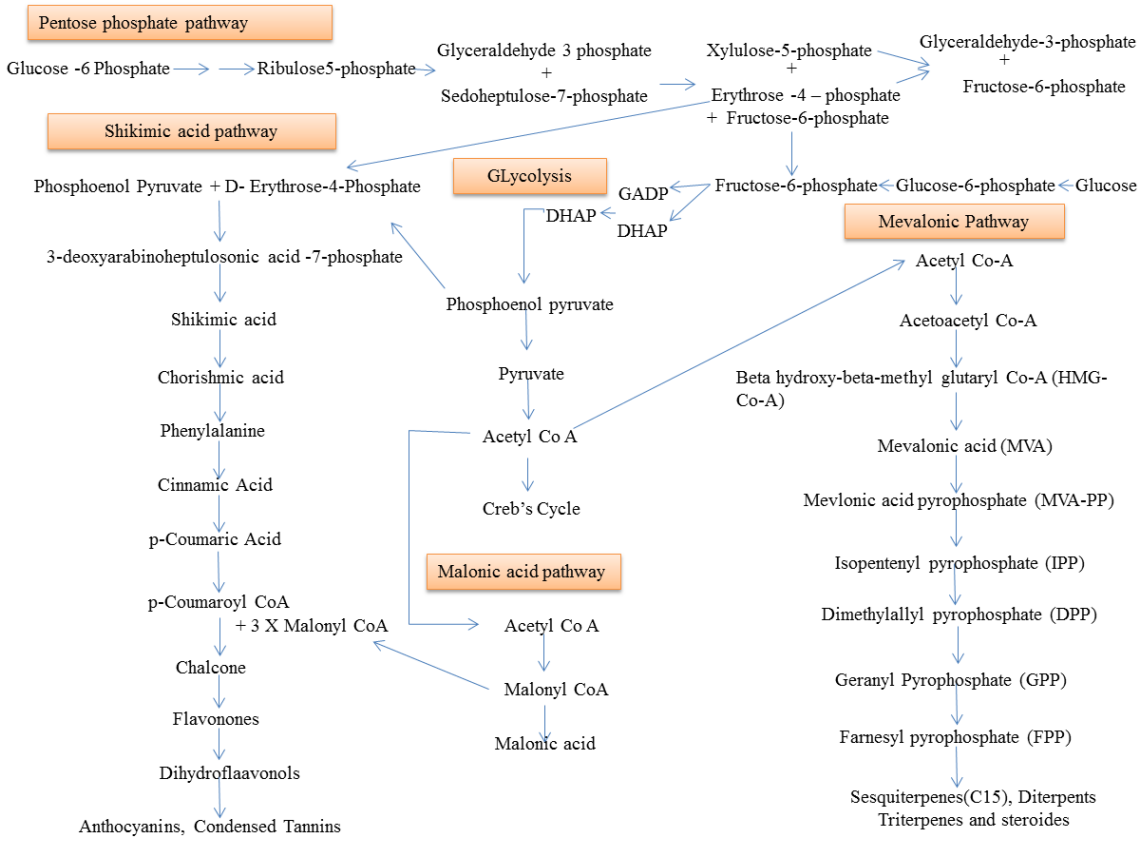

Figure - 3: Interconnection between Biosynthetic pathways for Secondary metabolites

5. Secondary Metabolites from *Terminalia* Genus

The Combretaceae family consists about 18 - 20 genera and 600 species of trees, shrubs and lianas. Plants belonging to this family are found in tropical and subtropical regions, mostly in Asian countries and African countries. *Combretum* and *Terminalia* are commonly found genus of Combretaceae. Plants from this genus show activity in treatment of many diseases and have important secondary metabolites with antioxidant activities (Georgieva *et al.,* 2021). Terminalia Linn, is a genus in the family Combretaceae with about 250 species in the world, is distributed mainly in southern Asia, Himalayas, Madagascar, Australia, and the tropical and subtropical regions of Africa. Many species are used widely in many traditional medicinal systems, e.g., traditional Chinese medicine, Tibetan medicine, and Indian Ayurvedic medicine practices, *Terminalia* plants in southern Asia have been intensively studied phytochemically due to their wide usage in Asian (India, Tibetan, and Chinese) traditional medicine systems, for example the fruits of *Terminalia bellirica* and *Terminalia chebula*, together with *Phyllanthus emblica* (*Euphorbiaceae*) which form the herbal remedy, *Triphala*, in Tibetan medicine, have received much attention because of its extensive and remarkable effectiveness in the treatment of anticancer, antifungal, antimicrobial, antimalarial, antioxidant (Zhang *et al.,* 2019). As like above mentioned species this genus have many valuable species, among them our book chapter is focused on *T. arjuna* and *T.chebula,* these two plant species because of their wide range of secondary metabolites which are used in tradtional as well as modern medicines.

Table - 1: Methods for Extraction and Characterization of Secondary metabolites

Plant	Method used for extraction	Compounds extracted	References
T. arjuna	Soxhlet apparatus extraction	Phenols, flavonoids, tannins, saponins, alkaloids, glycosides, phytosterols, carbohydrates	Muddapur *et al.* (2023)
T. chebula	Ultrasound-assisted extraction (UAE)	Phenolic compounds	Sheng *et al.* (2018)
	Supercritical fluid extraction (SFE)	Essential oils, flavonoids, total phenolic compounds, coumarins, and diterpenoids, among other substances	Sheng *et al.* (2018)

5.1. *Terminalia arjuna*

Terminalia arjuna is an evergreen tree, it is a large-sized deciduous tree The plant has a long history of medicinal uses in India. The uses are firstly mentioned by Vagbhata (a famous ayurvedic expert in ancient times) as per Bhavaprakasha. *Terminalia arjuna* is widely seen in the Indian Subcontinent, Africa, Southern Asian

countries, Australia and South America. It is commonly known as s Arjuna, Dhavala, Kaubha, Nadisaraja, Veeravrikskha, Partha and Indradru (Jaiswal *et al.,* 2021).

5.2. *Terminalia chebula*

Terminalia chebula (*Haritaki*) is an umbrella medium-sized deciduous tree. The flowers are short-stemmed, monoecious, dark white to yellow, with a strong, unpleasant odor, and in simple terminal spikes or short panicles. It is a deciduous tree having sizes from moderate to large, attains a height of 25 – 30 m and usually has a slow growth rate (Gupta, 2000). *Terminalia chebula* is a plant to the genus *Terminalia*, family *Combretaceae*. It called black myrobalan in English. It is also known as *Harada* (Marathi & Gujrati), *Haritaki* (Sanskrit and Bengali), *Harad* (Hindi), *Kadukkaya* (Tamil), *Karkchettu* (Telugu). The Sanskrit name '*Haritaki'* is rich with meaning, referring to the yellowish dye (Harita) that it cures all the diseses (Chattopadhyay and Bhattacharyya, 2007).

Table - 2: Secondary Metabolites in Selected Plants

S.No	Plant	Extract	Secondary metabolites	Reference
1	*Terminalia arjuna*	Bark	Triterpenoids - Arjugenin, Arjunic acid, Arjungenin, Terminic acid, Arjunolic acid	Dwivedi and Chopra (2014)
			Glycosides- Arjunetin, Arjunoside I& II, Arjunolone, Arjunolitin, Terminoside A, Terminic acid Flavonoids	Saha *et al.* (2012); Gaikwad and Jadhav (2018)
			Phenolics- Arjunone, luteolin, Baicalein, ethyl gallate, gallic acid, kaempferol, quercetin, Tannin- punicallin, Castalagin, casuarinin, punicalagin, Terflavin C	Saha *et al.* (2012)
		Leaves	Alkaloids, cardiac glycosides, flavonoids, tannins, phenols, terpenoids	Singh *et al.* (2018)
		Roots	Arjunoside, Arjunolic acid, Terminic acid, Arjunic acid	Amalraj and Gopi (2017)
2	*Terminalia chebula*	Leaves	Chebulagic acid, Tannins	Li *et al.* (2011)
		Fruits	Gallic acid, Tannins, Chebulic acid, Ellagic acid, chebulagic acid, Neo chebulic acid, corilagin, Flavanol, aglycones	Sharma *et al.* (2011); Prasad *et al.* (2006)
		Seeds	Chebulagic acid, Ellagic acid, Chebulagic acid	Kannan *et al.* (2012); Bhagavan *et al.* (2011)

6. Pharmacological Potential of These Secondary Metabolites

Various pharmacological activities were observed by the *Terminalia arjuna* and *Terminalia chebula*. All plants part extracts were evaluated against these activities. The extracts were rich in secondary metabolites. In this section, various pharmacological activities were assessed.

6.1. Antimicrobial Activity

Terminalia arjuna: An antibacterial activity of methanol extracts of *Terminalia arjuna* against was reported against multi drug resistance *Salmonella typhi*. *Terminalia arjuna* extract from bark have also reported to have antibacterial activity as compare to chloramphenicol, a standard drug. *Terminalia arjuna* holds significant antibacterial activity against *Pseudomonas aeruginosa, Escherichia coli*, *Klebsiella aerogenes*, and *Proteus vulgaris* (Vijayalaxmi *et al.,* 2023).

Terminalia chebula: The plant secondary metabolites showed antibacterial activity against various Gram positive and Gram negative bacteria such as *Salmonella typhi*, *Staphylococcus epidermidisis*, *Staphylococcus aureus*, *Bacillus subtilis* and *Pseudomonas aeruginosa*. These were the suggested broad spectrum for antibacterial remedy. *Terminalia chebula* fruit extract had strong antibacterial activity against intestinal bacteria, *Clostridium perfingens*, *Escherichia coli*, *A. baylyi and P. aeruginosa* (Mandeville and Cock, 2018). Methanolic, aqueous and ethyl acetate extracts of *Terminalia chebula* fruit displayed strong antimicrobial activity against bacteria involved in the autoimmune inflammatory diseases except *K. pneumoniae*, for which only moderate inhibition was observed.

6.2. Antioxidant Activity

Terminalia arjuna: The crude extract has a significant effect to augment endogenous antioxidant compounds. Free radicals scavenging activities are also increased in polymorphonuclear cells by arjungenin and its glucoside, arjun glucoside II. Antioxidant activity of *Terminalia arjuna* Methanolic Extract (TAME) and *Terminalia arjuna* ethyl acetate extract (TAEAE) finds out by using different in-vitro models. It includes Free radical scavenging activity of DPPH, Ferric reducing antioxidant power, Total flavonoid content and Total phenolic content. The plant contains much number of Phenolic compounds and Flavonoids. Plant shows significant antioxidant activity (Jaiswal *et al.,* 2021).

Terminalia chebula: The ethanolic fruit extract known to have high phenolic content and effectively inhibit lipid peroxidation. The extract significantly reversed the t-BHP-induced cell cytotoxicity and lactate dehydrogenase leakage, exhibited *in vitro* ferric-reducing antioxidant activity and 2,2-diphenyl-1-picryhydrazyl free radical-scavenging activities (Lee *et al.,* 2005). The xanthine/xanthine oxidase inhibition activity was reported for aqueous extract of *Terminalia chebula* (Bag *et al.,* 2013).

6.3. Antidiabetic potential

Terminalia arjuna: reduces the increased level of ROS and RNS (Reactive Oxygen Species, Reactive Nitrogen Species) and also regulates the pathway leading to apoptotic cell death, thus arjunolic acid has beneficial role against diabetes. It reduces oxidative, nitrosative stress, and multiple foci of hemorrhagic necrosis and cloudy swelling in tubules of the kidney. In diabetic lab mouse oral administration of *T. arjuna* (250 and 500 mg/kg body weight) for 30 days showed significant reduction in glucose, The bark powder of Terminalia arjuna can lower serum lipids in rats fed a cholesterol-rich diet (Jaiswal *et al.,* 2021).

Terminalia chebula: The chloroform extract of *T. chebula* seeds produced dose-dependent reduction in blood glucose of diabetic rats and comparable with that of standard drug, glibenclamide in short term study. It also produced significant reduction in blood glucose in long term study (Nalamolu and Nammi, 2006).

6.4. Antihepatic properties

Terminalia arjuna: Cytoprotective activity of Arjunolic acid protects arsenic induced cytotoxicity in murine hepatocytes (Hafiz *et al.,* 2014). The antioxidant activity or the inhibition of the generation of free radicals is important in providing protection against hepatic damage. *Terminalia arjuna* also exhibited hepatocurative effects when animals were given acetaminophen (400 mg/kg) for 3 days to damage the liver followed by the treatment with the plant extract (400 mg/kg) for 5, 10 and 15 days. The results also indicated hepatocurative activities, as the elevated serum levels of hepatic enzymes were inclining to normal ranges in a time-dependent manner (Khan *et al.,* 2020).

Terminalia chebula: The fruit is one of the most widely used herbal drug in Traditional medicine prescriptions including those for liver diseases. In the screening of bioactive constituents that have potential hepatoprotective activity, chebulinic acid (CA) which is a major chemical constituent of *Terminalia chebula* fruit showed potent activity (Feng

et al., 2021). *Terminalia chebula* fruit extract strongly inhibited in vivo lipid peroxidation in rat liver (Bag *et al.,* 2013)

6.5. Antimalarial Properties

Seed acetone extract of *Terminalia chebula*, also known as Black Myrobalan or Hard, has been shown to have antiplasmodial activity. This makes it a good candidate for isolating anti-protozoal compounds (Bagavan *et al.,* 2011). Unfortunately, very scanty reports are available on antimalarial activity of *Terminalia arjuna*.

6.6. Anticancer Activity

Terminalia arjuna: The extract can deplete GSH levels and promote oxidation induction that results in apoptosis of HepG2 cells, due to the accumulation of p53 protein and proteolytic cleavage of caspase-3 protein (Jaiswal *et al.,* 2021). It also exhibited anti-inflammatory and analgesic activities. The mechanisms of anti-inflammatory activity may be related to the antiphlogistic action of the tannins.

Table - 3: Pharmacological activities of *Terminalia arjuna*

S. No	Secondary metabolites	Pharma Activity	References
1.	Triterpenoids	Antioxidant and cardiovascular properties.	Dwivedi and Chopra (2014); Mandal *et al.* (2013)
		Free radical scavenging activity	Pawar and Bhutani (2005)
		Cardiovascular properties	Anka *et al.* (2020)
		Anticancer properties	Moulisha *et al.* (2010)
2.	Glycosides	Free radical scavenging activity	Pawar and Bhutani (2005)
		Anti-asthmatic properties	Anka *et al.* (2020)
3.	Phenolic compounds	Free radical scavenging action	Amalraj and Gopi (2017)
		Cardioprotective	Kumar *et al.* (2021)
4.	Tannins	Wound healing, antioxidant, anticancer and antimicrobial activity	Yadav *et al.* (2022)

Flavonoids and other phenolics compounds of plant origin have been reported as antioxidants and as scavengers of free radicals (Sumitra *et al.,* 2014). It down regulate anaerobic metabolism by inhibiting the activity of lactate dehydrogenase in lymphoma bearing mice, which was elevated in untreated cancerous mice. The results indicate the antioxidant action of aqueous extract of *Terminalia arjuna*, which may play a role in the anticarcinogenic activity by reducing the oxidative stress along with inhibition of anaerobic metabolism (Verma and Vinayak, 2008).

Terminalia chebula: The methanolic extract of fruit showed in vitro anticancer effect in the range of 75 % - 95 % against four human cancer cell lines of colon, melanoma, prostrate and lung origin. *T. chebula* fruit extract has induced apoptosis in lung cancer cells by regulating the Bcl-2 family protein-mediated mitochondrial pathway (Heer *et al.,* 2022).

6.7. Anti-inflammatory activity

Terminalia arjuna: Leaves and fruits had a stronger anti-inflammatory effect than the methanol extract of the bark. This potent inhibitory effect of HRBCs lysis may refer to the high content of saponins, tannins and flavonoids in the extracts (Abo-Elghiet *et al.,* 2022). It exhibited anti-inflammatory and analgesic activities. The mechanisms of anti-inflammatory activity may be related to the antiphlogistic action of the tannins. Flavonoids and other phenolics compounds of plant origin have been reported as antioxidants and as scavengers of free radicals (Vijayalaxmi *et al.,* 2023).

Terminalia chebula: Tannins from *Terminalia chebula* have an anti-inflammatory activity that inhibits inflammatory mediators TNF-α, reduction in beta-glucuronidase and lactate dehydrogenase enzyme, aqueous extract showed highest anti-inflammatory action. Ethanolic extract showed highest anti-inflammatory action. Both the aqueous and ethanolic extracts showed potent anti-inflammatory action compared to standard. The aqueous extract showed higher anti-inflammatory activity at low concentrations, when compared with ethanolic extract.

Table - 4: Pharmacological activities of *Terminalia chebula*

S. No	Secondary Metabolites	Pharma Activity	References
1	Chebulic acid	Free radical scavenging activity, antioxidant property	Mahesh *et al.* (2009); Naik *et al.* (2003)
		Chemo preventive activity	Prasad *et al.* (2006)
		Cytoprotective activity	Dhingra *et al*. (2022)
		Hepatoprotective activity	Choi *et al.* (2015)
2	Gallic acid	Radioprotective	Lee *et al.* (2010)
		Antibacterial activity	Khan and Jain (2009)
		Antifungal activity	Bonjar (2004)
		Antiviral activity	Mard *et al.* (2011)
		Antispasmodic activity	Mard *et al.* (2011)
		Immunomodulatory activity	Dwivedi *et al.* (2008)
3	Tannins	Antimutagenic	Grover and Bala (1992)
		Cardioprotective activity	Suchalatha and Shyamala (2004)
		Wound healing activity	Li *et al.* (2011)
4	Ellagic acid	Anticarcinogenic activity	Saleem *et al.* (2002)
		Antiprotozoal activity	Bagavan *et al.* (2011)
5	Neochebulic acid	Hepatoprotective activity	Li *et al.* (2011)
6	Chebulagic acid	Antidiabetic and renoprotective activity	Saleem *et al.* (2002)
		Anti-inflammatory	Moeslinger *et al.* (2000)
		Antiarthritic activity	Nair *et al.* (2010)
7	Chebulinic acid and corilagin	Hypolipidemic	Moeslinger *et al.* (2000)
		Hypocholesterolemic activity	Moeslinger *et al.* (2000)

6.8. Immunomodular Activity

Terminalia arjuna bark powder as a promising immunomodulator in *Labeo rohita* fish. This supplementation significantly improved various immune parameters, enhancing both specific and non-specific immune responses crucial for pathogen defense (Meena *et al.,* 2024).

Terminalia chebula: The crude extract of *T. chebula* stimulates cell-mediated immune response in experimental amoebic liver abscess in golden hamsters, Alcoholic extracts of *T. chebula* increase phagocytic activity in male Wistar rats (El-Shamarka *et al.,* 2024).

6.9. Hypolipidemic Activity

Terminalia arjuna: Solvent ether and ethanolic fractions caused a decrease in the plasma levels of lipids in tritonas well as in High fat diet (HFD) fed models of hyperlipidemia in hamsters. The efficacy of arjuna fractions was found to be in the order: Ethanol fraction solvent ether fraction petroleum ether fraction (Dwivadi, 2014, Chander, 2014). This study shows that the ethanolic extract of *Terminalia arjuna* tree bark in doses of 100 mg/kg and 500 mg/kg significantly reduced total and LDL cholesterol levels in hypercholesterolaemic rabbits. The bark powder of *Terminalia arjuna* can lower serum lipids in rats fed a cholesterol-rich diet. A 2010 study found that rats treated with Haritaki had significantly lower levels of total cholesterol, triglycerides, and total protein. The study also found that Haritaki increased high density lipoprotein cholesterol (Maruthappan and Shree, 2010).

6.10 Effects on Central Nervous System

Terminalia arjuna: An aqueous extract of TA bark was shown to improve neurological outcome in a rat model of transient focal cerebral ischemia, also the aqueous extract of TA bark was also shown to reduce blood-brain barrier damage in the same model, Alcoholic bark extract of TA has been shown to have a neuroprotective effect against brain injury (Shekhar *et al.,* 2017; Kaliyappan *et al.,* 2021). Some people use TA to help reduce stress and anxiety, as it is believed to have a calming effect on the mind.

Terminalia chebula: The plant can improve emotional memory in stressed animals by reducing the loss of neural spines in the hippocampus and amygdala. It can also reduce oxidative stress and increase total antioxidant capacity (TAC) in the brain (Khazani *et al.*, 2024). *T. chebula* extract can reduce oxidative stress, improve brain integrity, and promote insulin release in diabetic rats. It can also decrease the severity of nuclear

pyknosis and degeneration in the cerebral cortex, hippocampus, and striatum (El-Shamarka *et al.*, 2024).

6.11. Cardioprotective Activities

Terminalia arjuna: It acts as a cardiotonic due to glycoside in its bark. Glycoside also resulted in enhancing blood pressure. Bark stem of arjuna possesses diuretic, inotropic, and chronotropic properties (Dwivadi, 2014.) Alcoholic extract of bark increases the force of contraction of frog heart. Later studies confirmed that intravenous administration of alcoholic extract of *Terminalia arjuna* enhances auricular and ventricular contraction in rabbits. Aqueous bark extract injected into rabbit dose (1024 µg/ml) resulted in to rise in coronary flow, Hypotensive effects – effect of Terminalia arjuna on blood pressure was studied quite late whereas earlier it was used as an antihypertensive. The stem of *Terminalia arjuna* is used as a cardioprotective agent in hypertension, heart diseases, hypocholesterolemic, and antioxidants effect in humans (Gupta 2021). Myocardial ischemia was protected by *Terminalia arjuna* in rabbits (Jaiswal *et al.,* 2021).

Terminalia chebula: preliminary clinical investigation confirms the immediate and long term beneficial effect as well as the safety of *Terminalia chebula* adjuvent therapy in patients with otherwise unresponsive congestive heart failure, giving a sustained relief from symptoms and signs of congestive heart failure, with improvement in the quality of life (Bharani *et al.,* 1995) The histopathological observations of the heart tissue of *T. chebula* extract pretreated animals showed a near normal pattern, supporting its role as a promising cardioprotective agent (Suchalatha and Devi, 2003).

7. Conclusions

The plant secondary metabolites play importance of plants in the development of new medicines. They are an important source of bioactive or inspiring molecules. *Terminalia arjuna* and *Terminalia chebula* has tremendous potential to prevents and cure diseases and its associated complications. The authors of the current editorial hope that this special issue stimulates further research, in particular, research involving clinical trials.

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Chapter - 17

Phytomedicine Innovations: The Future of Plant – Based Therapies
ISBN: 978-81-977907-4-4
First Edition
Chapter – 17, Page: 273 - 287

17

STRUCTURAL AND MOLECULAR MECHANISMS OF ANTIOXIDANT ACTIVITY: COMPUTATIONAL ANALYSIS OF NATURAL PHYTOCONSTITUENTS

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Abstract

Nature possesses a rich source of antioxidants and the consumption of natural products is involved in managing many physiological functions as well as oxidative stress. Many natural compounds are involved in scavenging the free radicals generated in our biological system specifically curcumin-like molecules easily absorb and reduce the cell damage caused by the stress. In this study, the analysis of various natural phytoconstituents was discussed and different computational analyzing techniques were exposed to study the structural features that play a significant role in the process of antioxidant activity. Also, the different proteins are analyzed for the interaction with phytoconstituents and illustrated molecular level studies to explain the mechanism of antioxidant properties by the natural compounds.

Keywords: Phytoconstituents, SAR, Curcumin, Oxidative stress management and Computer-aided oxidative stress analysis.

1. Introduction

Antioxidants are essential molecules that protect our body's cells from the damaging effects of free radicals and oxidative stress. Free radicals are highly reactive atoms or molecules with unpaired electrons, making them prone to interact with cellular components like DNA, proteins, and lipids (Zhang *et al.,* 2024). This interaction can cause significant cellular damage, contributing to the development of chronic diseases such as cancer, cardiovascular diseases, and neurodegenerative disorders. The body has natural defence mechanisms that include endogenous antioxidants like superoxide dismutase, catalase, and glutathione peroxidase. These enzymes work to neutralize free radicals and reduce their harmful impact. However, the efficiency of these mechanisms can diminish due to aging, environmental pollutants, poor diet, and other lifestyle factors (Yu *et al.,* 2023). Consequently, exogenous antioxidants obtained from dietary sources become crucial in supporting the body's defence system. Exogenous antioxidants are abundant in fruits, vegetables, nuts, and seeds. Common dietary antioxidants include vitamins C and E, beta-carotene, selenium, and polyphenols. These compounds have been extensively studied for their health benefits and potential therapeutic applications (Maciej Serda *et al.,* 2013; Liu *et al.,* 2024). For example, vitamin C, also known as ascorbic acid, is a potent antioxidant that donates electrons to neutralize free radicals and regenerate other antioxidants in the body. Vitamin E, which includes tocopherols and tocotrienols, protects cell membranes from oxidative damage by scavenging lipid peroxyl radicals (Becker, 2004).

Polyphenols, a diverse group of naturally occurring compounds found in plants, have received significant attention for their antioxidant properties. These include flavonoids, phenolic acids, stilbenes, and lignans. Flavonoids, such as quercetin, catechins, and anthocyanins, are particularly notable for their ability to scavenge free radicals and chelate metal ions, preventing the formation of new free radicals. Phenolic acids, such as caffeic acid and ferulic acid, contribute to the antioxidant defense system by neutralizing Reactive Oxygen Species (ROS) and enhancing the activity of endogenous antioxidant enzymes. In addition to their direct antioxidant activity, many of these compounds exhibit anti-inflammatory, anti-carcinogenic, and cardioprotective effects. For instance, resveratrol, a stilbene found in grapes and red wine, has been shown to activate sirtuins, a family of proteins involved in cellular stress resistance and longevity (Ruan *et al.,* 2022). Curcumin, the active component of turmeric, exhibits strong anti-inflammatory properties by

inhibiting the activity of nuclear factor-kappa B (NF-κB), a key regulator of inflammatory responses.

Understanding the mechanisms of action of antioxidants is crucial for developing effective strategies to combat oxidative stress-related diseases. Antioxidants can exert their effects through various pathways, including the direct scavenging of free radicals, chelation of metal ions, and modulation of signalling pathways involved in the oxidative stress response. For example, the Nrf2-Keap1 signalling pathway plays a pivotal role in regulating the expression of antioxidant and detoxification enzymes. Under oxidative stress conditions, Nrf2 dissociates from its inhibitor Keap1, translocate to the nucleus, and binds to Antioxidant Response Elements (AREs) in the promoter regions of target genes, thereby enhancing the expression of antioxidant enzymes (Badr *et al.,* 2019; Freer *et al.,* 2019; *Molecular Design of Antioxidant Lubricating Oil Additives via QSPR and Analysis Dynamic Simulation Method – Science Direct*, n.d.). Despite the promising benefits of antioxidants, it is important to approach supplementation with caution. While moderate intake of antioxidant-rich foods is beneficial, excessive supplementation can potentially lead to adverse effects. For instance, high doses of vitamin E supplements have been associated with an increased risk of haemorrhagic stroke, while excessive beta-carotene intake may increase the risk of lung cancer in smokers. Therefore, a balanced diet rich in natural antioxidants is generally recommended over high-dose supplementation. The bioavailability of antioxidants is a critical factor influencing their efficacy. Bioavailability refers to the proportion of an ingested nutrient that reaches systemic circulation and is available for use or storage in the body. Factors such as the food matrix, preparation methods, and individual differences in metabolism can affect the absorption a utilization of antioxidants. For example, the bioavailability of polyphenols can be enhanced by consuming them in combination with other nutrients, such as fats, which facilitate their absorption. In recent years, there has been growing interest in developing functional foods and nutraceuticals enriched with antioxidants (Singh *et al.,* 2024). These products aim to provide health benefits beyond basic nutrition by incorporating bioactive compounds that can help prevent or manage chronic diseases. For instance, adding polyphenol-rich extracts to beverages, cereals, and dairy products has been explored to enhance their antioxidant capacity and health-promoting properties.

Advances in biotechnology and food processing techniques have opened new avenues for enhancing the stability and bioavailability of antioxidants. Techniques such as microencapsulation, nanotechnology, and fermentation can improve the delivery and efficacy of antioxidants in functional foods and supplements. For example, microencapsulation involves enclosing antioxidants in protective coatings, which can protect them from degradation during processing and storage and facilitate their controlled release in the digestive tract. In conclusion, antioxidants are essential compounds that play a crucial role in protecting the body from oxidative stress and its associated health risks. While endogenous antioxidants form the first line of defence, exogenous antioxidants obtained from a balanced diet rich in fruits, vegetables, nuts, and seeds provide additional support. Understanding the diverse mechanisms through which antioxidants operate, as well as the factors influencing their bioavailability, is key to maximizing their health benefits (Abubakar *et al.,* 2022). Ongoing research and innovation in the field of functional foods and nutraceuticals hold promise for developing effective strategies to harness the potential of antioxidants in promoting health and preventing disease. Antioxidants play a key part in maintaining our health by shielding our cells from oxidative damage triggered by free radicals. These unstable free radicals can lead to various health issues, including aging (Lobo *et al.,* 2010), inflammation, and chronic diseases. Fortunately, nature provides us with abundant sources of antioxidants through various foods and incorporating them into our diet can have numerous health benefits (Deledda *et al.,* 2021).

1.1. Natural Sources of Antioxidants

Colourful fruits and vegetables are rich in antioxidants. Citrus fruits (grape fruits, oranges), Berries (such as strawberries, blueberries, and raspberries), and leafy greens (spinach, kale) contain vitamins (like vitamin C) and phytochemicals (such as flavonoids and carotenoids) that act as powerful antioxidants (Ayaz *et al.,* 2024). These compounds neutralize free radicals and support overall health. Culinary spices and herbs like cinnamon, oregano, turmeric, and cloves are contains rich antioxidant phytoconstituents. For instance, curcumin in turmeric has potent anti-inflammatory properties, while cinnamon contains polyphenols that contribute to its antioxidant effects (Yashin *et al.,* 2017). Including these herbs and spices in your meals can enhance your antioxidant intake. Whole grains (such as brown rice, oats, and quinoa) and nuts (like almonds, walnuts, and pecans) provide essential nutrients and antioxidants (Călinoiu and Vodnar, 2018). Vitamin E, selenium, and various phenolic compounds found in whole grains and nuts play a protective role against oxidative stress. Dark chocolate (with a high cocoa content) contains flavonoids, particularly flavanols.

These compounds improve blood flow, reduce inflammation, and act as antioxidants. Enjoying a small piece of dark chocolate can be a delightful way to boost your antioxidant intake (Samanta *et al.,* 2022).

1.2. *Curcuma longa* Linn.

Turmeric is one of the antioxidant-rich herbs and possesses sesquiterpenes, polyphenols, triterpenoids, diterpenes, alkaloids and sterols (more than 300 biologically active phytoconstituents). Specifically, the yellow-pigmented curcuminoids represent 2 % - 5 % of the turmeric root (El-Saadony *et al.,* 2023). Among these, curcumin constitutes approximately 85 %, while demethoxycurcumin and bisdemethoxycurcumin make up the remaining percentages. Curcumin exhibits strong antioxidant activity due to its ability to scavenge Reactive Oxygen Species (ROS) and Reactive Nitrogen Species (RNS). ROS are produced by enzymes like NAD(P)H oxidases and xanthine oxidases, while RNS are generated by nitric oxide synthase (Hewlings and Kalman, 2017). By neutralizing these harmful radicals, curcumin helps protect cells from oxidative damage and reduces the risk of chronic diseases.

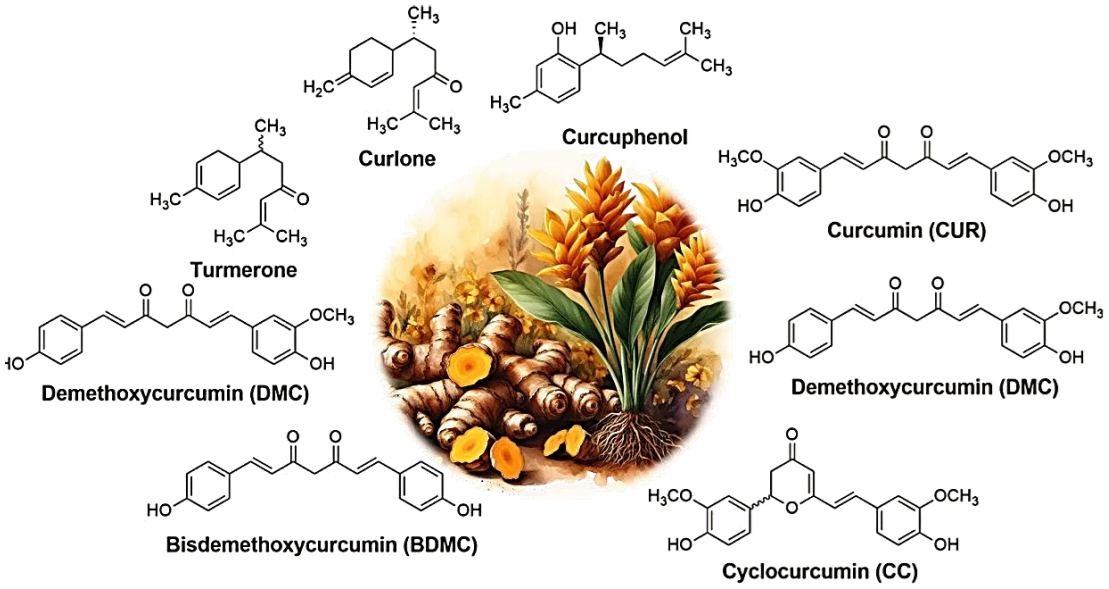

Figure - 1: **Structures of Major Phytoconstituents of *Curcuma longa***

Curcumin's antioxidant effects are attributed to its ability to donate hydrogen atoms from its phenolic groups. While many antioxidants rely on hydrogen atom donation, curcumin's primary central CH_2 group involves H-atom abstraction. This unique property allows curcumin to scavenge free radicals effectively and maintain

cellular health (Ahmadinejad *et al.,* 2017; Chaudhary *et al.,* 2023). In summary, curcumin acts as a potent antioxidant, it was depicted in Figure 1. safeguarding our cells against oxidative stress and contributing to overall well-being. Incorporating turmeric into our diet can provide these beneficial effects. These scavengers employ various mechanisms to counteract reactive free radicals, including inhibiting and promoting the endogenous production of Glutathione (GSH), reducing lipid peroxidation, and increasing intracellular GSH levels and spin trapping. The mechanism involved in scavenging free radicals by the natural phytoconstituents is difficult to explain at the molecular level (Jakubczyk *et al.,* 2020; Sharifi-Rad *et al.,* 2020). But, the current computational techniques made possible of it.

2. Natural Antioxidative Phytoconstituent and the Mechanism Analysis

α-tocopherol, a lipid-soluble antioxidant, acts as a 'chain breaker' during lipid peroxidation in cell membranes and various lipid particles, including low-density lipoprotein (LDL).(Collin, 2019) Its role is to intercept lipid peroxyl radicals (LOO˙) and halt the lipid peroxidation chain reactions.

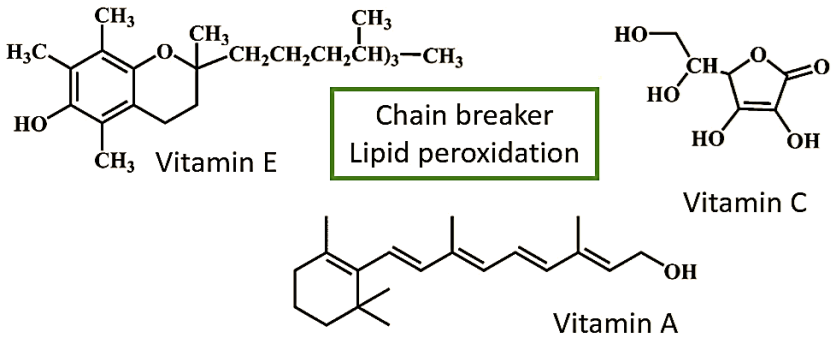

Figure - 2: **Lipid-soluble antioxidant Vitamins E, A, C**

Flavonoids, found abundantly in fruits and vegetables, possess powerful antioxidant properties. These natural compounds, including flavanols (like quercetin and myricetin), flavones (such as apigenin and luteolin), and anthocyanidins (like cyanidin and delphinidin), exhibit various biological effects, including free radical scavenging. Notably, they safeguard against DNA damage caused by hydroxyl radicals. One protective mechanism involves chelating metal ions (such as copper or iron), which prevents the generation of Reactive Oxygen Species (ROS).

Carotenoids, including lycopene, β-carotene, zeaxanthin, and lutein, are lipid-soluble phytonutrients. Among the numerous compounds, lycopene and β-carotene are particularly noteworthy (Tapiero *et al.,* 2004). The biosynthetic pathway demonstrates how carotenoids are synthesized from phytoene, which is derived from two geranylgeranyl pyrophosphate molecules. Carotenoids exhibit superior scavenging ability against peroxyl radicals compared to other Reactive Oxygen Species (ROS). These peroxyl radicals, generated during lipid peroxidation, can harm cell wall lipids. By disrupting the reaction sequence, carotenoids prevent lipid damage (Metibemu and Ogungbe, 2022). Their long unsaturated alkyl chains contribute to their high lipophilicity. Carotenoids are known to play an important role in the protection of cellular membranes and lipoproteins against the Reactive Oxygen Species (ROS) due to their peroxyl radical scavenging activity (Imran *et al.,* 2020). They deactivate the peroxyl radicals by reacting with them to form resonance-stabilized carbon-centered radical adduct.

Lycopene, naturally found in various fruits and vegetables, acts as a potent antioxidant. Its multiple conjugated double bonds give it exceptional singlet oxygen quenching ability, surpassing that of α-tocopherol (vitamin E) it was illustrates in Figure 3. or β-carotene. Speaking of β-carotene, this orange-colored carotenoid is abundant in yellow-orange fruits and dark-green leafy vegetables. It also exhibits antioxidant properties due to its chemical structure and interaction with biological membranes. Interestingly, β-carotene is more effective at quenching singlet oxygen than α-tocopherol (Moazzen *et al.,* 2022). Additionally, the (Z)-isomers of β-carotene demonstrate antioxidant activity *in vitro*. Moreover, enzymatic cleavage by β-carotene-15,15'-dioxygenase can convert β-carotene into two molecules of vitamin A.

Hydroxycinnamic acids, including ferulic acid, caffeic acid, sinapic acid, and p-coumaric acid, play a crucial role in preventing oxidative damage to Low-density lipoproteins (LDL). *In vitro* studies using human LDL as the oxidizing substrate demonstrate that hydroxycinnamic acids have higher antioxidant activity compared to corresponding hydroxybenzoic acids (Sökmen and Akram Khan, 2016). The antioxidant efficiency of free hydroxycinnamates on human LDL oxidation decreases in the following order: Caffeic acid > Sinapic acid > Ferulic acid > p-coumaric acid.

The presence of the o-dihydroxy group in the phenolic ring (as seen in caffeic acid) enhances the antioxidant activity of hydroxycinnamic acids against human LDL oxidation in vitro. The radical scavenging mechanism of hydroxycinnamic acids is similar to that of flavonoids due to their ability to donate a hydroxyl hydrogen and

stabilize resulting antioxidant radicals through resonance (Nimse and Pal, 2015). Additionally, the o-dihydroxy substituents allow metal ion chelation, similar to flavonoids.

Curcumin exhibits chain-breaking antioxidant ability comparable to vitamin E. Its free radical scavenging activity correlates with the phenolic OH group and the CH2 group of the β-diketone moiety. Curcumin can undergo electron transfer or abstract H-atom from either of these two sites. Although pulse radiolysis and other biochemical methods credit curcumin's antioxidant activity to its phenolic OH group, the Scheme 14 depicts the autoxidation mechanism initiated by hydrogen abstraction from one of the phenolic hydroxyl groups. The phenoxy radical moves into the carbon chain, leaving a quinone methide that eventually quenches with water molecules. The methide radical undergoes a 5-exo-cyclization with the double bond, generating a carbon-cantered radical.

Curcumin reacts with Molecular Oxygen (O_2) to form peroxyl radicals. These radicals are then reduced to hydroperoxides by abstracting hydrogen atoms from other curcumin molecules, propagating an autoxidation chain reaction. Subsequently, the hydroperoxide loses water and rearranges into a spiro-epoxide. Hydrolysis of the epoxide by water-derived hydroxyl groups results in the final bicyclopentadione product. Notably, the copper complex of curcumin (Curcumin – Cu[II]) exhibits promising superoxide dismutase (SOD) activity, demonstrating improved antioxidant efficacy (Moazzen *et al.,* 2022). The O_2 scavenging activity of the Curcumin–Cu(II) complex is depicted in Scheme 15. When O_2 reacts with the Curcumin–Cu(II) complex, a major fraction of O_2 interacts with the Cu_2^+ moiety, while only a small fraction reacts with curcumin. This reaction reduces Cu_2^+ to Cu^+. The Cu^+ then undergoes subsequent oxidation by another molecule of O_2, regenerating the parent complex. The catalytic activity primarily arises from reversible redox reactions within the Cu_2^+/Cu^+ couple in the complex. However, in the presence of excess O_2, the phenolic moiety undergoes oxidation, resulting in the production of phenoxyl radicals. Then these phenoxyl radicals can generate

2.1. QSPR Technique

Advanced Quantitative Structure-Property Relationship (QSPR) study of phenolic compounds structure on the radical scavenging properties related to antioxidant activity. Specifically, the study investigated how basic structural features, such as the number of -OH (hydroxyl groups), and in conclusion the Bors criteria (is

one of the major criteria that influence the Oxygen Radical Absorbance Capacity (ORAC). It was shown on Figure - 3. PCA (principal component analysis) statistical technique compared Bors criteria with *in vitro* antioxidant assays result (Platzer *et al.,* 2022). The results revealed that the substitution and its numbers in the basic fragment alter antioxidant behavior rather than the Bors criteria and steric hindrance not affecting the antioxidant property of the molecules. A molecule pentahydroxyflavone (Morin), which has 5 -OH and 2 Bors criteria, achieved an AUC of $3.64 \pm 0.08 \times 10^5$, compared to quercetin-7-D-glucoside making a better antioxidant.

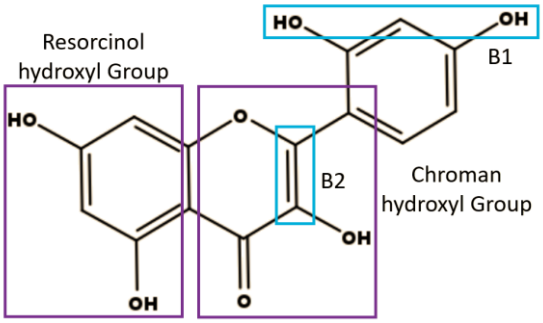

Figure – 3: Schematic representation of Bors criteria using QUR. Bors 1: catechol group on the B-ring; Bors 2: double bond between C-2 and C-3 and a carbonyl group at C-4 on the C-ring; Bors 3: hydroxyl groups at C-3 and C-5 on the A- and C-rings and 4-oxo group on the C-ring

Furthermore, the structural analysis of radical scavenging compounds in the assays such as DPPH (2,2-diphenyl-1-picrylhydrazyl), FC (Folin-Ciocalteu) ABTS and ABTS (2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) it was shown on Figure - 4. dependent based on the various reaction mechanism and number of hydroxyl group compare to the bors criteria.

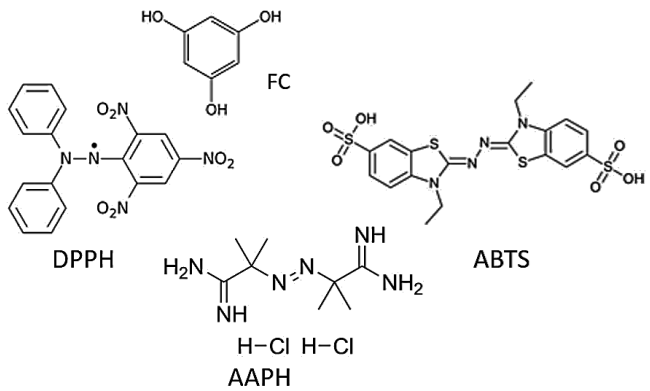

Figure - 4: Schematic representation of Bors criteria using QUR. Bors 1: catechol group on the B-ring; Bors 2: double bond between C-2 and C-3 and a carbonyl group at C-4 on the C-ring.

2.2 DFT and MD Simulation Technique

In our computational study, we investigated the antioxidant activities and non-covalent inhibition of the SARS-CoV-2 main protease (Mpro) by isorhamnetin. Isorhamnetin, flavonoid rich in hydroxyl groups, it shown on Figure 5. plays a crucial role in the antioxidant capacity of polyphenols.(Irfan *et al.,* 2023; Mohammed Zaidh *et al.,* 2023; Navabshan *et al.,* 2021) It is naturally found in Chinese sea buckthorn juice and can be extracted from various sources, including *Ginkgo biloba*, *A. roxburghii*, and *Hippophae rhmnoides* L. Moreover, isorhamnetin is a metabolite of quercetin, further emphasizing its significance. Notably, even when only quercetin is consumed, isorhamnetin concentrations remain high in human plasma.

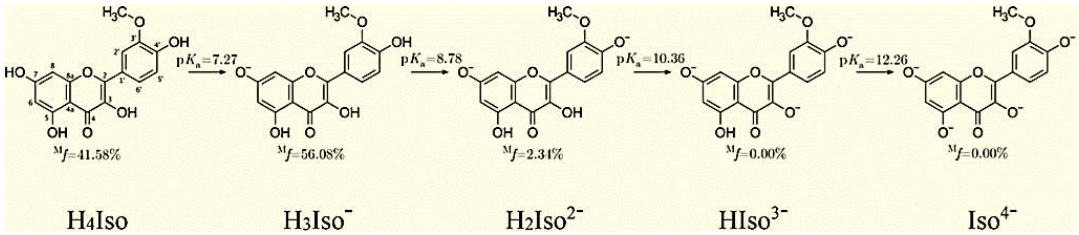

Figure – 5: Flavan -3-ols derivatives on antioxidative compounds

Enzymatic antioxidants and nonenzymatic antioxidants play crucial roles in modulating free radical reactions. The body's defense against Reactive Oxygen Species (ROS) involves enzymatic antioxidant mechanisms. These antioxidant enzymes help reduce levels of lipid hydroperoxide and Hydrogen peroxide (H_2O_2), thereby preventing lipid peroxidation and maintaining cell membrane structure and function. Examples of enzymatic antioxidants include Catalase (CAT), Glutathione peroxidase (GSHPx), Superoxide dismutase (SOD), and Peroxiredoxins I–IV.

Superoxide Dismutases (SODs), located in the cytosol and mitochondria, play a critical role in converting superoxide anions ($O_2^{\cdot}-$) into oxygen and hydrogen peroxide (H_2O_2). This catalytic process relies on metal ion cofactors such as copper (Cu), zinc (Zn), or manganese (Mn). Additionally, the enzyme catalase (CAT), found in peroxisomes, efficiently converts H_2O_2 to water and oxygen. Glutathione peroxidase (GSHPx), present both in the cytoplasm and extracellularly, further contributes by converting H_2O_2 into water. GSHPx exhibits robust activity against both H_2O_2 and fatty acid hydroperoxides. Another enzyme, it wa depicted in Figure - 6. peroxiredoxin, facilitates the reduction of H_2O_2, Organic Hydroperoxides, and Peroxynitrite (ONOO). The diverse expression profiles, sub-cellular locations, and

substrate specificities of these antioxidant enzymes highlight the intricate nature of Reactive Oxygen Species (ROS) biology. Overall, these enzymes play a crucial role in preventing oxidative damage. Fukai and Ushio-Fukai (2011) represented the synergistic effect of CAT, GSHPx, and SOD in scavenging.

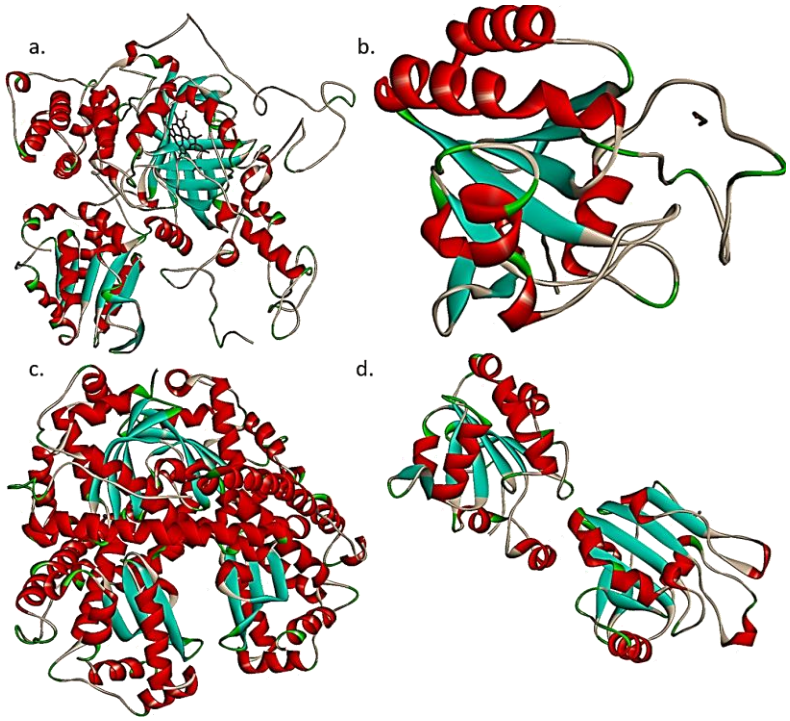

Figure - 6: **Glutathione Peroxidase Enzymes**

3. Current Trends and Future Directions

In recent years, there has been increased interest in studying free radicals and antioxidants in relation to human health. Research has shown that even in the absence of degenerative diseases, aging is associated with neuronal and behavioural changes. Recent studies highlight the link between lower dietary antioxidant levels and cognitive decline. Evidence from experimental, clinical, and epidemiological studies suggests that consuming foods rich in antioxidants can help prevent or reduce the risk of cognitive deterioration. Tempol, a novel SOD mimetic drug, effectively alleviates acute and chronic pain while minimizing tissue damage caused by inflammation. To better understand the relationship between radical damage and disease, further research is essential. Collectively, efforts should focus on unravelling the mechanisms underlying the free radical scavenging activities of known antioxidants to develop potent therapeutic options.

4. Conclusion

Reactive oxygen species (ROS), the radical derivatives of oxygen, play a crucial role in biological systems. These harmful byproducts are generated during normal cellular functions. Maintaining an adequate antioxidant status through natural antioxidants is essential for proper physiological functioning. Evidence suggests that dietary antioxidants contribute to disease prevention. These antioxidant compounds engage in one-electron reactions with free radicals in vitro, preventing oxidative damage. Understanding the reaction mechanisms between antioxidants and free radicals is crucial. Such knowledge helps evaluate the antioxidant activity of naturally occurring compounds. This review elaborates on the mechanisms of natural antioxidants and discusses assays for evaluating their antioxidant properties

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Phytochemical and Pharmacognostic Characterisation and Elucidation of Therapeutic Potential of Cleome gynandra

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Chapter - 18

Phytomedicine Innovations: The Future of Plant – Based Therapies
ISBN: 978-81-977907-4-4
First Edition
Chapter – 18, Page: 288 - 306

18

PHYTOCHEMICAL AND PHARMACOGNOSTIC CHARACTERISATION AND ELUCIDATION OF THERAPEUTIC POTENTIAL OF *Cleome gynandra*

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Abstract

The study titled "Phytochemical and Pharmacognostic Characterization and Elucidation of Therapeutic Potential of *Cleome gynandra aims* to explore the medicinal properties and bioactive compounds of the plant *Cleome gynandra.* Synthetic drugs often cause significant side effects, leading to a resurgence in interest in plant-based traditional medicines for treating various diseases. This research focuses on the Pharmacognostic and Phytochemical properties of *Cleome gynandra*, analyzing its antibacterial, antioxidant, and anti-ulcer activities. Various extraction methods were employed to prepare plant extracts, which were then tested for their efficacy against multiple drug-resistant bacterial strains, as well as their potential to prevent ulcers in animal models. The study also included the biosynthesis of silver nanoparticles from *Cleome gynandra* extracts, which showed promising results in controlling pathogenic bacterial growth and exhibited significant antioxidant properties. Molecular docking studies further validated the potential of phytochemicals isolated from *Cleome gynandra* for their binding affinity against specific target proteins involved in disease

mechanisms. The findings indicate that *Cleome gynandra* could be a valuable source of bioactive compounds for developing new therapeutic agents, with potential applications in managing microbial infections, oxidative stress, and gastric ulcers.

Keywords: *Cleome gynandra,* Secondary metabolites, Antioxidant activity, Herbal medicines and Silver nanoparticles.

1. Introduction

The *Cleome gynandra* L. plant is commonly called Nalvezhala and belongs to the family Cleomaceae is a naturally occurring species. *Cleome gynandra* is a widely occurring herb in the southern part of Africa and various African countries. It is a globally distributed plant found mainly in tropical and subtropical regions. It grows as a weed in paddy fields and also in road sides and in open grasslands. In India it is never cultivated but grows spontaneously everywhere. Different species of *Cleome* can be found in all states of India. In India, this plant grows best during the months of August –November (Sandhya *et al.*, 2018). It is an erect glandular-pubescent annual herb up to 250 – 600 mm tall which is popularly used in the Ayurveda, Siddha, Folk, and Tibetan systems of medicine (Moyo *et al.*, 2017; Sivakumar *et al.*, 2018). The leaves and seeds of this herb are used as medicine in several countries (Mishra *et al.*, 2011). Sap from leaves possess curator properties and are used as an analgesic to treat headaches, earache, etc. Fresh leaves are squashed into the ears, nose, and eyes. It is also used to treat epileptic fits. An infusion of leaves or root is used in conditions such as to facilitate childbirth to treat severe threadworm infection, stomach ache and constipation, conjunctivitis and in reducing chest pains. Leaves are used to treat arthritis. They are also applied as a poultice or rubbed on the affected parts to cure rheumatism, neuralgia, and headache. In order to prevent sepsis, the leaves could be applied externally over the wounds. Researchers have proved its properties such as analgesic, anti-inflammatory (Bose *et al.*, 2007), anticancer potentials and antipyretic activities scientifically.

Figure – 1 to 3: *Cleome gynandra* is an erect yellowish green herb, stem is glandular in nature, leaves are 3-5 foliate, leaflet Elliptic oblong and entire, Flowers are white in colour with Corymbose-racemes type

2. Morphological Characterization

Cleome species are annual or perennial herbs. Stems are Simple or sparsely branched, glabrous or glandular pubescent, Foetid or sometimes with scattered prickly appendages. Leaves Are 5 foliate pinnately compound; leaf stalk is 20 – 50 mm long with glandular hairs. Inflorescence racemes, solitary to many Flowered, terminal or axillary. Flowers bisexual, zygomorphic or rarely actinomorphic, pedicellate, bracts membranous or Leaflike, caducous or persistent, sepals 4, equal, valvate, free or Slightly fused at the base, subtending nectary glands at the base, Pubescent, petals 4, equal or unequal, usually clawed at base, longer than the sepals. Stamens 4 - 6, filament inserted on a Discoid, declinate, glabrous, anthers linear oblong. Ovary Superior, bicarpellary, sessile or on short gynophore, Unilocular, ovules many on parietal 2 placentae, style short (Figure – 1 to 3).

Powder microscopy revealed the presence of a xylem Element, which showed dense spiral lining lateral wall Thickenings. There are wide rectangular parenchyma cells Which form one below the other forming vertical strands. The Cell wall is fairly thick and inside cells are seen as dark particles. There are other types of parenchymal cells which are wider with thick walls and dense cytoplasm. There are fibres with Varying thickness and length. This is another vessel element Which has a long conical and thick tail at one end. The other End is blunt. There are wide circular perforations. The cell has Thick cell wall and there are numerous circular bordered pits. In the powder, bundles of fibres and parenchymal cells were Seen. They are occurring in vertical compact rows. The fibres Are narrow thick walled with narrow lumen. The parenchyma Cells vertically rectangular compactly arranged one below Another. Some of the parenchymal cells exhibit prominent Nucleus. Many parenchyma cells are seen which are long, Narrow and wide. The narrow parenchyma cells are separated and two celled. It has prominent nuclei. Some parenchymal Cells are wide, long and septate. There are also fibres which Are narrow thick walled and lignified (Figure – 4 to 7). Size of the various elements found in *C. gynandra* were in Table - 1.

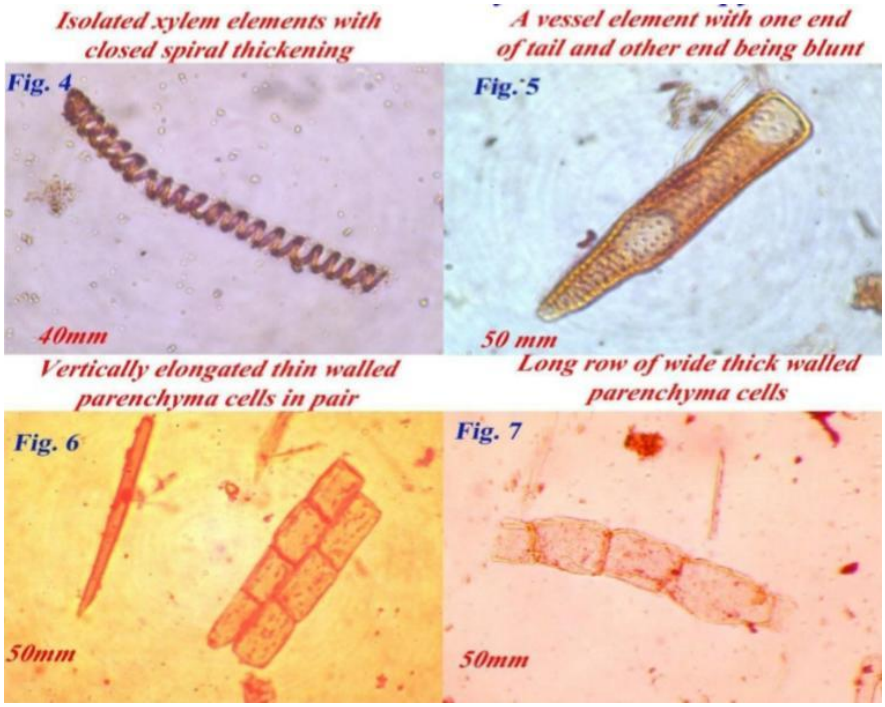

Figure - 4 to 7: Presence of a xylem element, which showed dense spiral lining lateral wall thickenings. There are wide rectangular parenchyma cells which form one below the other forming Vertical strands

Table - 1: Morphological Characterization of *Cleome gynandra*

Specifications	Characteristics
Native	Asian And African Countries
Morphology	Erect Plant With 250-600 mm Tall
Soil type	Black mostly with waste place
Habitat	Annual herb
Leaves	Mostly 5 foliate pinnately compound; leaf stalk is 20 - 50 mm long with glandular hair
Fruits	Fruits are in capsule form
Inflorescence	Corymbose – racemes
Flower colour	White or yellow
Androecium	6
Gynoecium	Gynandrophore 1cm long
Capsule	4-9 cm in length
Flowering and Fruiting	August - December

3. Microscopic Characterization

3.1. Seed Characteristics

Dark brown, oily; Fragments of epidermis from the testa (seed coat) consist of thin-walled, polygonal cells; Groups of cells resemble stone cells, reddish-brown with non-lignified walls; Numerous oval, rounded, or irregularly shaped protein bodies, Starch and crystals absent.

3.2. Leaf Anatomy

Thickness Ranges from 112 - 398 µm. Upper Epidermis consists of Single-layered with large, slightly deep tubular cells and a thick lamellar cuticle. Mesophyll Composed of palisade cells (Adaxial, single-layered, long rectangular cells with abundant chloroplasts and little intercellular space) and spongy parenchyma (2-3 layered, with large intercellular spaces). Vascular Bundles having Large, collateral, and arc-shaped in primary veins; small and round in secondary veins. Xylem is towards the adaxial (upper) side, and phloem is on the abaxial (lower) side. Lower Epidermis have Single-layered, large, thick-walled cells. Guard cells are thick-walled and vertically embedded with subsidiary cells (Anbazhagi *et al.*, 2009).

Table - 2: Microscopic characters of powder of *Cleome gynandra* whole Plant powder

Xylem element	600 µm long and 80 µm thick
The strand is	140 µm long
Individual cells	40 µm long and 20 µm wide
Parenchyma cells	70 µm long and 40 µm wide
The vessel element	110 µm long and 50 µm thick

4. Systematic Position

Kingdom: Plantae
Division: Angiosperms
Class: Dicotyledones
Order: Capparidales (Capparales)
Family: Cleomaceae
Genus: *Cleome*
Species: *gynandra*

5. Taxonomy of *Cleome Gynandra*

This plant belongs to the Kingdom Plantae, Phylum Spermatophyta, Division Magnoliophyta, Class Magnoliopsida, Order Brassicales and Family Cleomaceae. Out of 200 Species in Cleome, 15 are found in India. Genus *Cleome* and the species *Cleome gynandra* (L.) Briq.

6. Major Phytochemical Composition

6.1. Chemical Constituents

The total phenolic content (mg GAE/g DW) of *Cleome gynandra* was significantly higher than that of *Berberis vulgaris* and *Brassica oleracea* similar trend was observed for total flavonoid content (CE/g DW). However, β-carotene content (mg/100 g DW) was significantly greatest in *Berberis vulgaris*, followed by *Cleome gynandra* and *Cleome oleracea*. The concentration of β-carotene was 21.9 times higher in *Cleome gynandra* compared to *Brassica oleracea.* On the other hand, the concentration of ascorbic acid (mg/100 g DW) was observed to significantly decrease in the order: *Cleome gynandra* >*Berberis vulgaris* > *Brassica oleracea*. In particular, the concentration of ascorbic acid in *Cleome gynandra* was 3.2 and 4.7 folds higher than that of *Berberis vulgaris* and *Brassica oleracea*, respectively.

Varying concentrations of both hydroxybenzoic acids and hydroxycinnamic acids were identified and quantified in the three vegetables. Compared to *Berberis vulgaris, Brassica oleracea* and *Cleome gynandra* exhibited significantly high concentrations of protocatechuic acid, p-hydroxybenzoic acid and salicylic acid. The content of p-hydroxybenzoic acid was 11 and 6 folds higher in *Cleome gynandra* compared to *Brassica oleracea* and *Berberis vulgaris*, respectively. For protocatechuic acid and salicylic acid, the concentration in *Cleome gynandra* was at least 2 times greater than that of Berberis vulgaris and *Brassica oleracea.* The identified and quantified hydroxycinnamates were caffeic acid, p-coumaric acid, sinapic acid, and ferulic acid. The concentration of caffeic acid (2.27 µg/g DW) and p-coumaric acid (23.9 µg/g DW) was significantly high in *Cleome gynandra* compared to the other two leafy vegetables. On the other hand, *Brassica oleracea* and Berberis vulgaris had the highest sinapic acid and ferulic acid content, respectively. In fact, the sinapic acid concentration in *Brassica oleracea* was 27 times more than that of *Cleome gynandra*.

7. QUANTITATIVE ANALYSIS

7.1. Quantification of Total Phenolics and Flavonoids

Following the extraction method described by Amoo *et al*. (2012), the determination of total phenolic content for the three vegetable samples was performed using the Folin and Ciocalteu method (Singleton and Rossi, 1965) with slight modifications as outlined by Fawole *et al*. (2009). Gallic acid was used as the standard for plotting the calibration curve. Total phenolic content was expressed in mg Gallic acid equivalents (GAE) per g Dry weight (DW).

The flavonoid content of the three vegetable samples was quantified using the aluminum chloride colorimetric method as described by Zhishen *et al*. (1999). Catechin was used as a standard for the calibration curve and total flavonoid content was expressed in mg Catechin Equivalents (CE) per g DW. The Histochemical features express the following, Flavonoids are detected on the basis of yellow colouration with diluted Ammonia and H_2SO_4. Presence of alkaloids are indicated by the Presence of brown colouration by the addition of Dragendorff's reagent. Dark blue colour formation with ferric Chloride indicates the presence of tannin. Plant powder Treated with 5 drops of acetic anhydride and 5 drops of H_2SO To give Blue to light green colour indicates the presence of Steroids. Toludine blue treatment with plant powder gives Bluish green colour indicating the presence of polyphenol. Orange colouration with Dinitrophenylhydrazine (few drops) Showed the presence of Terpenoids. Plant powder treated with few drops of Sulphuric acid provides the presence of Saponins with the formation of yellow colour (Figure – 8 to 13).

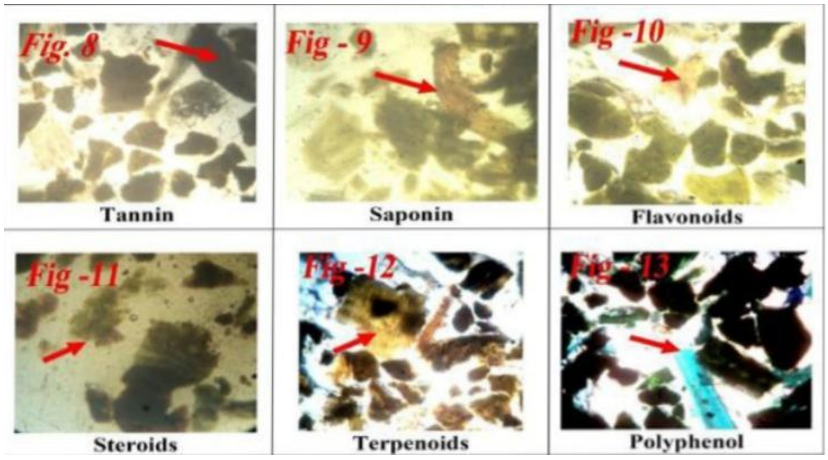

Figure – 8 to 13: Histochemistry – Flavonoids -yellow, alkaloids -brown colouration; Tannins – blue colouration

7.2. Determination of β-Carotene

β-Carotene extraction and quantification using HPLC-PDA were done as described by Biehler *et al*. (2010) with modifications. In brief, samples were extracted (0.1 g/ml) with ice-cold hexane: acetone (1:1, v/v). The mixture was vortexed for 2 min before centrifuging at 2,000 rpm for 2 min. The organic phase was decanted into a tube containing saturated sodium chloride solution and placed on ice. The remaining residue was similarly re-extracted until the extract is colorless. Each time, the extracts were combined in a saturated sodium chloride solution tube. The separated organic phase was filtered through a 0.45 µm syringe filter before injection into HPLC. The analysis was carried out on the Prominence-i HPLC-PDA model system equipped with sample cooler LC-2030C (Shimadzu, Kyoto, Japan). Chromatographic separation was achieved using a C18 Luna® column (150 × 4.6 mm, 5 µ) maintained at 35 °C. An isocratic mobile phase which consisted of Acetonitrile: Dichloromethane: Methanol (7:2:1) was used with a flow rate of 1 ml/min, an injection volume of 20 µl and the detection at 450 nm. Peak identification and quantification were achieved based on the authentic β-carotene standard, which was used for plotting the calibration curve.

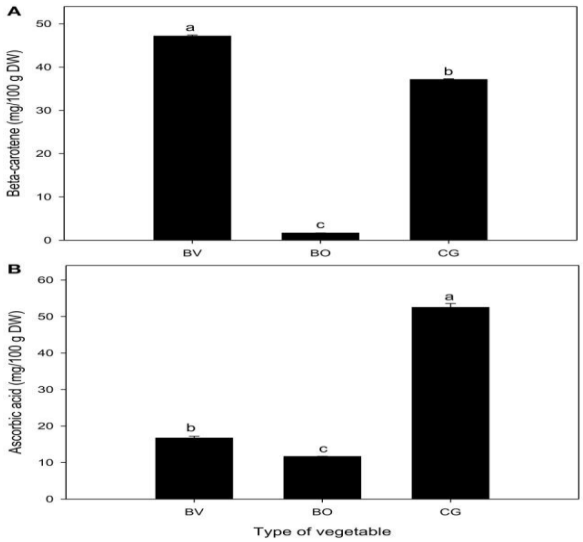

Figure - 14: β-Carotene Quantification

Twenty compounds were detected in ethanol mixed Crude preparation of *Cleome Gynandra* via GC-MS peak analysis (Figure - 15). The prevailing compounds Are 2-Hexadecen-1-ol, 3,7,11,15-tetramethyl-,9,12-Octadecadienoic acid (Z,Z), 9,12,15-Octadecatrienoic acid and methyl ester, (Z, Z, Z). The presence of various

bioactive Compounds justifies the use of the plant for various ailments by traditional practitioners.

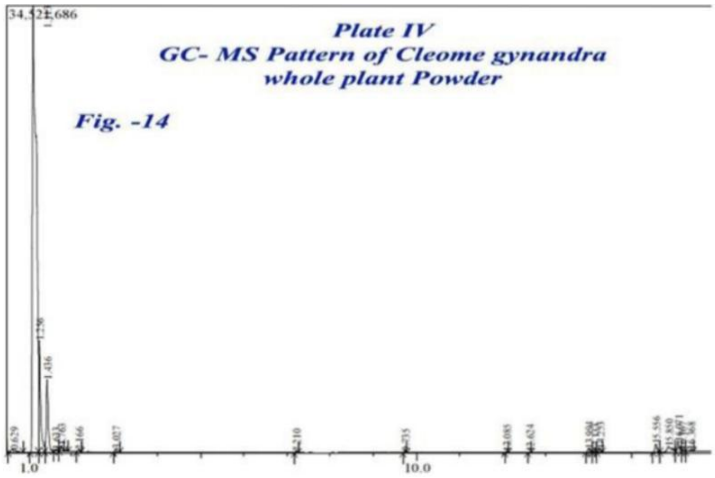

Figure - 15: GC MS pattern – The prevailing compounds are 2-Hexadecen-1-ol, 3,7,11,15-tetramethyl-,9,12-Octadecadienoic acid (Z, Z), 9,12,15-Octadecatrienoic acid and methyl ester, (Z, Z, Z)

8. Fluorescence Analysis of C*leome gynandra*

The chromogenic nature of phytochemicals was assessed by Fluorescence analysis which indirectly revealed the presence of Phytochemicals present in the plant powder. The powder of *Cleo*me *gynandra* showed mostly black colouration under long Wavelength of UV (365nm). Powder preparations observed Under visible light showed characteristic green, dark green, yellowish green, blackish brown, yellowish brown and brown colouration.

Table – 4: Fluorescence Analysis of *Cleome gynandra*

Test	Visible light	Short UV (254nm)	Long UV (365 nm)
Plant powder	Green	Green	Black
Plant powder+ water	Green	Light yellowish green	Black
Plant powder+ Hexane	Green	Green	Black
Plant powder + Chloroform	Green	Dark green	Black
Plant powder + Methanol	Green	Black green	Black
Plant powder + Acetone	Black Green	Black	Black
Plant powder + 1N NaOH	Yellowish green	Yellowish green	Black
Plant powder + 1N HCL	Brownish green	Brown	Black
Plant powder + H_2SO_4 + Water	Black	Black	Black
Plant powder + HNO_3+water	Black	Brown	Violet brown

8.1. Quantification of Ascorbic acid

The method described by Odriozola-Serrano *et al.* (2007) and Parbhunath *et al.* (2014) was followed with slight modifications. Individual sample was weighed (1 g) into a tube, followed by the addition of 5 % metaphosphoric acid (10 ml). It was sonicated in an ice-cold water bath for 15 min before centrifugation and filtration. The analysis was carried out on the Prominence-i HPLC-PDA model system described above. Chromatographic separation was achieved using a C18 Luna® column (150 × 4.6 mm, 5 µl) maintained at 25 °C. An isocratic mobile phase made up of water: acetonitrile: formic acid (99:0.9:0.1) at a flow rate of 1 ml/min was used. The injection volume was 20 µl and the detection was set at 245 nm. Sample quantification was achieved based on the calibration curve plotted using L-ascorbic acid.

8.2. Quantification of Individual Phenolic Acids

Freeze-dried samples of the three vegetables were homogenized with 80% methanol (40 mg/ml) in a 1.5 ml Eppendorf tube, using an oscillation ball mill (MM 301, Retsch, Haan, Germany) at a frequency of 25 Hz for 3 min. Deuterium-labeled internal standards were added to the extraction solvent prior to plant material homogenization. The extracts were centrifuged for 10 min at 26,000 g and the supernatant was filtered through 0.45 µm nylon microfilters (Alltech, Breda, Netherlands). The concentration of phenolic acids in vegetable extracts was determined using UHPLC (Waters, Milford, MA, USA) linked to a Micromass Quattro micro® API benchtop triple quadrupole mass spectrometer (Waters MS Technologies, Manchester, UK) as originally described by Gruz *et al*. (2008). The analyses were performed using three replicates per sample.

8.3. 2,2–Diphenyl−1–picryl hydrazyl (DPPH) Free Radical Scavenging Activity

The determination of free radical scavenging activity of the three vegetable extracts was carried out as described by Amoo et al. (2012) using freshly prepared methanolic DPPH (100 µM). Decrease in the purple colouration of the reaction mixtures was read at 517 nm using a UV/VIS Specord 210 plus (Analytik Jena, Germany) spectrophotometer. Ascorbic acid was used as a standard antioxidant. Methanol, which was used for extraction, served as the negative control. The assay was performed in triplicate. The free Radical Scavenging Activity (RSA) of the vegetable extracts was calculated according to the formula:

$$RSA\ (\%) = 100 \times (1 - AE/AD)$$

where AE is the absorbance of the reaction mixture containing the sample extract or standard antioxidant, and AD is the absorbance of the negative control.

8.4. Oxygen Radical Absorbance Capacity (ORAC)

The oxygen radical absorbance capacity (ORAC) was measured as described by Ou et al. (2001). Fluorescein (100 µl, 500 mM) and vegetable extracts (25 µl) were added into each working well in a 96-well microplate and shaken. The reaction was initiated by the addition of AAPH (25 µl, 250 mM) pre-incubated at 37°C. The fluorescence (Ex. 485 nm, Em. 510 nm) was read every 3 min over 90 min in a microplate reader Infinite M200 Pro (Tecan, Switzerland) incubated at 40°C. The net area under the curve was used to calculate antioxidant capacity in trolox equivalents (µmol TE/g). The analysis was carried out in triplicate.

8.5. Data Analysis

Statistical significance was determined using One-way Analysis of Variance (ANOVA) followed by a post hoc test (Duncan's multiple range or Tukey's multiple comparison tests). Data on total phenolic content, total flavonoid content, β-carotene, ascorbic acid and DPPH free radical scavenging activity were subjected to ANOVA followed by Tukey's post hoc test using GraphPad Prism version 5.02 (GraphPad Software Inc., San Diego, USA). SPSS version 16 (SPSS Inc., Chicago, IL, USA) was used to evaluate significant differences in the concentrations of phenolic acids. Differences in phenolic acid concentrations were further separated using Duncan's multiple range test. All analyses were done at a probability of $\alpha = 0.05$. Normality of residuals and equality of variance were tested using the Kolmogorov-Smirnov and Levene's tests (SPSS version 16). Percentage data were arcsine transformed prior to being subjected to ANOVA.

9. Pharmacognostic Characterization

9.1. Antioxidant activity

A dose-dependent increase in radical scavenging activity was demonstrated by the three vegetable extracts. Across the three tested concentrations (3.125, 50, and 200 µg/mL), *Cleome gynandra* exhibited a significantly high DPPH radical scavenging activity compared to both *Brassica oleracea* and *Berberis vulgaris*. The radical scavenging activity of *Brassica oleracea* was consistently the lowest at all tested concentrations.

Based on the oxygen radical absorbance capacity model, *Cleome gynandra* extract had the highest ORAC (200.57 µmol TE/g). This activity was 11 and 1.6 fold greater than *Brassica oleracea* and *Berberis vulgaris*, respectively. Overall, *Cleome gynandra* exhibited higher antioxidant activity in both the DPPH and ORAC model systems used in this study.

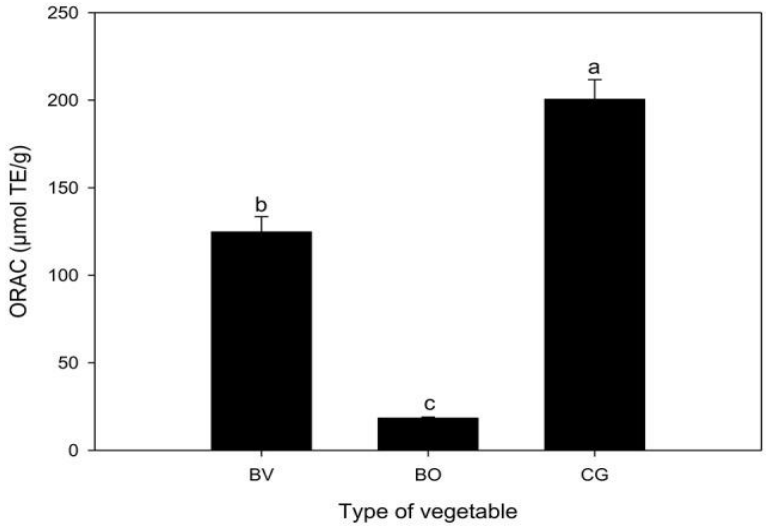

Figure - 16: Antioxidant activity in ORAC Model System

9.2. Anti-inflammatory agent

In 2008 a group of scientists uncovered the anti-inflammatory action of *Cleome gynandra*. They utilized thermal stimuli in hotplate test and the writhing reaction of the tested animals to an intraperitoneal infusion. From the outcomes, it was clear that the aqueous extract, to an intraperitoneal infusion. From the outcomes, it was clear that a notable antinociceptive activity in the hotplate test and writhing response, which is similar to that of the standard. Studies show that different flavonoids, for example, luteolin, rutin, hesperidin, quercetin, and bioflavonoids produced substantial antinociceptive and anti-inflammatory activities.A couple of reports on tannins as anti-inflammatory activities and antinociceptive properties. NSAIDs; nonsteroidal anti-inflammatory drugs in peripheral tissues can hinder cyclooxygenase, thus interfering with the transduction mechanism. The antinociceptive activity could be because of the flavonoid-mediated peripheral mechanism. Most of the NSAIDs have all around adjusted mitigating and ulcerogenic exercises, which are thought to be because of prostaglandins synthetase inhibitor activity.

9.3. Anticancer agent

Anticancer activity of methanolic extract of *Cleome gynandra* was assessed against Ehrlich Ascites Carcinoma cell line at the doses of 400 and 200 mg/kg body weight intraperitoneally. The outcome indicated significant decline in tumor volume, viable cell count, tumor weight, and raised the life expectancy of tumor-bearing mice when compared with normal control mice. Hemoglobin, red blood cell, white blood cell, and lymphocyte count returned to the normal level in treated mice. Result reveals the extract has potent dose-dependent anticancer activity.

9.4. Immunomodulator

Aqueous and alcoholic extracts of *Cleome gynandra* significantly diminishes the level of serum immunoglobulin G (IgG) in correlations with the level of IgG. Both aqueous and alcoholic extracts separately influenced IgM and IgG levels. Among the two tested samples, alcoholic extract demonstrated better activity even with lower amounts. The general pharmacological examinations strongly show the immunosuppressant activity of the alcoholic extracts and the aqueous extract of *Cleome gynandra.* Therefore, T cell-dependent antigen shown the inhibitory effect of both the extracts on T cells. The ethanolic extract of *Cleome gynandra* demonstrations better action; inhibition about 92.74 % cell-induced hypersensitivity in the albino rat to evaluate the impact of the division on cell-mediated immunity.

9.5. Antidiabetic agent

Herbal formulation of plants containing minor and trace elements in bioavailable that positively impacts glucose resistance and potentially increases self-ability to improve the diabetic condition. Essential nutrients such as Mg, Na, Fe, Ca, Se, Cu, and Zn have confirmed that many Indian herbs like Eugenia jambolana are responsible for curing diabetes by providing fundamental supplements. In some places of western Orissa, the leaves and roots are utilized by tribal people and conventional healers as an antidiabetic medicine. The reason for *Cleome gynandra* to be used in diabetes might be anticipated for its antioxidant activities, its nutritive capacity, and immunomodulatory properties. The glucose oxidation enhancing pathway, because of the dynamic phytochemicals is probably to be its polyphenolic compounds. A diabetic inconvenience like Diabetic Nephropathy (DN) is a serious and life-threatening complexity of chronic diabetes. As one of the primary factors of renal disorder, the prevention and treatment of DN in its beginning phase, and the decrease of DN

advancement are of most extreme significance and are emerging subjects current research. Natural products enriched with antioxidants.

10. Phytochemical Importance of *Cleome gynandra*

A good number of phytochemicals have been isolated from different parts of white mutant *Cleome gynandra* which confirms its current understanding of nutritional claims and pharmacological evidence, whereas a few compounds, namely, clenbuterol, stearin compound, bicyclohexyl derivatives, and (5Z,8Z)-3-hydroxypropyl dodeca-5,8-dienoate only been isolated from the pink mutant variety, only available in North east states. Samples (stems and leaves) of the plant (*Cleome gynandra*) were obtained from the germplasm maintained at the Faculty of Science and Technology of Dassa (FAST Dassa) in Benin. They were washed thoroughly under running tap water followed by sterile distilled water, cut into smaller pieces and dried under shade for 9 days. The dried plant parts were ground using an electric blending machine and the powdery samples obtained were sieved using two sieves of 0.2 mm (mesh size) and stored in airtight sterile containers until needed. Qualitative phytochemical screening was carried out on the powdery samples, after extraction with aqueous solvent, using the standardly employed precipitation and coloration reactions as described by Houghton and Raman (1998) and Dougnon *et al*. (2013). Major secondary metabolites essayed and the methods used were as follow: Alkaloids (Mayer's test), Quinone derivatives (Born-Trager reaction), Cathetic tannins (Stiasny test), Gallic tannins (Ferric chloride test after saturation with Sodium acetate), Flavonoids (Shinoda test and Magnesium powder), Cyanogenic derivatives (Picric acid test), Triterpenoids (Acetic acid test + Mixture of Acetic anhydride and Sulfuric acid), Steroids (Kedde reaction), Saponins (test index foam), Cardiac glycosides (Raymond Marthoud reaction), Anthocyanins (test with hydrochloric acid and ammonia diluted to half), Leucoanthocyanes (Shinoda test), Mucilage (Test of Absolute alcohol), Reducing compounds (Test with Fehling's solution), Coumarins (Test with Ether and Ammonia), Free anthracene derivatives (Test with Chloroform and Ammonia) and Combined anthracene derivatives (Test with Chloroform and Ammonia).

11. Cultivation of *Cleome gynandra*

Cleome gynandra is adapted to various soil types, ranging from sandy to clay loams and requires soil pH that range between 5.5 and 7.0 (DAFF, 2013). This leafy vegetable favors well-drained, medium-textured soils and is highly susceptible to

poorly drained or heavy clay soils (Shilla *et al*., 2019). The study of Schippers (2002) indicated that the application of fertilizers containing a substantial amount of nitrogen increased the leaf number and size. Mauyo *et al*. (2008) indicated that applying nitrogen fertilizer at the rate of 80 kg ha^{-1} increased plant height, number of leaves and fresh leaf of *Cleome gynandra.* The seeds of *Cleome gynandra* enter physiological dormancy for 4 – 5 months after harvest and only germinate after 6 months of harvest (Chweya, 1990; Ramphele *et al*., 2020). The process of germination is important in the domestication of crops and this is because lack of uniform seed germination can lead to poor seedling establishment and subsequently affect total yield (Kwarteng *et al*., 2018). Several studies attempted to break dormancy of *Cleome gynandra* seeds using different methods. For example, Kamotho (2004) demonstrated that storing freshly harvested seeds for the duration of one year could break dormancy; however, it was specified that seed storage conditions determine the success of breaking the dormancy. The effect of temperature, light and pre-germination treatments were tested on *Cleome gynandra* seeds, and it was revealed that alternating temperatures of 20 – 30 °C under dark conditions produced high germination percentages (Ochuodho, 2005; Ochuodho and Modi, 2005; Ochuodho and Modi, 2007). Ochuodho and Modi (2005) and Tibugari *et al*. (2012) made recommendations of puncturing the dormant seeds at the radicle to improve germination as the most effective pre-treatment method. The seeds of *Cleome gynandra* are negatively photoblastic and exposure to light for longer periods of 12 hours per day will reduce their germination due to photo inhibition (Ekpong, 2009; Raboteaux and Anderson, 2010). Others indicated that treating seeds with plant growth regulators like gibberellic acid was also found to be effective in breaking dormancy by disrupting metabolic processes that impede seed germination (Bewley and Black, 1994). Others demonstrated that farmyard manure was used to enhance the growth and yield of this leafy vegetable (Ngetich *et al*., 2012). According to Kumar *et al*. (1984), this plant has been empirically proven to tolerate salt and water stress, which is important for soil erosion control. Even though *Cleome gynandra* produces well with adequate water supply due to its ability to tolerate certain levels of water stress; nevertheless, prolonged moisture stress could delay flowering and senescence stages (Van Rensburg *et al*., 2007). Despite these advantages, indigenous vegetables like *Cleome gynandra* often produce low economic yield and are less productive when compared to commercial vegetable cultivars (Moyo and Aremu, 2022).

12. Medicinal Importance of *Cleome gynandra*

Table - 5: Medicinal Importance

S.No	Listed Diseases	Species *(Cleome gynandra)*	Organs used
1	Anemia	+	Leaves
2	Vomiting	-	Leaf
3	Ulcer	-	Leaf, stem, fruit
4	Malaria	+	Leaf
5	Jaundice	+	Leaf
6	Fever	-	Leaf, stem, fruit
7	Difficult delivery	-	Leaf, stem, fruit
8	Headache	+	Leaf
9	Dizziness	+	Leaf
10	Tooth sores	-	Root
11	Sexual weakness	+	Leaf
12	Infection	+	Root
13	Earaches	+	Leaf
14	Abscesses and wound	+	Leaf
15	Cold	-	Leaf

13. Clinical Studies and Human Trials

In traditional medicine, the whole plant of *Cleome gynandra* L. is used to treat a variety of cancers, inflammatory conditions, diabetes, parasite infections, and serves as an antioxidant and lysosomal stability promoter. Additionally, plants are employed as medicinal alternatives for tumors, piles, and stomach pain. Furthermore, the leaves are utilized topically to treat pneumonia. Moreover, iron deficiency-related anemia can be treated with a *Cleome* leaf infusion. Several plant species' external *Cleome* leaf infusions contain vesicant, rubefacient, and diaphoretic qualities that make them useful for treating ulcers and wounds. The leaf sap is used as an analgesic, notably for headaches, as a pain reliever, especially for cerebral pain, and for the treatment of severe. This genus of plants has demonstrated a greater range of genotypic, chemotypic, and biological activities in many ecological settings across the globe. These plant species have a wide range of therapeutic applications among the indigenous people and traditional healers of India. *Cleome* species exhibit a range of advantageous medicinal properties, including anthelmintic, antiseptic, antiscorbutic, carminative, febrifuge, immune-modulatory, antipyretic, psychopharmacological,

anti-inflammatory, anti-diarrheal, and hepatoprotective effects. These plant species are utilized as gulma (any tumor, lump, or diverticulosis), karnaroga (ear illnesses), asthila (prostate enlargement), kandu (pruritus), and krmiroga (worm infections) in the Ayurvedic medical system.

14. Conclusion

Africa has been characterized in the worldwide media as a continent that suffers from starvation, with images of undernourished children perpetuating this idea for a generation. Eating wild leafy greens or vegetables has the ability to nourish a great number of people both within and outside of the continent. The current study's results on the chemical, nutritional, and antioxidant qualities of Cleome gynandra, a popular wild leafy vegetable in many parts of sub-Saharan Africa, offer strong scientific support for the plant's potential to diversify diets and help millions of people meet their daily nutritional needs. Nevertheless, a lot of things need to come together for this "dream" to come true, such large funding for studies on underutilized foods, especially wild green vegetables. Chemical components, nutritional value, and antioxidant capacity of vitamin C. Cleome genus has a variety of phytochemical compounds such as essential oils, terpenes, flavonoids, glucosinolates, and alkaloids in its whole plants or plant parts (i.e., aerial plants, seeds, flowers, and roots). This genus also possesses a variety of pharmacological effects correlated with their phytoconstituents, including analgesic, anti-inflammatory, antipyretic, antidepressant, anticancer, antimicrobial, anti-arthritic, and anti-diabetic properties. The study confirmed that *Cleome gynandra* is a valuable source of bioactive compounds with significant antimicrobial, antioxidant, and anti-ulcer properties. Through various extraction methods and in-vitro assays, the aqueous and ethanolic extracts showed promising results against Multidrug-resistant (MDR) bacterial isolates and exhibited strong antioxidant activities. Additionally, the anti-ulcer potential of the extracts was validated in animal models, suggesting its effectiveness in managing gastric disorders. The research also explored the synthesis of silver nanoparticles using Cleome gynandra extracts, demonstrating their efficiency as antibacterial agents against pathogenic bacteria and as cytotoxic agents against cancer cell lines. Molecular docking studies further revealed the binding interactions of phytomolecules with key proteins, highlighting the therapeutic relevance of the identified compounds.

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Euphorbia hirta - Biofabrication of Metal Oxide Nanoparticles and Biomedical Applications

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Chapter - 19

Phytomedicine Innovations: The Future of Plant – Based Therapies
ISBN: 978-81-977907-4-4
First Edition
Chapter – 19, Page: 307 - 325

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Euphorbia hirta - BIOFABRICATION OF METAL OXIDE NANOPARTICLES AND BIOMEDICAL APPLICATIONS

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Abstract

Herbal medicine, the oldest form of medicine known to humanity, was the cornerstone of many early civilizations and remained the most widely practised form of medicine globally. This study aims to provide a comprehensive review of the green synthesis of metal and metal oxide nanoparticles using *Euphorbia hirta* and their biological applications. *Euphorbia hirta*, commonly known as the asthma plant (Amman Pacharisi in Tamil), is a small herb from the Euphorbiaceae family. Traditionally, *E. hirta* is renowned for treating respiratory conditions (such as asthma, bronchitis, and coughs) and gastrointestinal issues (like diarrhoea and dysentery). *E. hirta* exhibits various properties, including antidiarrheal, antispasmodic, anti- inflammatory, antifungal, anticancer, antimalarial, antiamoebic, antibacterial, and antihelminthic activities. Scientific studies on *E. hirta* have identified a variety of chemical compounds, including alkaloids, flavonoids, terpenoids, phenols, and phytosterols. Green synthesis methods are more suitable for developing nanoparticles ranging from 1 to 100 nm compared to other methods due to their safety, eco-friendliness, non-toxicity, and cost- effectiveness. Research indicates that plant-based synthesized nanoparticles, such as Gold (AuNPs), Silver (AgNPs), Copper (CuNPs), Zinc (ZnNPs), Iron (FeNPs), and Titanium oxide (TiO_2) exhibit anticancer, antibacterial, antifungal, larvicidal activity, antioxidant, and anti- inflammatory properties. The cytotoxic activity of metal oxide nanoparticles synthesized from *E. hirta* has been tested on various cancer cell lines, including lung, liver, colon, ovarian, and prostate cancer cells

Keywords: *Euphorbia hirta*, phytochemicals, Metal oxide Nanoparticles and Anticancer activity.

1. Introduction

Euphorbia hirta is a small herb, that belongs to the family Euphorbiaceae, distributed throughout the hotter part of India. It is commonly known as an Asthma plant, Dove milk, or Garden Spurge. The plant typically reaches a height of 30 – 40 cm, with hairy stems and leaves. All species of the Euphorbiacea family are characterized by the presence of milky latex. The plants are widely used as a traditional medicine in treating gastrointestinal disorders, respiratory disease, wound healing, pulmonary disorders, tumours, lactation in women, urinogenital disorders etc. *E. hirta* and its active constituents possess wide array of pharmacological potential viz anti-inflammatory, antioxidant, antitumour, antidiabetic and free radical scavenging, anti-allergic, analgesic and anti-anaphylactic, anxiolytic, sedative, antiarthritic, antidiarrhoeal, spasmogenic, anti-thrombocytopenic, diuretic, gastrointestinal tract, burn wound healing, immune-stimulatory, sperm motility, genotoxic, synergic, antiviral, antihelmentic, immune prophylaxis, antimalarial, antimicrobial, herbicidal and larvicidal property.

Table – 1: Botanical classification of *Euphorbia hirta*

Kingdom	Plantae
Division	Spermatomatophyta
Class	Dicotyledonae
Order	Malpighiales
Family	Euphorbiaceae
Genus	*Euphorbia*
Species	*Euphorbia hirta (E. hirta)*

2. Vernacular Names of *Euphorbia hirta*

E. hirta has diverse synonyms and vernacular names vary from region to region. In India it is known as Asthma plant – English; Dubhy, dudhi – Hindi; Amampatcharishi – Tamil; Dudeli – Gujarat; Daun bijii kacang – Indonesia; Ambin Janyan, Keremak susu - Malaysia; Boro kerui – Bangladesh.

3. Nativity and Distribution

The plant species *E. hirta* is native to Central America. It is cosmopolitan in distribution, widely distributed Throughout tropical or temperate regions of India, Asia, Africa, and Australia. It prefers dry and humid conditions, from sea level up to 2200 meters altitude. It commonly grows in paddy fields, gardens, lowlands, waste places near the roadside.

4. Phytochemicals of *Euphorbia hirta*

The primary group of bioactive phytochemicals identified in *Euphorbia hirta*, includes flavonoids, steroids, terpenoids, coumarins, tannins, and polyphenols. Phytochemical analysis of leaf extract revealed the presence of carbohydrates, terpenoids, alkaloids, reducing sugars, steroids, tannins, proteins, fats, oils, mucilages, glycoside, saponin, coumarin, anthroquinones, chlorophyll, and carotenoids. The compounds present in the plant extract are: Flavonoids (Euphorbianin, Leucocyanidol, Camphol, Quercitrin and Quercitol); Polyphenols (Gallic acid, myricitrin, 3,4-di-O-galloylquinic acid, 2,4,6-tri-O-galloyl-D- glucose, 1,2,3,4,6-penta-O-galloyl-β- D-glucose); Tannins (Euphorbins A, B, C, D, E); Triterpenes and phytosterols(β-Amyrin, 24-methylenecycloartenol, and β-Sitosterol); Alkanes (Heptacosane, n-nonacosane) (Asha *et al.*, 2015).

Figure - 1: *Euphorbia hirta*

Table - 2: Phytochemical constituents of *Euphorbia hirta*

S.No	Phytoconstituents	Aqueous	Ethanol	Methanol
1	Carbohydrates	+	-	-
2	Proteins and amino acids	+	-	-
3	Alkaloids	-	+	+
4	Flavonoids	-	+	+
5	Saponins	+	+	+
6	Tannins	+	+	+
7	Steroids	+	+	+
8	Terpenoids	-	+	+
9	Phenolic compounds	+	+	+

5. Pharmacological activity

Euphorbia hirta Linn. exhibits a broad range of pharmacological properties, including antibacterial, antifungal, anti-inflammatory, antidiarrheal, sedative, anxiolytic, anticancer, antipyretic, antioxidant, anti-asthmatic, antitumor, antimalarial, diuretic, electrolyte-enhancing, antidiabetic, and antiviral activities.

5.1. Anti-oxidant activity

The methanolic extract of *Euphorbia hirta* demonstrated antioxidant activity comparable to that of green and black tea. The phenolic acids extracted from the aqueous leaf solution exhibited antioxidant properties. The efficacy of these phenolic extracts was confirmed through Ferric Reducing Antioxidant Power (FRAP) and 1,1-Diphenyl-2-picryl-hydrazyl (DPPH) assays. The phenolic acids from *E. hirta* showed enhanced free radical scavenging activity and provided protection against oxidative damage to proteins. The antioxidant potential of the leaf extract was further evidenced by the presence of lipid peroxides, hydroperoxides, and both enzymatic and non-enzymatic antioxidants.

5.2. Anti-microbial activity

Euphorbia hirta has been extensively studied and validated by numerous research efforts. Vijaya *et al*. (1995*),* examined the antibacterial effects of methanolic extracts of *E. hirta* against *Shigella dysentereae* using vero cell lines. The decoction demonstrated significant antibacterial activity against the bacteria responsible for dysentery. The plant extract's non-cytotoxic concentrations were tested for antibacterial activity against various doses of the pathogen, proving to be both non-cytotoxic and effective. Additionally, the antimicrobial activity was assessed using nystatin and methanol extracts from *E. hirta* leaves on *Candida albicans*, yielding positive results.

The antibacterial properties of the crude ethanolic extract of *Euphorbia hirta* have been studied against *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Bacillus subtilis*. The results demonstrated significant antibacterial activity against the tested bacterial strains. The ethanolic extracts of *E. hirta* were more effective against Gram-positive bacteria compared to Gram-negative bacteria (Jackson *et al.*, 2009). The antimicrobial activity of *Euphorbia hirta* is attributed to compounds such as tannins, flavonoids, alkaloids, glycosides, proteins, sterols, and saponins. Suresh *et al*. (2008) demonstrated antibacterial effects of ethanolic extract of *E. hirta* against *Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa, and Bacillus subtilis.*

The extract showed greater antibacterial activity against Gram-positive bacteria compared to Gram-negative bacteria. The plant is rich in caffeic acid and epicatechin 3-gallate acid, both known for their antibacterial properties. This explains its traditional use in Malaysia for treating gastrointestinal, respiratory, and bronchial ailments caused by nosocomial infectious agents.

5.3. Anti-inflammatory activity

The method for studying inflammatory activity, inspired by Sy *et al.* (2019) involved using ethanolic extracts of *Euphorbia hirta*. The study was conducted on 30 Wistar rats, with inflammatory edema induced using a 2 % Formalin solution. The rats were divided into five groups of six rats each. The first group served as the control and received physiological water, while the second group, the reference group, received diclofenac. The remaining groups were administered ethanolic extracts of *Euphorbia hirta*. The percentage increase in edema was then measured across these groups. The extracts significantly reduced edema in rats from the third to the fifth hour compared to the control group. This indicates that the ethanolic extracts of *Euphorbia hirta* possess anti-inflammatory properties

5.4. Anticancer activity

Euphorbia hirta contains a variety of compounds, including flavonoids, terpenoids, phenols, and essential oils. The major constituents of its essential oils include 3,7,11,15-tetramethyl-2-hexadecon-1-ol, 6,10,14-trimethyl-2-pentadecanone, hexadecanal, phytol, and n-hexadecanoic acid (Nyeem *et al.,* (2017). Among the flavonoids, *E. hirta* includes quercetin, quercitrin, quercitol and its derivatives, rhamnose, quercetin rhamnoside, chlorophenolic acid, rutin, leucocyanidin, leucocyanidol, myricitrin, cyanidin 3,5-diglucoside, pelargonidin 3,5- diglucoside, camphol, hentriacontane, myricyl alcohol, inositol, tetraxerol, friedelin, β- sitosterol, ellagic acid, and kaempferol. The triterpenoids found in this plant include α-amyrin, β-amyrin, friedelin, teraxerol, taraxerone, 11α, 12α-oxidoteraxerol, cycloartenol, 24- methylene-cycloartenol, and euphorbol hexacosonate (Chi *et al.,* 2012).

Euphorbia hirta also contains β-sitosterol, campesterol, cholesterol, and stigmasterol. The plant extract is rich in various tannins, including dimeric hydrolysable dehydro ellagic tannins, euphorbins A, B, C, E, and terchebin, as well as monomeric hydrolysable tannins like geraniin, 2,4,6-tri-o-galloyl-β-D-glucose, and 1,2,3,4,6-penta-O-galloyl-β-D-glucose. Additionally, it contains esters such as 5-O-caffeoyl quinic acid (neo chlorogenic acid), 3,4-di-o-galloyl quinic acid, and benzyl gallate. *E. hirta* is also rich in ellagic, gallic, maleic, and tartaric acids (Birndha *et al.,* 2010).

Shao-Ming Chi *et al.* (2012) isolated a new cyclopentanone derivative, (1'R,5'R)-5- (5'carboxylmethyl-2'-oxocyclopentyl)-3Z-pentenyl acetate, from *Euphorbia hirta*. Using 1D and 2D NMR spectroscopic analysis, they elucidated its structure. They also assessed the cytotoxicity of the ethanol extract against K562 (human leukemia) and A549 (lung cancer) cell lines. The results showed that the ethanol extract exhibited weak activity against A549 cells and was inactive against K562 cells.

Sandeep *et al.* (2011) investigated the antitumor activity of *Euphorbia hirta.* They used the aerial parts of the plant to obtain ethanol, chloroform, and petroleum ether extracts, all of which contained tannins, saponins, alkaloids, and flavonoids. The chloroform and ethanol extracts increased the mean survival time and reduced solid tumour mass in mice.

5.5. Antidiabetic activity

The anti-diabetic activity of ethanolic and ethyl acetate extracts of *Euphorbia hirta* was investigated using the α-glucosidase inhibitor method in vitro. A significant reduction in blood glucose levels was observed in streptozotocin-induced diabetic mice treated with ethanolic extracts from the leaves, flowers, and stems of the plant. Subramanian *et al*. (2011) also treated experimental diabetic rats with the leaf extract of *E. hirta* and confirmed its anti-diabetic properties.

Shilpa *et al.* (2020), performed in vitro antidiabetic potential of *Euphorbia hirta* was evaluated using an alpha-amylase inhibition assay. The findings revealed that this plant's leaves are nutritionally valuable and possess significant inhibitory activity against alpha-amylase. Goldie Uppal *et al.* (2012) investigated the anti-diabetic activity of the ethanol extract of *Euphorbia hirta Linn* using animal models. Diabetes was induced in rats using alloxan for 21 days. The study found that the ethanol extract significantly reduced blood glucose levels in these diabetic rats, demonstrating a hypoglycemic effect.

Widharna *et al*. (2010) conducted both *in vivo* and *in vitro* studies on the anti-diabetic activity of *Euphorbia hirta*. *In vitro* experiments showed that the ethanol extract and ethyl acetate fractions inhibited α-glucosidase activity, while n-hexane, chloroform, butanol, and water fractions did not. The in vivo tests confirmed these results, indicating that the ethanolic and ethyl acetate extracts of *Euphorbia hirta* possess anti-diabetic properties through α-glucosidase inhibition.

5.6. Antiasthmatic activity

Euphorbia hirta is reported to have antiasthmatic activity due to its relaxing effect on the bronchial tubes and its depressant action on respiration. In a study, the trachea of an adult goat was isolated immediately after sacrifice, cut into small rings, and arranged in a series. These rings were then suspended in Krebs solution and aerated at 37 °C. The Dose-Response Curve (DRC) of Histamine was measured after administering 80 micrograms per milliliter of *Euphorbia hirta* extract. The results showed the percentage of maximum contractile response to the concentration of the plant extract (Pravin Shelke *et al.,* 2014).

6. Nanotechnology

Nanotechnology involves the creation, manipulation, and utilization of materials at the nanometer scale. With technological advancements and enhanced scientific understanding, there has been significant progress in integrating nanotechnology with Herbal and Medicinal Plant Biology. A notable example of this intersection is the use of plant sources for the green synthesis of nanoparticles. Nanoparticles are tiny particles that range in size from 1 to 100 nanometers (Drexler, 1986). Due to their small size, they exhibit unique physical and chemical properties that differ significantly from their larger counterparts.

6.1. Methods for Synthesis of Nanoparticles

Nanoparticles can be produced through various techniques, which are broadly divided into two primary approaches: Bottom-up and Top-down methods.

a) *Top-down method:* The top-down approach, often referred to as a destructive method, involves breaking down bulk materials into smaller fragments, which are then converted into nanomaterials. Examples of this method include lithography, mechanical milling or ball milling, laser ablation, sputtering, electron explosion, arc discharge, and thermal decomposition.
b) *Bottom-up method:* The bottom-up method, also known as the constructive method, involves the building of material from atoms to clusters to nanoparticles. CVD, sol-gel, spinning, pyrolysis, and biological synthesis are all examples of bottom-up methods.

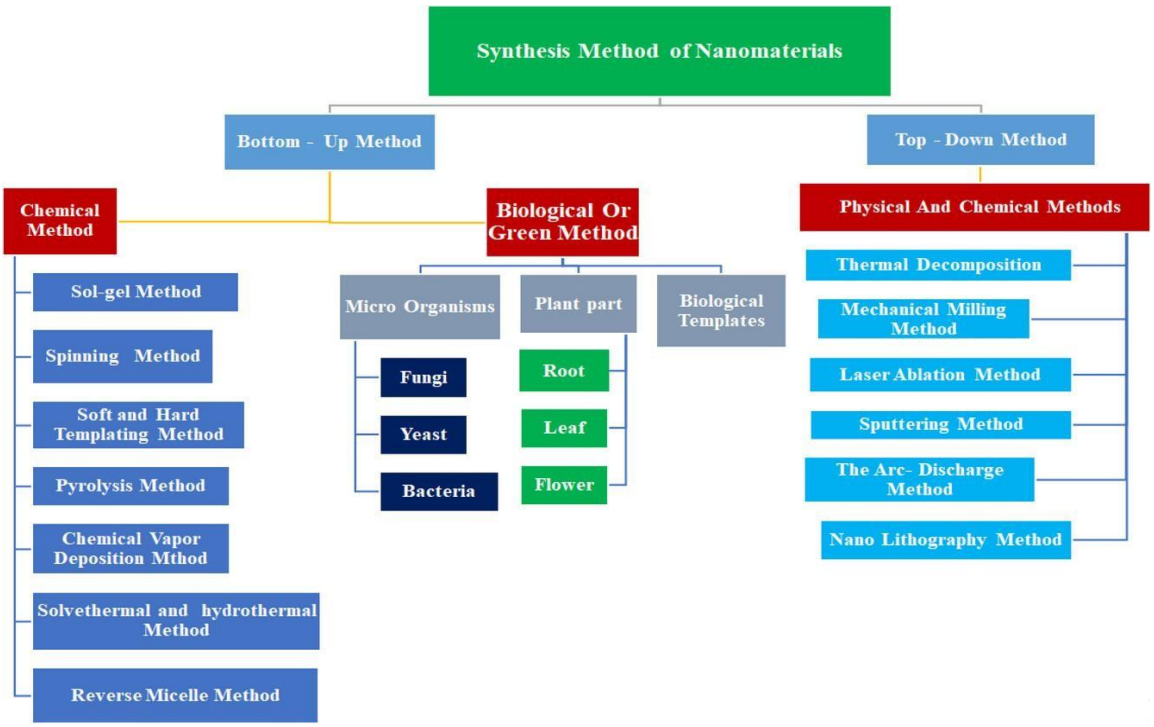

Figure - 2: Synthesis Methods of Nanoparticles

6.2. Biosynthesis of Nanoparticles from Plant extract

Green synthesis of nanoparticles has been an arising research region nowadays. The progression of green synthesis over chemical and physical methods are better for the environment. It is cost-effective and easily scaled up for large-scale syntheses of nanoparticles, furthermore, there is no need to use high temperature, pressure, energy and toxic chemicals. The use of plants for producing nanoparticles has gained significant attention due to its rapid, eco- friendly, non-pathogenic, and cost-effective approach, offering a straightforward technique for green synthesis processes. A mix of biomolecules such as proteins, amino acids, enzymes, polysaccharides, alkaloids, tannins, phenolics, saponins, terpenoids, and vitamins facilitates the reduction and stabilization of metal ions. These biomolecules, present in medicinal plant extracts, are environmentally friendly and chemically complex. The different parts of plant such as stem, root, fruit, seed, callus, peel, leaves and flower are used to synthesis of metallic nanoparticles in various shapes and sizes by biological approaches. Numerous plants have been reported to aid in the synthesis of metal nanoparticles (Roy *et al.,* 2015).

6.3. Characterization of Nanoparticles

Characterizing nanoparticles` involves a variety of techniques to measure their physical and chemical properties. These properties include size, shape, surface area, crystallinity, and elemental composition

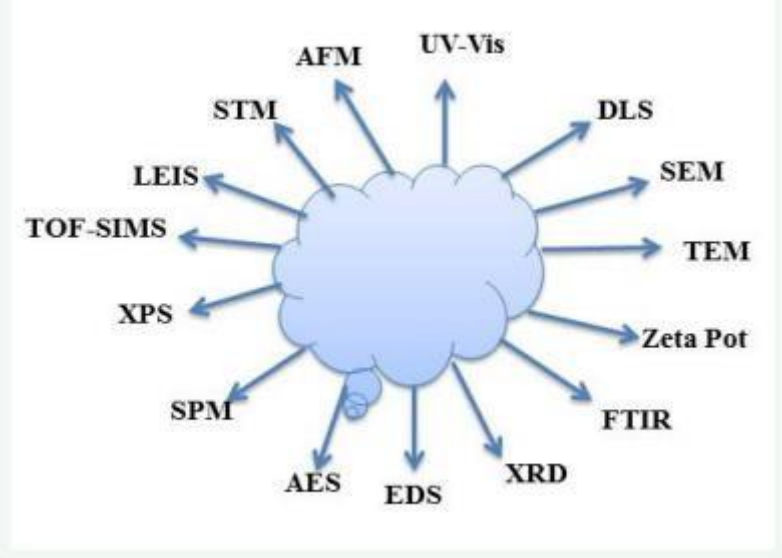

Figure - 3: Characterization of Nanoparticles

6.4. Applications of Nanoparticles

Medicine

i) *Drug Delivery:* Nanoparticles can deliver drugs directly to targeted cells, enhancing efficacy and minimizing side effects.
ii) *Imaging:* Used as contrast agents in MRI and other imaging techniques to improve the visibility of internal structures.
iii) *Therapeutics:* Utilized in cancer treatments, such as photothermal therapy, where nanoparticles are used to destroy cancer cells with heat.

Electronics

i) *Nanoelectronics:* Development of smaller, faster, and more efficient electronic components.
ii) *Sensors:* High sensitivity sensors for detecting chemical and biological substances.

Energy

i) *Solar Cells:* Increasing the efficiency of photovoltaic cells.
ii) *Batteries:* Enhancing the performance and capacity of batteries and supercapacitors.

Environmental Applications

i) *Water Purification:* Removing contaminants from water through adsorption and catalytic processes.
ii) *Pollution Control:* Degrading pollutants in the environment.

Catalysis

i) *Chemical Reactions:* Nanoparticles act as catalysts to accelerate chemical reactions in industrial processes.

Agriculture

i) *Pesticides and Fertilizers:* Controlled release of agrochemicals to improve crop yield and reduce environmental impact.

Food Industry

i) *Packaging:* Nanoparticles are used in food packaging to enhance barrier properties and extend shelf life.
ii) *Food Additives:* Improving the texture, flavor, and nutritional value of food products.

Cosmetics

i) *Skincare Products:* Used in sunscreens and anti-aging creams for better skin penetration and protection (Ramsden and Jeremy, 2016).

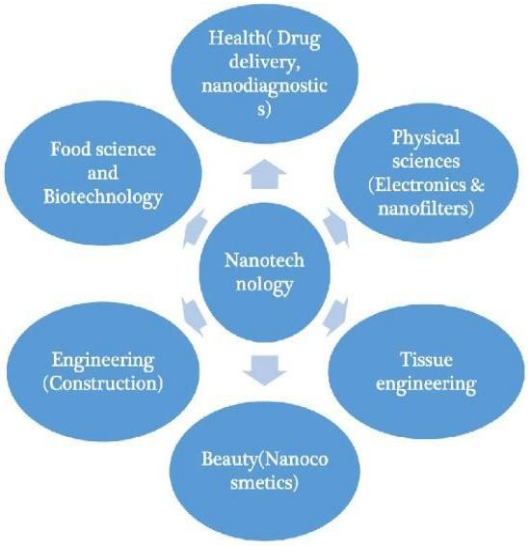

Figure - 4: Applications of Nanotechnology

7. Metal Oxide Nanoparticle Fabrication Using *Euphorbia hirta*

7.1. Silver Nanoparticles

Anti-microbial activity

Elumalai *et al.* (2010) have discussed that the aqueous extract from shade-dried leaves of *Euphorbia hirta* L. was utilized for synthesizing Silver (Ag) nanoparticles. UV-visible spectroscopy was employed to confirm the formation of Ag nanoparticles while Scanning Electron Microscopy (SEM) characterized them. SEM images revealed that the silver nanoparticles were quite poly dispersed, with sizes ranging from 40 nm to 50 nm. These silver nanoparticles demonstrated effectiveness against *Bacillus cereus* and *Staphylococcus aureus*. The approach of extracellular synthesis of Ag nanoparticles using dried biomass is both cost- effective and eco-friendly compared to conventional nanoparticle synthesis methods. The green synthesis of nanoparticles was found to be highly toxic against five clinically isolated bacterial species. At a concentration of 30 µl, silver nanoparticles exhibited significant antibacterial activity against *Bacillus cereus* and *Staphylococcus aureus*. In contrast, they showed moderate activity against *Escherichia coli, Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*.

Melchias *et al.* (2014) have synthesized silver nanoparticles using the *E. hirta* plant, after exposing the silver ions to *E. hirta* the rapid reduction of silver ions is observed and leading to the formation of silver nanoparticles. The synthesized nanoparticles are characterized using UV- visible spectroscopy, FTIR, FESEM and particle size analyser. FESEM image divulges that silver nanoparticles are quite poly-dispersed, the size ranging from 5.1642 nm to 98.65 d.nm. The antibacterial activity was examined and the zone of inhibition was noticed against the bacteria *Bacillus subtilis, vibrio cholera and salmonella typhi* the zone of inhibition was 17,13,18 for 20 µl of concentration.

Elumalai *et al*. (2010) have synthesized silver nanoparticles using a 1 mM $AgNO_3$ solution and the leaf extract of *Euphorbia hirta* L. as both a reducing and capping agent. The nanoparticles were characterized using UV-VIS absorption spectroscopy. These Green synthesized Silver nanoparticles demonstrated Antifungal activity against *Candida albicans, Candida kefyr, and Aspergillus niger*. The green synthesis of nanoparticles demonstrated significant toxicity against seven clinically isolated fungal species. At a concentration of 50 µl, silver nanoparticles exhibited strong antifungal activity against *Candida albicans*, *Candida kefyr*, and *Aspergillus niger* with a zone of inhibition was noticed at 16.25±0.03, 15.00±0.02, 13.24±0.01 mm.

Anti-larvicidal activity

Chellasamy Pannerselvam *et al*. (2012) have noticed the activity of Silver nanoparticles (AgNPs) synthesized using the leaf extract of *Euphorbia hirta* (*E. hirta*) against the malarial vector *Anopheles stephensi* (*A. stephensi*) was evaluated. Various concentrations of synthesized AgNPs (3.125, 6.25, 12.5, 25, and 50 ppm) and methanol crude extract (50, 100, 150, 200, and 250 ppm) were tested against *A. stephensi larvae*. Characterization of the synthesized AgNPs was performed using UV-vis Spectroscopy, Scanning Electron Microscopy (SEM), and X-ray diffraction (XRD). SEM analysis revealed that the AgNPs, measuring 30 – 60 nm in size, were clearly distinguishable.

The synthesized AgNPs demonstrated larvicidal effects after 24 hours of exposure, with the highest larval mortality observed in the synthesized AgNPs against the first to fourth instar larvae and pupae, with LC50 values of 10.14, 16.82, 21.51, and 27.89 ppm, respectively, and LC90 values of 31.98, 50.38, 60.09, and 69.94 ppm, respectively. The LC50 and LC90 values for pupae were 34.52 and 79.76 ppm, respectively. The methanol extract showed larval toxicity against the first to fourth instar larvae and pupae, with LC50 values of 121.51, 145.40, 169.11, and 197.40 ppm, respectively, and LC90 values of 236.44, 293.75, 331.42, and 371.34 ppm, respectively. The LC50 and LC90 values for pupae were 219.15 and 396.70 ppm, respectively. No mortality was observed in the control group. These findings suggest that synthesized silver nanoparticles offer a rapid, eco-friendly, and single-step approach, with potential as effective mosquito larvicidal agents. The AgNPs synthesized from *E. hirta* exhibited higher toxicity compared to the methanolic crude extract against *A. stephensi*.

Anticancer activity

Selvam *et al*. (2019) have synthesized and characterized silver nanoparticles (AgNPs) were synthesized using the bioreduction method with an ethanolic extract from the aerial parts of *Euphorbia hirta* L. (EH-ET). The formation of AgNPs was indicated by a color change in the solution and confirmed through UV-Visible spectroscopy. The nanoparticles were characterized using Scanning Electron Microscopy (SEM), Fourier Transform Infrared Spectroscopy (FT-IR), and Zeta potential analysis. The anticancer activity of EH-ET AgNPs was evaluated against Neuroblastoma (SH-SY5Y) and Breast cancer (MCF-7) cells, with cytotoxicity tested on vero cells using the MTT assay.

Preliminary confirmation of AgNP synthesis was indicated by a reddish-brown color and an absorption peak at 429.5 nm. SEM images showed that the AgNPs were spherical, with sizes between 2.9 and 206.3 nm. FT-IR spectra identified functional groups such as C=O, -C=C, and -OH, which played roles in the bioreduction and stabilization processes. The AgNPs were found to be polydispersed and showed some agglomeration.

The synthesized AgNPs demonstrated significant anticancer activity against neuroblastoma and breast cancer cells, with IC_{50} values of 29.85 and 335 µg/mL, respectively, while showing no cytotoxicity towards Vero cells. These findings suggest that AgNPs synthesized using the ethanolic extract of *Euphorbia hirta* L. could be effective cytotoxic agents for cancer treatment. Bennet Rohan *et al.* (2020) have reported that the aqueous extracts of *Euphorbia hirta* were utilized to synthesize Silver nanoparticles through a bioreduction method. The nanoparticles were characterized using UV-Vis spectroscopy, SEM, EDX, AFM, and XRD analyses. Their antibacterial activity was tested against *Pseudomonas aeruginosa* and *Bacillus subtilis*. The Minimum Inhibitory Concentration (MIC) for the synthesized nanoparticles was determined, with the lowest concentration being 0.5 µg/ml. Additionally, swarming motility and protein leakage assays were conducted. The results indicated that the silver nanoparticles were highly effective.

Rajalakshmi Ramachandran *et al.* (2022) their study planned to evaluate the anticancer efficacy of Silver nanoparticles (AgNPs) synthesized using *Euphorbia hirta* (Eh) on human lung adenocarcinoma A549 cell. The Eh-AgNPs were characterized using UV-spectroscopy, X-ray diffraction, Transmission Electron Microscopy, and Fourier-Transform Infrared Spectroscopy. The antibacterial efficacy of Eh-AgNPs was assessed using the agar well diffusion method, while their cytotoxicity on A549 cells was evaluated using the MTT assay. The results indicated that Eh-AgNPs exhibited significant antibacterial activity against bacterial pathogens and demonstrated dose-dependent cytotoxicity on A549 cells, inducing apoptosis. This was evidenced by increased lipid peroxidation and decreased antioxidant levels. Eh-AgNPs significantly promoted early apoptosis in A549 cells in a concentration-dependent manner.

Treatment with Eh-AgNPs reduced Bcl-2 expression while increasing the expression of p53, Bax, and cleaved caspase-3 and -9. Additionally, Eh-AgNPs treatment led to a reduction in PI3Kγ, phospho-PI3K, phospho-Akt, phospho-mTOR, and p70S6K levels. These findings suggest that Eh-AgNPs induce reactive oxygen species-mediated apoptosis by upregulating p53 and Bax and inhibiting the PI3K/Akt/mTOR/p70S6K Signaling pathway.

7.2. Gold Nanoparticles

Annamalai *et al.* (2013) have studied the gold nanostructures with unique physicochemical properties were produced using the leaf extract of *Euphorbia hirta* L. The eco-friendly and non-toxic Gold nanoparticles (AuNPs) were synthesized biologically, confirmed by a colour change from pale yellow to purple and surface plasmon resonance spectra around 530 nm. The synthesized nanoparticles ranged in size from 6 nm to 71 nm. Various techniques such as TEM, XRD, EDAX, AFM, particle size analyzer, FTIR, and Raman spectra were used to characterize the Au NPs.

Antibacterial activity

The antibacterial activity of these green-synthesized Au NPs was tested against *Escherichia coli*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae* using the MIC method, showing high effectiveness. At 200 µg/ml an inhibition of 88 % for *Escherichia coli*, 86 % for *Pseudomonas aeruginosa* and 94 % for *Klebsiella pneumoniae* was found.

8. Copper Oxide Nanoparticles

Vaitheeswari Balakrishnan *et al*. (2021) synthesized the metal nanoparticles using green methods is eco-friendly and non-toxic, offering several benefits to emerging research fields, particularly in inhibiting bacterial and cancer growth. In this study, Copper oxide nanoparticles (CuO NPs) were synthesized using *Euphorbia hirta* leaf extract. The formation of CuO NPs was confirmed by the Surface Plasmon Resonance (SPR) peak in the UV spectrum. Functional groups responsible for reduction and stabilization were identified through FTIR, while GC-MS analysis revealed the phytochemicals in *Euphorbia hirta* extract that facilitate the synthesis of CuO NPs. XRD analysis confirmed the crystalline nature of the nanoparticles, and SEM and TEM analyses verified their size and spherical morphology. CuO NPs demonstrated effective antibacterial activity against pathogens, strong antioxidant and anti-inflammatory activities, and excellent anticancer activity against the Ht-29 cell line. They also proved to be good catalysts for the effective degradation of Methylene blue.

9. Zinc Oxide Nanoparticles

Waseem Ahmad and Divya Kalra (2020) have proposed a green method for synthesizing ZnO nanoparticles using *Euphorbia hirta* leaf extract has been developed. ZnO nanoparticles are known for their wide range of applications, particularly as antimicrobial agents. While various methods exist for synthesizing

ZnO nanoparticles, using plant material is an excellent and eco- friendly alternative. The leaf extract acts as a biological reducing agent to synthesize ZnO nanoparticles from zinc nitrate. The synthesized nanoparticles were characterized using several analytical and spectroscopic techniques, including UV-visible spectroscopy, Fourier Transform Infrared Spectroscopy (FT-IR), X-ray Diffraction (XRD), and Scanning Electron Microscopy (SEM). The antimicrobial activity of the biosynthesized nanoparticles was evaluated using the disc diffusion method against clinical and standard strains of *Streptococcus mutans, Streptococcus aureus, Clostridium absonum, Escherichia coli, Arthogrophis cuboida, Aspergillus fumigatus, and Aspergillus niger.*

10. Titanium Dioxide Nanoparticles

Maheswari *et al*. (2021) have reported that Three medicinal herbs, namely *Plectranthus amboinicus* (Karpooravalli), *Phyllanthus niruri* (Keezhanelli), and *Euphorbia hirta* (Amman Pacharisi) were utilized to modify the surface of TiO_2 nanoparticles. These synthesized nanoparticles underwent various characterization techniques. The samples were then subjected to an MTT assay to assess cell viability, using KB oral cancer cells to determine the anticancer properties of both the pure and bio-modified nanoparticles. It was observed that the TiO_2 nanoparticles modified with *Plectranthus amboinicus* and *Phyllanthus niruri* exhibited superior anticancer activities compared to other bio-modified and pure samples.

The antibacterial activities of the samples were tested against three Gram-negative bacterial strains (*Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa*) and two Gram- positive bacterial strains (*Staphylococcus aureus and Streptococcus mutans*). Among the modified and pure samples, those modified with *Plectranthus amboinicus* demonstrated significant antibacterial activity against both Gram-positive and Gram-negative bacteria. Flow cytometry analysis revealed that the *Plectranthus amboinicus – Phyllanthus niruri*-modified TiO_2 nanoparticles induced the expression of the p53 protein, indicating their anticancer potential. To evaluate the toxicity of these modified nanoparticles on normal cells, an MTT assay was conducted using normal L929 cells, revealing that the nanoparticles were safer and less toxic to normal cells.

Table - 3: Nanoparticles and their Applications

Nanoparticles	Biological Activity	Reference
Silver	Antibacterial activity	Elumalai *et al.* (2010)
	Antibacterial activity	Melchias *et al. (*2014)
	Larvicidal agent	Chellasamy Pannerselvam *et al*. (2012)
	Anticancer activity	Selvam *et al*. (2019)
	Antifungal activity	Elumalai *et al.* (2010)
	Antibacterial activity	Bennet Rohan *et al* (2020)
	Anticancer activity	Rajalakshmi Ramachandran *et al.* (2022)
Gold	Antibacterial activity	Annamalai *et al.* (2013)
Copper oxide	Antibacterial, Antioxidant, anti-inflammatory and Anticancer activity	Vaitheeswari Balakrishna *et al.* (2021)
Zinc oxide	Antibacterial activity	Waseem Ahmad and Divya Kalrai (2021)
Iron oxide	Antibacterial activity	Waseem Ahmad *et al.* (2021)
Titanium oxide	Antibacterial activity	Maheswari *et al.* (2021)

11. Conclusion

Research on the synthesis of metal nanoparticles using various methods, particularly plant extracts, has significantly contributed to fields like medicine and industrial applications. Green synthesis is an environmentally friendly, cost-effective, bioefficient, and non-carcinogenic approach. This method is eco-friendly, non-toxic, and economical. This review summarizes information on the synthesis, characterization, and applications of plant-based synthesized metal and metal oxide nanoparticles, which are used to analyze antibacterial, antifungal, antioxidant, and anticancer properties. These studies strongly recommend the green synthesis approach for developing metal and metal oxide nanoparticles due to their beneficial responses in biomedical applications. Furthermore, it is concluded that most recent studies follow the synthesis method, physicochemical characterization, and in vitro evaluation using different cell lines or microbes, depending on their application. Numerous research studies have demonstrated the antioxidant and larvicidal activity of these nanoparticles. Therefore, the environmentally friendly synthesis of nanoparticles and their biomedical applications still require special attention in future studies.

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Biomedical Exploration of Ayurvedic Phytomedicines: From *Traditional Formulations to Modern Drug Development Paradigms*

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Chapter - 20

Phytomedicine Innovations: The Future of Plant – Based Therapies
ISBN: 978-81-977907-4-4
First Edition
Chapter – 20, Page: 326 - 349

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BIOMEDICAL EXPLORATION OF AYURVEDIC PHYTOMEDICINES: FROM TRADITIONAL FORMULATIONS TO MODERN DRUG DEVELOPMENT PARADIGMS

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Abstract

The biomedical investigation of Ayurvedic phytomedicines is a dynamic interface of ancient traditional medicine on drug discovery and therapeutic uses. Ayurveda offers a diverse application of plant-based medicines with their multi-target activity in the treatment of chronic, inflammatory, metabolic, and neurodegenerative diseases. The bioactive molecules such as the alkaloids, flavonoids, terpenoids, glycosides, and polyphenols, that find source in their pharmacological activity. Advanced analytical methods, including High-Performance Liquid Chromatography (HPLC), Mass Spectrometry (MS), and Nuclear Magnetic Resonance (NMR) spectroscopy, have made it possible to isolate and characterize these phytoconstituents and delineate their mechanisms of action in anti-inflammatory, antioxidant, hepatoprotective, antidiabetic, and cardioprotective activities. The omics technologies like the genomics, proteomics, metabolomics and computational technologies like the molecular docking, systems biology has further revealed the

polypharmacological synergies embedded in Ayurvedic polyherbal formulations such as Triphala and Chyawanprash. Several challenges including standardization, bioavailability, regulatory harmonization, and clinical validation. Modern drug delivery systems such as nanoencapsulation and liposomal formulations are being used to improve the bioavailability and targeted delivery of these phytochemicals. In addition, integration of Ayurveda's preventive, personalized approach with precision medicine highlights its health care. Nonetheless, ethical issues, intellectual property rights, and sustainable sourcing of medicinal plants continue to be important concerns. Ayurvedic phytomedicines multidisciplinary collaboration with the use of artificial intelligence, blockchain-based quality assurance, and clinical trials to connect ancient wisdom with evidence-based medicine. Ayurvedic phytomedicines can be moved from alternative medicine to biomedical use, that provides the sustainable, multi-targeted approaches to worldwide health problems. This chapter highlights the revolutionizing applications of Ayurveda in contemporary paradigms for drug development that promoting a synergistic effects of traditional wisdom and advanced science for the future holistic and customized therapeutics in medicine.

Keywords: Ayurvedha, Phytomedicines, Traditional Formulations and Modern Drug Development.

1. Introduction

Ayurveda has been used for more than 5000 years for health and healing on the Indians. It has the used as the balance between the body, mind, and environment. Ayurveda provides a large pharmacopeia of plant-derived medicines, often referred to as phytomedicines, that have been traditionally used for the prevention and treatment of a great variety of conditions. The pharmacological potential of Ayurvedic phytomedicines results from the worldwide biomedical community's growing potential in natural and plant-based remedies (Brantley *et al.,* 2014). The medicinal richness of traditional formulations into the paradigms of modern drug discovery and development, this modern approach strives to the historical wisdom inherent in ancient Ayurvedic with the modern scientific research methods. Ayurvedic formulations often complicated from the mixes of herbs and minerals that have the ethnopharmacological significance that poses both the health and medicine (Hankey, 2001). Unlike conventional single-compound drugs, these formulations depend on synergistic interactions among several bioactive compounds, thus advanced analytical tools including High-Performance Liquid Chromatography (HPLC), Mass Spectrometry (MS), Nuclear Magnetic Resonance (NMR) Spectroscopy, and metabolomics are necessary to isolate, identify, and the mechanisms of action of individual phytoconstituents.

Ayurvedic phytomedicines' molecular foundations are being used in the modern *in vitro* and *in vivo* experimental models, computational methods like molecular docking, ADMET profiling, and systems biology. Moreover, the integration of omics technologies like genomics, proteome, transcriptomics, and metabolomics has given a stage for mapping the impacts of ayurvedic formulations on biological systems and multi-target drug development. Significant issues phytochemical-based treatments have been demonstrated by the biomedical

investigation of phytochemicals including Curcumin from *Curcuma longa*, Withanolides from *Withania somnifera,* Boswellic acids from *Boswellia serrata*, and Glycyrrhizin from *Glycyrrhiza glabra* (Dori *et al.,* 2020). These have shown anti-inflammatory, antioxidant, anticancer, neuroprotective, and immunomodulating effects. The safety, effectiveness, and repeatability, turning these age-old treatments into evidence-based medications. The preclinical validation, pharmacokinetic profiling, toxicity assessment, and clinical evaluation. Standardizing formulations, guaranteeing quality control, and enabling worldwide adoption all depend on regulatory frameworks including those supplied by AYUSH, WHO, and international bodies. Moreover, the use of advanced formulation technologies including nanoencapsulation, liposomal delivery, and transdermal systems together with Good Manufacturing Practices (GMP) has improved the bioavailability and targeted delivery of phytoconstituents for the solubility and absorption problems (Islam *et al.,* 2021).

The pharmacologists, biotechnologists, and regulatory authorities working together to have integrated healthcare solutions has also resulted from the systems with modern science. Furthermore, the ethical, cultural, and intellectual property rights elements of using traditional knowledge have to be negotiated and guarantee equitable distribution of benefits to indigenous people. Ayurveda's function is being reinterpreted in this changing terrain as a fundamental source of fresh pharmacological ideas and complete therapeutic approaches rather than only as an alternative or complementing system. Ayurvedic phytomedicines provide a viable path for creating safe, efficient, and sustainable treatments for chronic illnesses, infectious diseases, and lifestyle-related diseases as the global health paradigm moves toward personalized medicine and prevent-oriented care (Fu *et al.,* 2018). Ayurvedic phytomedicines' present biomedical research is therefore a convergence of tradition and innovation into modern pharmacotherapeutics by strong scientific investigation. Ayurvedic phytomedicines have great potential to be included into modern drug development paradigms by translational medicine, technology-enabled analysis, and interdisciplinary research by lowering drug-related toxicity, and fostering wellness through natural-inspired remedies (Jayakumar, 2010).

2. History of Ayurvedic Phytomedicines

Ayurveda is a healthcare system originating over 5000 years ago in the Indian subcontinent, is based on sacred Vedic texts like the Rigveda and Atharvaveda that include hymns and references to medicinal plants and their therapeutic uses. Classical books like the Charaka Samhita, Sushruta Samhita, and Ashtanga Hridaya systematized and expanded the knowledge of medicinal plants for their complex formulations, diagnostic techniques, and therapeutic regimens that still influence

Ayurvedic practices. Ayurvedic phytomedicines have evolved over the centuries, reflecting the pharmacodynamics and pharmacokinetics before these ideas were formalized in Western science (Ifeoma and Oluwakanyinsola, 2013). Trade routes throughout Asia, the Middle East, and Europe helped to share medical knowledge, and Ayurvedic traditions, local healers, and classical institutions despite disturbances during colonial times when Western biomedicine was imposed as the dominant paradigm. The phytochemistry, molecular biology, pharmacology, and biotechnology have made the Ayurvedic phytomedicines possible with modern drug discovery models. Several Ayurvedic-derived compounds and formulations have been preclinical and clinically tested under alternatives involving Ayurvedic, biomedical researchers, and pharmaceutical industries, showing potential for managing chronic conditions like diabetes, arthritis, neurodegenerative diseases, cardiovascular disorders, and cancers (George, 2011).

3. Significance of Ayurvedic phytomedicines in modern biomedicine

Ayurvedic phytomedicines offer a therapeutic potential and a holistic approach to health, aligning with modern trends in integrative and personalized medicine. They provide a rich supply of bioactive chemicals that treat the underlying causes of illnesses rather than just relieving symptoms. Major disciplines like ethnopharmacology, phytochemistry, and molecular docking studies have helped Ayurvedic phytomedicines be included in modern biomedical research (Ernst, 2007). Technologies like high-throughput screening, omics platforms, and artificial intelligence have advanced Ayurvedic drug mechanisms on gene expression modulation, immune system enhancement, and gut microbiota control. Ayurvedic medicine emphasizes preventive care, treatment based on prakriti (body constitution), and the use of Rasayanas (Rejuvenative therapies). Ayurvedic phytomedicines treat not only physical diseases but also mental and emotional well-being, complementing the increasing understanding of mind-body relationships in contemporary medicine. Some Ayurvedic phytochemicals show efficacy against multi-drug-resistant bacteria, providing fresh scaffolds for antibiotic development. Ayurvedic phytomedicines are important for oncology, with agents like *Tinospora cordifolia, Phyllanthus nirri*, and *Ocimum sanctum* for their immunomodulating, anti-proliferative, and radioprotective properties. They must be translated into biomedical applications for standardized production techniques, and regulatory compliance (Denaro *et al.,* 2020).

4. Types of Ayurvedic Medicinal Plants

Ayurvedic medicinal plants are known for their rich phytochemical compositions and therapeutic properties, have been used in traditional healing practices for centuries. These botanicals, including Vata, Pitta, and Kapha, have been used to balance the body's doshas and treat various diseases, including preventative

ones. Modern studies have found withanolides as main bioactive compounds responsible for increasing endurance, lowering cortisol levels, and possibly helping in neurodegenerative disease management (Fernández-Ochoa *et al.,* 2021). Ashwagandha is known for its adaptogenic, antistress, neuroprotective, and immunomodulating properties. Turmeric is a pillar of Ayurvedic medicine, has strong anti-inflammatory, antioxidant, and anticancer agents, used in conditions such as arthritis, metabolic syndrome, cardiovascular disease, and Alzheimer's disease. Tulsi is also known as holy basil, is widely regarded for its antimicrobial, antidiabetic, and cardioprotective activities. Neem, another multifarious Ayurvedic plant, has shown efficacy in antimicrobial, antimalarial, anti-inflammatory, and antitumor applications. Guduchi, a "divine herb," shows immunostimulant, hepatoprotective, and anti-inflammatory properties, often used in managing fever, diabetes, and immune-related diseases (Jiang *et al.,* 2010). Triphala, a synergistic mix of three fruits, shows antioxidant, anti-aging, detoxifying, and gut-modulating properties. Ayurvedic herbs like Amalaki, Shatavari, and Safed Musli have become increasingly important for their rejuvenating and fertility-boosting qualities, showing potential in reproductive health.

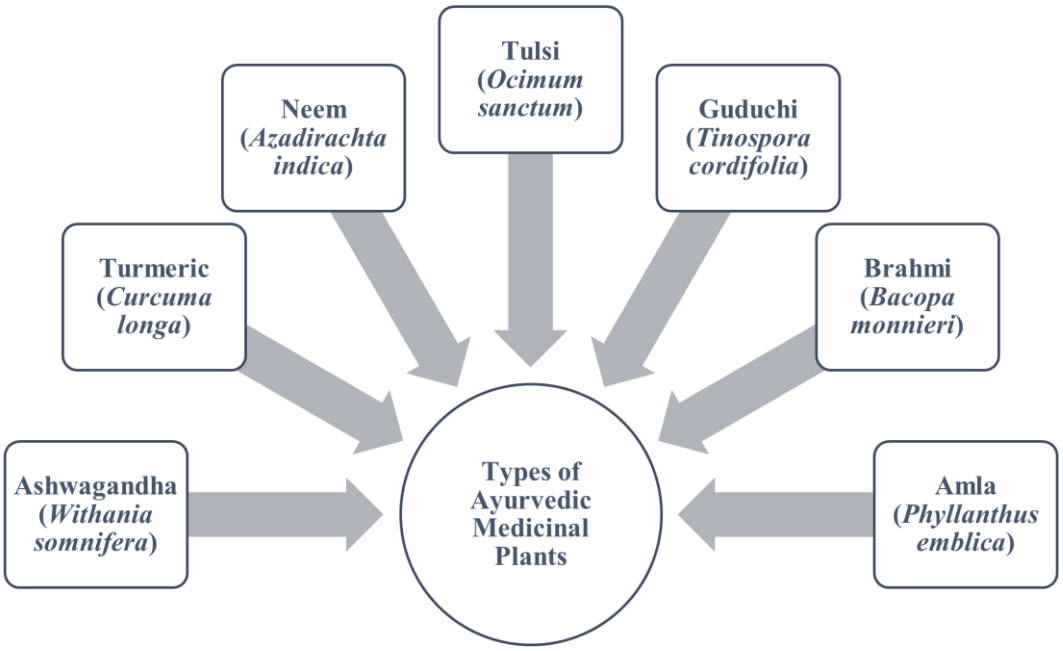

Figure – 1: Types of Ayurvedic Medicinal Plants

4.1. Ashwagandha (*Withania somnifera*)

Ashwagandha is an adaptogenic herb in Ayurveda, has gained significant importance in biomedical research due to its numerous medicinal effects. It is also known as the "Indian ginseng," and has been used to boost vitality, lower stress, and improve cognitive performance. Recent research has shown its value in neuroprotection, immunomodulation, anti-inflammatory action, and even anticancer uses. Ashwagandha's bioactive compounds, particularly withanolides, alkaloids, and sitoindosides, contribute to its antioxidant activity. It has shown potential in neurological diseases like Alzheimer's disease by lowering beta-amyloid plaques, enhancing memory in dementia, and decreasing anxiety and sadness through GABAergic and serotonergic regulation (Karimi *et al.,* 2015). Its immunomodulating properties improve lymphocyte proliferation and macrophage activity in autoimmune diseases and post-chemotherapy recovery. Ashwagandha's cardioprotective, antidiabetic, and thyroid-regulating properties make it suitable for metabolic diseases. Clinical studies confirm its safety and efficacy in stress relief, cognitive improvement, and chronic illness management. The nanoparticle-based administration of withanolides to improve bioavailability.

4.2. Turmeric (*Curcuma longa*)

Turmeric is a golden-hued rhizome in Ayurveda, is gaining attention for its therapeutic potential in biomedical research. Its main bioactive compound, curcumin, is known as "haridra" in Sanskrit and is widely used as a culinary spice. Curcumin acts in anti-inflammatory and immunomodulating applications by blocking inflammatory mediators, managing chronic inflammatory conditions like rheumatoid arthritis, inflammatory bowel disease, and asthma. Its strong antioxidant activity makes it a therapeutic agent in oxidative stress-related disorders, including neurodegenerative diseases, cardiovascular diseases, and aging. It also crosses the blood-brain barrier in neuroprotection, modulating pathways linked to Alzheimer's disease, Parkinson's disease, and depression (Jităreanu *et al.,* 2022). It induces apoptosis, inhibits angiogenesis, and suppresses metastases in many cancers, augmenting its anticancer potential with adjunctive use in chemotherapy. Turcumin's cardiometabolic benefits include improving lipid profiles, enhancing endothelial function, and exerting antihypertensive effectsmanage atherosclerosis, diabetes, and metabolic syndrome. Modern drug development paradigms are looking at combination therapy to maximize turmeric-derived synthetic analogues.

4.3. Neem (*Azadirachta indica*)

Neem is also known as "Nature's Pharmacy" in Ayurveda, is a versatile therapeutic plant with over 140 bioactive compounds. These compounds have various biological applications, including antimicrobial, anti-inflammatory, immunomodulating, anticancer, antidiabetic, hepatoprotective, and dermatological effects. Neem's broad-spectrum activity against bacteria, viruses, fungi, and parasites makes it valuable for developing new antimicrobial agents. It also improves wound healing through angiogenesis and collagen synthesis, and its anti-inflammatory and immunomodulating effects show potential in treating autoimmune disorders. Neem's anticancer potential is extensively investigated, particularly nimbolide that induces apoptosis, inhibits angiogenesis, and prevents metastases in various cancers (Fu *et al.,* 2018). Neem leaf extracts and seed oil show notable antidiabetic action in metabolic diseases, raising insulin sensitivity, lowering blood glucose levels, and preserving pancreatic β-cells. Its hepatoprotective ability shields against alcohol, drug, and toxin-induced liver damage through antioxidant processes and improved detoxification paths. Neem's multifunctional therapeutics for its low toxicity, and cost-effectiveness for future drug development to the global health challenges like antimicrobial resistance, chronic inflammation, and metabolic syndrome.

4.4. Tulsi (*Ocimum sanctum*)

Tulsi is also known as the "Queen of Herbs" in Ayurveda, is a powerful adaptogen with numerous therapeutic benefits. This aromatic plant belongs to the Lamiaceae family and contains bioactive phytochemicals like eugenol, ursolic acid, rosmarinic acid, carvacrol, linalool, and apigenin. These phytochemicals contribute to its adaptogenic, immunomodulating, anti-inflammatory, antioxidant, antimicrobial, cardioprotective, antidiabetic, neuroprotective, and radioprotective properties. Tusi's antiviral activity against respiratory pathogens like influenza and SARS-CoV-2 has gained attention during recent pandemics. It also has immunomodulating properties, making it beneficial for autoimmune condition treatment and resistance against infectious diseases (Dori *et al.,* 2020). Tusi modulates the hypothalamic-pituitary-adrenal axis, lowers cortisol levels, and increases stress resilience by controlling neurotransmitters. Its antioxidant capacity protects against oxidative stress-induced damage in cardiovascular, neurodegenerative, and metabolic diseases. Its cardioprotective capabilities include lipid-lowering effects, anti-hypertensive action, and antiplatelet activity. It also has anti-ulcer, hepatoprotective, and carminative properties in gastrointestinal health.

4.5. Guduchi (*Tinospora cordifolia*)

Guduchi is also known as "Amrita" in Ayurveda, is a versatile plant with significant potential in modern biomedical research. Its rich array of bioactive compounds, including berberine, tinosporaside, cordioside, tinosporaside, and arabinogalactan polysaccharides, confer immunomodulating, anti-inflammatory, hepatoprotective, antidiabetic, antioxidant, anti-arthritic, neuroprotective, and adaptogenic properties, making it a prime candidate for integrated medicine approaches. Guduchi's selective immunosuppression shows anti-autoimmune effects, making it valuable in conditions like frequent infections, rheumatoid arthritis, and multiple sclerosis (Ifeoma and Oluwakanyinsola, 2013). It enhances both innate and adaptive immunity by stimulating macrophage activity, increasing immunoglobulin levels, and promoting lymphocyte proliferation. Its hepatoprotective potential is remarkable, showing efficacy against alcohol-induced liver damage, drug-induced hepatotoxicity, and non-alcoholic fatty liver disease. Guduchi's antidiabetic properties have shown comparable efficacy to metformin in clinical trials for type 2 diabetes management. Its neuroprotective effects show promise in Alzheimer's disease, Parkinson's disease, and cognitive improvement. Its chemopreventive and adjuvant therapeutic potential in oncology involves inducing death in cancer cells, inhibiting angiogenesis, and protecting normal cells from radiation and chemotherapy-induced damage. Modern drug development is investigating Guduchi's potential in targeted therapies, with the immunomodulating polysaccharides and alkaloids for autoimmune diseases and cancer immunotherapy.

4.6. Brahmi (*Bacopa monnieri*)

Brahmi is a plant native to India and tropical areas, has been scientifically validated as a powerful neuroprotective and cognitive-enhancing agent. Its unique combination of bioactive compounds, including bacosides A and B, bacosaponins, alkaloids like brahmine, and antioxidants like apigenin and luteolin, confers nootropic, neuroprotective, anxiolytic, antidepressant, antioxidant, anti-inflammatory, adaptogenic, and even hepatoprotective properties. Brahmi's cognitive enhancement and neuroprotection have shown unparalleled efficacy in improving memory formation, learning capacity, and information retention, making it valuable for age-related cognitive decline, Alzheimer's disease, and other neurodegenerative disorders. Its anxiolytic and antidepressant effects, mediated through GABAergic modulation, serotonin and dopamine control, and cortisol reduction, provides a natural alternative to synthetic psychotropics for managing generalized anxiety disorder, depression, and stress-related cognitive impairment. Brahmi's strong antioxidant capacity extends its therapeutic potential to ischemic stroke prevention, Parkinson's disease management, and radiation-induced oxidative damage mitigating

(Hankey, 2001). The bioavailability, and clarifying dose-response relationships have pharmaceutical approaches such as mucoadhesive delivery systems, phospholipid complexes, and nanoemulsions. Brahmi is leading Ayurvedic phytomedicines transitioning to mainstream medicine, offering solutions to modern challenges including neurodegenerative epidemics, stress-related cognitive disorders, and the limits of single-target synthetic drugs.

4.7. Amla (*Phyllanthus emblica*)

Amla is a medicinal plant in Ayurveda as the ultimate Rasayana (rejuvenator), is a highly scientifically validated plant with therapeutic potential in preventive, curative, and regenerative medicine. Its antioxidant capacity, including gallic acid, ellagic acid, quercetin, kaempferol, phyllanthin, hydroxy tannins Emblican A and B, and gallic acid, offers protection against oxidative stress-related disorders, including neurodegenerative diseases and cancer prevention. Amla's detoxification enzyme modulation, reduction of inflammatory cytokines, and inhibition of hepatic stellate cell activation provide protection against alcohol-induced liver damage, drug hepatotoxicity, non-alcoholic fatty liver disease (NAFLD), and hepatic fibrosis. Its immunomodulating potential makes it valuable for immune enhancement in immunodeficiency and immunobalancing in autoimmune conditions. Amla's cardiovascular benefits include lipid-lowering effects, antihypertensive action, anti-atherosclerotic activity, and antiplatelet aggregation properties (Ekor, 2014). It also shows hypoglycemic effects in diabetes management through insulin secretion stimulation, α-amylase and α-glucosidase inhibition, enhanced glucose absorption, and protection of pancreatic β-cells. Amla's neuroprotective effects show promise in Alzheimer's disease, Parkinson's disease, and ischemic stroke recovery. Modern drug development is derived at Amla-derived lead compounds for synthetic analogues its ancient reputations.

5. Phytochemistry of Ayurvedic Herbs

Ayurvedic medicinal plants are rich in chemical diversity, have been used for centuries for traditional therapeutics and modern drug development. These botanicals contain a variety of secondary metabolites, including alkaloids, flavonoids, terpenoids, phenolic acids, glycosides, saponins, tannins, and polysaccharides that interact synergistically to produce holistic therapeutic effects. Terpenoids from herbs like Ashwagandha and Tulsi show remarkable anti-inflammatory, adaptogenic, and anticancer properties by modulating NF-κB, COX-2, and apoptotic pathways. Phenolic acids from Triphala constituents show antimicrobial, antidiabetic, and chemopreventive actions (Islam *et al.,* 2021). Flavonoids from Bhringraj and Amla exhibit strong antioxidant, cardioprotective, and neuroprotective effects via free

radical scavenging, metal chelation, and upregulation of endogenous antioxidant systems. Saponins from Brahmi and Yashtimadhu target neurological and metabolic disorders through interactions with neurotransmitter systems and insulin signaling pathways. Polysaccharides from Kutki and Shatavari show immunostimulative and gut microbiome-modulating effects.

Modern analytical techniques have identified over 10,000 bioactive compounds from over 300 Ayurvedic plants, with the spatial and temporal variability of these phytochemicals providing both challenges and opportunities for standardization. Ayurvedic herbs offer an unparalleled chemical variety that is now being methodically explored using phytochemomics approaches, combining metabolomics with bioinformatics, to decode the molecular basis of traditional formulations and accelerate targeted discovery of multi-mechanistic therapeutics for complex diseases (Ekor, 2014).

6. Bioactive Compounds and their Chemical Properties

Ayurvedic herbs contain a variety of bioactive compounds with unique chemical properties, including alkaloids, terpenoids, phenolic compounds, and specialized metabolites. Alkaloids, such as piperine and reserpine, have analgesic, antihypertensive, and psychoactive effects due to their interactions with neuronal receptors and ion channels. Terpenoids, the largest class, show lipophilicity and membrane permeability, allowing them to modify intracellular signaling pathways, leading to anti-inflammatory, adaptogenic, and anticancer properties. Phenolic compounds, like flavonoids, tannins, and lignans, have redox-modulating capacity, making them potent antioxidants, metal chelators, and enzyme inhibitors (Katoch *et al.,* 2017). Specialized metabolites, like curcuminoids and iridoids, have unique electrophilic reactivity with thiol groups, enabling them to activate detoxifying enzymes and modulate redox-sensitive transcription factors. Modern medication research uses these natural features to generate semi-synthetic analogues, such as tetrahydrocurcumin and withaferin. Ayurvedic alkaloid-rich plants, like *Rauvolfia serpentina, Catharanthus roseus*, and *Argemone mexicana*, have been used for millennia and have been validated by modern science. Modern analytical methods, such as LC-MS/MS and NMR fingerprinting, provide exact characterization of alkaloid profiles in polyherbal compositions. The exact molecular architecture of Ayurvedic phytochemicals presents unmatched opportunities for multi-target drug development, especially for complex chronic diseases where polypharmacology is advantageous.

6.1. Alkaloids

Alkaloids, nitrogen-containing compounds in Ayurvedic medicinal plants, are crucial for drug development due to their diverse pharmacological activities. These secondary metabolites, ranging from simple pyrrolidines to complex polycyclic complexes, directly affect their bioavailability, target selectivity, and mode of action. Ayurveda's alkaloid-rich plants, such as *Rauvolfia serpentina, Catharanthus roseus*, and *Argemone mexicana*, have been used for millennia and have been validated by modern science. Their potency is attributed to their interactions with biological membranes and receptors. Chemical alterations of natural alkaloids have led to semi-synthetic derivatives with improved characteristics. However, challenges in alkaloid-based drug development include potential toxicity, poor water solubility, and complicated stereochemistry (Kunle *et al.,* 2012). Modern analytical methods like LC-MS/MS and NMR fingerprinting provide precise characterization of alkaloid profiles in polyherbal compositions. The integration of Ayurvedic knowledge about alkaloid-containing plants with modern pharmacology continues to reveal new therapeutic applications, demonstrating how these ancient molecular treasures can address modern medical challenges through targeted drug design and synergistic formulation approaches.

6.2. Flavonoids

Flavonoids are polyphenolic secondary metabolites found in Ayurvedic medicinal plants, with their structural diversity highlighting their biological activities and therapeutic potential. These compounds, classified into subgroups like flavones, flavonols, and flavanones, have been validated for their antioxidant, anti-inflammatory, and immunomodulating properties through molecular studies. Traditional plants like *Ocimum sanctum, Glycyrrhiza glabra*, and *Cyperus rotundus* have been used for their antioxidant, anti-inflammatory, and therapeutic efficacy. Modern drug development has utilized these features to create standardized extracts and synthetic analogues, such as silymarin for hepatoprotection and flavopiridol for cyclin-dependent kinase inhibitors (Jordan *et al.,* 2010). Flavonoids faces challenges such as metabolic instability, complicated pharmacokinetics, and herb-drug interactions. Advanced analytical methods like UPLC-QTOF-MS and NMR metabolomics allow for the analysis of flavonoid profiles in conventional Ayurvedic formulations. Ayurveda combined with contemporary pharmacology for the applications of flavonoids, demonstrating these ancient phytochemicals can be optimized through modern drug development paradigms to health challenges holistic therapeutics.

6.3. Tannins

Tannins are water-soluble polyphenolic compounds with molecular weights ranging from 500 to 3000 Daltons, are essential in Ayurvedic medicinal plants for wound healing, anti-inflammatory, and antimicrobial purposes. These complex phytochemicals, including hydrolyzable tannins, condensed tannins, and phlorotannins, have unique structural features that provide astringency and protein-binding capacity. They have been used in Ayurvedic formulations like Triphala and Khadirarishta for their therapeutic effects on gastrointestinal diseases, skin conditions, and metabolic imbalances (Muyumba *et al.,* 2021). Modern scientific studies have clarified the molecular pathways by tannins exert their biological actions, including free radical scavenging, enzyme inhibition, and modulation of cellular signaling cascades. Modern medication research has utilized these features through structural alteration, enhanced extraction methods, and nanoformulation strategies. Tannin challenges such as hepatotoxicity at high dosages, varying composition depending on plant source and processing techniques, and form insoluble complexes with proteins and minerals.

6.4. Terpenoids

Terpenoids are derived from isoprene, are a significant class of natural products in Ayurvedic medicinal plants. These secondary metabolites, categorized according to carbon skeleton, have wide-ranging biological activities and therapeutic applications in Ayurveda. Traditional Ayurvedic formulations heavily rely on terpenoid-rich plants like *Boswellia serrata, Withania somnifera, Curcuma longa*, and *Commiphora wightii*. Modern pharmacological research has validated these traditional uses by understanding their molecular mechanisms and modulating key cellular targets. Terpenoids' unique chemical characteristics, such as their lipophilic character, stereochemical complexity, and functional group diversity, control their biological activities (Mardani *et al.,* 2013). Modern drug research has utilized these features through semi-synthetic changes, nanoformulations, and structure-activity. Terpenoid faces challenges such as complicated biosynthetic routes, limited natural abundance of certain bioactive analogues, and metabolic instability. Advanced analytical techniques, such as GC-MS, LC-MS/MS, and NMR-based metabolomics, enable thorough characterization of terpenoid profiles in classical Ayurvedic preparations. The integration of Ayurvedic knowledge with modern science continues to reveal new therapeutic uses for terpenoids, making them building next-generation Ayurvedic-inspired therapies.

6.5. Glycosides

Glycosides is a class of secondary metabolites in Ayurvedic medicinal plants, are crucial bioactive compounds that act as intermediates between traditional herbal formulations and modern pharmaceutical uses. These naturally occurring conjugates, such as cardenerolides, bufadienolides, anthraquinone glycosides, flavonoid glycosides, saponins, and cyanogenic glycosides, have a unique chemical architecture that affects their bioavailability, pharmacological activity, and therapeutic potential. Modern pharmacological research has validated their mechanisms of action, including Na+/K+-ATPase inhibition by cardiac glycosides, NF-κB pathway modulation by glycyrrhizin, and acetylcholine esterase inhibition by bacosides. The unique chemical architecture of glycosides, particularly the nature of the sugar and their biological activities. Modern medication research has leveraged these features through enzyme changes, semi-synthetic techniques, and nanocarrier systems. However, glycoside research presents challenges such as sensitivity to enzymatic hydrolysis in the gastrointestinal system, difficult purification techniques, and potential toxicity at therapeutic levels (Kumar *et al.,* 2016). The integration of Ayurveda with modern science continues to reveal fresh therapeutic applications for glycosides, particularly for cardiovascular, neurological, and metabolic diseases. The mix of targeted biological activity and improved bioavailability by their dual glycone-aglycone glycosides as promising candidates for evidence-based Ayurvedic-inspired drug development.

6.6. Polyphenols

Polyphenols is a class of phytochemicals found in Ayurvedic medicinal plants, are bioactive compounds with antioxidant, anti-inflammatory, and multi-target therapeutic properties. Their complex structural structure affects their bioavailability, biological activity, and therapeutic efficacy. Modern science has validated their molecular mechanisms, which involve modulating the Nrf2/ARE pathway, inhibiting NF-κB signaling, and controlling cellular redox homeostasis. Polyphenols are extensively used in Ayurvedic formulations for their rasayana, anti-inflammatory, and neuroprotective effects (Parasuraman *et al.,* 2010). Modern drug development has utilized these properties through nanotechnology-based delivery systems, structural modifications, and synergistic combinations with other bioactive compounds. The polyphenol faces challenges such as fast metabolism, excretion, interactions with traditional medications, and complicated structure-activity correlations. Advanced in silico approaches and analytical platforms help interpret polyphenolic actions. The integration of Ayurvedic knowledge with contemporary science continues to reveal new therapeutic applications for polyphenols while preserving their holistic therapeutics.

7. Biomedical Applications of Ayurvedic Phytomedicines

Ayurvedic phytomedicines, containing bioactive compounds such as alkaloids, flavonoids, tannins, terpenoids, glycosides, and polyphenols, are being studied for their pharmacological efficacy. Alkaloids, such as those found in *Rauwolfia serpentina* and *Catharanthus roseus*, have neuroactive, antibacterial, and anticancer effects, which align with Ayurveda's use of these herbs for mental health and chronic disorders. Flavonoids, found in turmeric and holy basil, show cardioprotective, anti-inflammatory, and antioxidant properties, supporting their traditional function in boosting immunity and lifespan. Tannins, found in *Terminalia chebula* and *Emblica officinalis*, help with wound healing, antibacterial action, and gastrointestinal health. Terpenoids, including curcuminoids and boswellic acids, are studied for their anti-inflammatory, anticancer, and neuroprotective properties. Glycosides, found in Aloe vera and Digitalis purpurea, demonstrate the role of sugar moieties in improving bioavailability and targeted therapy (Peltzer and Pengpid, 2019). Polyphenols found in green tea and amla provide multitarget advantages against oxidative stress, diabetes, and aging. Modern medication development issues such as standardizing and scalability using new technologies.

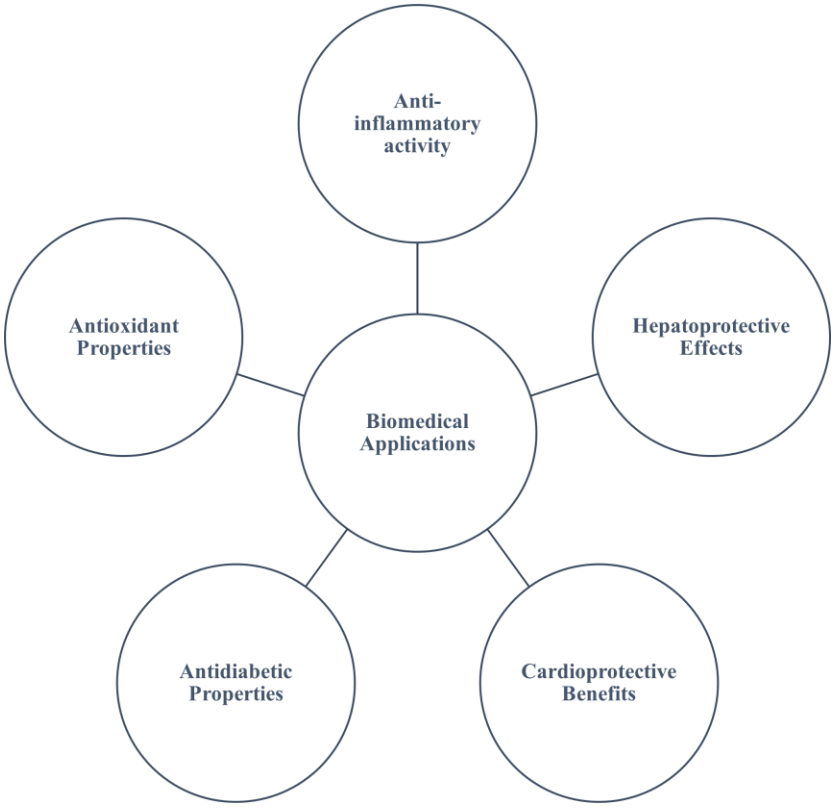

Figure – 2: Biomedical Applications of Ayurvedic Phytomedicines

7.1. Anti-inflammatory activity

Ayurvedic phytomedicines, such as curcuminoids, boswellic acids, withanolides, and gingerols, have been used as a substitute for standard anti-inflammatory medications due to their ability to modulate complex inflammatory pathways. The efficacy of these phytochemicals through molecular characterization, with boswellic acids from Boswellia inhibiting 5-LOX without affecting COX-1, while curcumin shows strong NF-κB suppression and downregulation of interleukin-6 and IL-1β. Ayurveda's approach is particularly evident in polyherbal formulations like Triphala and Dashmoola, where synergistic interactions between bioactive compounds produce enhanced anti-inflammatory effects (Patwardhan *et al.,* 2005). Modern drug development has addressed bioavailability issues of these phytochemicals through creative delivery systems, such as boswellic acid-phospholipid complexes for osteoarthritis management and nanocurcumin formulations for 20-40 times greater absorption than conventional curcumin. Advanced research techniques like transcriptomics, proteomics, and artificial intelligence-based predictive modeling are clarifying the systems-level effects of these botanicals and their capacity to target nodes in inflammatory networks.

7.2. Antioxidant Properties

Ayurvedic phytomedicines are rich in natural antioxidants that offer defense mechanisms against oxidative stress, a pathogen of chronic illnesses like neurotoxicity, cardiovascular diseases, diabetes, and aging. Modern research has identified bioactive compounds like emblicanin A and B, orientin, bacosides, and curcuma longa, which exhibit diverse redox-modulating capacity. Traditional formulations like Chyawanprash, Triphala, and *Brahmi Ghrita* use *Emblica officinalis* (Amla), *Ocimum sanctum* (Tulsi), *Bacopa monneri* (Brahmi), *and Curcuma longa* (Turmeric). These compounds operate through direct free radical scavenging, metal chelation, upregulation of endogenous antioxidant systems, and inhibition of pro-oxidant enzymes (Nooreen *et al.,* 2018). The chemical architectures of these compounds control their antioxidant efficacy, with ortho-dihydroxy phenolic groups in flavonoids enabling exceptional radical neutralization, curcumin enabling electron delocalization, and hydrolyzable tannins in Amla showing remarkable antioxidant capacity. Advanced delivery systems have enhanced the bioavailability and tissue targeting of these compounds. This also explores the mitochondrial-targeted antioxidant effects, epigenetic modulating capabilities, and potential in combating inflammation through simultaneous oxidative stress and inflammation control.

7.3. Hepatoprotective Effects

Ayurvedic phytomedicines, such as phyllanthin, andrographolide, kutkin, and berberine, have been found to have significant hepatoprotective properties. These compounds, traditionally used in formulations like Arogyavardhini Vati, Punarnavadi Mandur, and Kumaryasava with various hepatotoxic insults and protect against alcohol-induced liver damage. They also have antioxidant activity, enhance detoxification pathways, anti-inflammatory action, liver regeneration stimulation, and immunomodulation. Modern research has focused on silymarin, which increases hepatocyte protein synthesis by stimulating RNA polymerase I activity. Standardized Phyllanthus extracts achieve 50-60% hepatitis B surface antigen clearance rates, while andrographolide formulations dramatically lower serum transaminases in patients with alcoholic liver disease (Mirzaeian *et al.,* 2019). Silymarin shows equivalent efficacy to ursodeoxycholic acid in non-alcoholic fatty liver disease while exhibiting better safety profiles. Polyherbal formulations containing Picrorhiza, *Terminalia chebula*, and *Emblica officinalis* show 30 – 40 % greater hepatoprotective activity than their individual components. Combining Ayurvedic hepatoprotective techniques with modern medicine is producing creative ideas, such as developing hepatoprotective nutraceuticals for metabolic syndrome patients, adjunctive use with chemotherapy to minimize drug-induced hepatotoxicity, and combination therapies with conventional antivirals for hepatitis.

7.4. Antidiabetic Properties

Ayurvedic phytomedicines are derived from the ancient Indian system of medicine, have been found to have antidiabetic properties that could help the global diabetes crisis. These plants, including *Momordica charantia, Gymnema sylvestre, Tinospora cordifolia, Azadirachta indica*, and *Curcuma longa*, have been traditionally used to manage diabetes by improving insulin sensitivity, stimulating pancreatic β-cell function, inhibiting glucose absorption, and reducing oxidative stress. Modern scientific studies have confirmed these claims, revealing bioactive compounds that modulate metabolic pathways such as AMPK, PPARs, and NF-κB. These phytoconstituents control blood glucose levels and reduce diabetes-related complications like neuropathy, nephropathy, and cardiovascular diseases. Ayurvedic phytomedicines are being integrated into contemporary drug development using advanced technologies like metabolomics, network pharmacology, and high-throughput screening. Nanoformulations and phytosome-based delivery methods are being investigated to overcome constraints like low solubility and fast metabolism (Prakash *et al.,* 2017). Ayurveda's approach emphasizes individualized therapy based on individual Prakriti and Dosha balance that aligns with modern precision medicine techniques and provides a foundation for the antidiabetic treatments. This

convergence between traditional modern science could lead to the development of medication to metabolic health.

7.5. Cardioprotective Benefits

Ayurvedic phytomedicines, such as *Withania somnifera*, Allium sativum, Guggulu, and Bacopa monnieri, have been traditionally used to strengthen cardiac function, improve circulation, lower lipid accumulation, and prevent oxidative stress-induced damage to the cardiovascular system. Modern pharmacological research has found bioactive compounds such as flavonoids, saponins, alkaloids, and polyphenols that modulate key pathways, such as nitric oxide synthesis, lipid metabolism, Angiotensin-converting enzyme (ACE) inhibition, and anti-inflammatory signaling. These phytomedicines have shown potential in integrating into current cardiovascular treatments, but issues with standardizing, bioavailability, and clinical validation must be resolved. Novel drug delivery technologies, such as nanoformulations and liposomal encapsulation, are under investigation to improve bioavailability and targeted distribution. The development of new, affordable, sustainable cardioprotective treatments depends on cooperative research integrating conventional medications with biomedical science (Riaz *et al.,* 2023). This synergy supports Ayurveda for the identification of multi-target therapeutic candidates to solve the biomedical research of Ayurvedic phytomedicines marks a paradigm change from traditional single-target therapies as cardiovascular disorders worldwide. The Ayurvedic holistic beliefs with modern scientific developments, thus supporting the importance of traditional medicine in healthcare systems.

8. Quality Control of Herbal Medicines

Ayurvedic herbal treatments are standardized through quality control, ensuring safety, effectiveness, and repeatability while maintaining their holistic therapeutic values. Modern techniques like DNA barcoding, HPTLC, and macroscopic examination are used to verify raw materials and identify key bioactive markers (Isola, 2013). The heavy metal contamination, pesticide residues, and microbiological load are tracked using atomic absorption spectroscopy and microbial limit testing. *In vitro* and *in vivo* bioassays confirm pharmacological activity, while stability tests evaluate shelf-life under different conditions. Modern quality control also combines metabolomics and chemometrics to interpret the synergistic interactions in polyherbal formulations like Triphala and Chyawanprash (Brantley *et al.,* 2014). Artificial intelligence models and nanotechnology improve bioavailability monitoring for the regulatory harmonization among pharmacology that remains as a challenge to Ayurvedic medicines transition from empirical use to evidence-based therapeutics by quality control measures, allowing their integration into modern pharmacopeias and

fostering innovation in drug discovery. This preserves the integrity of traditional medicine systems that promoting the integration of Ayurvedic medicines into modern medicine (Boullata and Nace, 2000).

9. Formulations of Herbal Medicines

Ayurvedic herbal treatments combine ancient medicines with modern pharmaceutical research, utilizing various delivery methods to enhance therapeutic efficacy while maintaining the holistic principles of Ayurveda. These methods include fermentation processes in arishtas, specialized calcination in bhasma preparations, and careful preparation of powders, ghritas, avalehas, and bhasmas (Tnah *et al.,* 2019). Modern drug development has adapted these traditional systems into standardized extracts, nanoformulations, phytosomes, liposomes, and microencapsulated delivery systems to address challenges of solubility, stability, and targeted release. Ayurveda's emphasis on synergy, where several herbs to maximize therapeutic applications by polyherbal formulations like Triphala and Yashtimadhu (Aware *et al.,* 2022). Quality control is essential in formulation development, and advanced techniques like CRISpen and metabolomics are being used to maximize herb production for consistent phytochemical profiles. Regulatory challenges remain in harmonizing Ayurvedic formulations with global standards, and rigid pharmacokinetic studies, stability testing, and clinical trials are necessary to validate safety and efficacy. Ayurvedic formulations are poised to transform integrative medicine by traditional methods with cutting-edge technology, providing sustainable, holistic approaches to global health concerns, and paradigms for natural product medication development (Das *et al.,* 2019).

10. Integration of Ayurveda into Modern Biomedical Formulations

Ayurvedic phytomedicines are being integrated into modern biomedical formulations, combining ancient therapeutic wisdom with modern pharmaceutical innovation. Modern analytical techniques, such as metabolomics, transcriptomics, and network pharmacology, are used to decode the complex polypharmacological actions of traditional formulations like Triphala, Ashwagandha, and Brahmi, used to manage chronic diseases like diabetes, neurodegenerative disorders, and inflammation (Tulunay *et al.,* 2015). Ayurvedic compounds are standardized using advanced extraction and purification technologies, enhancing their bioavailability and therapeutic repeatability while maintaining their natural synergy. Modern drug delivery systems, such as nanoparticles, liposomes, phytosomes, and nanoemulsions, address pharmacokinetic restrictions of conventional preparations. Evidence-based standardized extracts bridge the gap between Ayurvedic empiricism and modern clinical practice. Regulatory harmonization efforts ensure quality control from farm to formulation, while Pharmogenomics and AI-driven predictive modeling investigate

Prakriti-based personalized medicine (Wen *et al.,* 2005). Collaborative research projects like the Council of Scientific and Industrial Research's New Millennium Indian Technology Leadership Initiative (NMITLI) program demonstrate the innovative drug discovery.

11. Challenges and Limitations

Ayurvedic phytomedicines presents significant challenges in drug development. Traditional formulations, often consisting of multiple herbs, are complex and difficult to isolate individual bioactive compounds.

Table – 1: Challenges and Limitations of Ayurvedic Phytomedicines

Category	Challenges and Limitations	References
Standardization and Quality Control	Lack of raw material collection, processing, and storage leading to variability in efficacy.	Hankey (2001)
Formulations	Ayurvedic medicines often contain multiple herbs, making it difficult to isolate active compounds and to evaluate the synergistic effects.	Aware *et al.,* (2022)
Pharmacological analysis	The mechanisms of action, bioavailability, and pharmacokinetics of Ayurvedic compounds.	Dori *et al.* (2020)
Regulatory approvals	Differences in traditional medicine systems and modern drug approval processes (e.g., FDA, EMA).	Fu *et al.* (2018)
Toxicity and Safety Concerns	Insufficient for long-term toxicity, herb-drug interactions, and indicators in modern clinical applications.	Fernández-Ochoa *et al.* (2021)
Dose Optimization	Traditional dosage forms (e.g., churna, asava) may not align with modern precision medicine requirements.	George (2011)
Intellectual Property Issues	Difficulty in natural compounds that leads to limited commercial products from pharmaceutical companies.	Jitareanu *et al.* (2022)
Clinical Designs	Challenges in designing the holistic and individualized nature of Ayurveda.	Ifeoma and Oluwakanyinsola (2013)
Sustainability	Harvesting of medicinal plants, lack of sustainable cultivation practices, and adulteration risks.	Fernández-Ochoa *et al.* (2021)
Bioavailability Issues	Poor solubility and absorption of plant-derived compounds, requiring advanced drug delivery systems.	Islam *et al.* (2021)

Traditional herbs lack thorough phytochemical characterization, leading to variability in raw material quality and poor bioavailability of important molecules (Singh *et al.,* 2022). Regulatory hurdles, such as the absence of globally harmonised standards, complicate approval in Western markets. Clinical validation is hindered by the lack of large-scale, well-designed RCTs that meet contemporary evidence-based medicine standards. The one-size-fits-all approach of traditional drug research conflicts with holistic Ayurvedic concepts, posing methodological difficulties in customized trials. The technological gaps and intellectual property issues like biopiracy and patentability complicate commercialization. Cultural and educational obstacles include training in integrative research techniques and a lack of multidisciplinary approaches between the Ayurvedic practitioners and scientists. Environmental sustainability issues like overharvesting of medicinal plants threatens the supply chain stability and biodiversity (Srivastava *et al.,* 2013). These challenges are required in omics technologies, for regulatory cooperation, and developing strong quality control protocols.

12. Future Perspectives

Ayurvedic phytomedicines are used to revolutionize biomedical research and medication development by their modern scientific discoveries with ancient medicines (Rinschen *et al.,* 2019). Major advances in omics technologies, such as genomics, proteomics, and metabolomics, will enable the decoding of Ayurveda's polyherbal synergies, validating traditional concepts like Yukti and Prakriti. Artificial intelligence and machine learning will revolutionize drug discovery from Ayurvedic herbs, while 3D bioprinting and nanotechnology will address bioavailability challenges. The combination of the Ayurvedha with the gut microbiome research will reveal pathways for prebiotic benefits in classic formulations for microbiome-targeted treatments in the metabolic diseases (Zhao *et al.,* 2013). Blockchain technology will ensure quality consistency and worldwide herbal supply chain. The connection between Ayurveda's holistic paradigms and evidence-based medicine requirements are used in the ethnopharmacology and digital twinning of classical formulations will conserve traditional medicines that allows for the high-throughput screening of medicines. Ayurvedic nutraceuticals are used by the IoT sensors will be commercialized, offering sustainable solutions for chronic diseases, antimicrobial resistance, and healthy aging (Roy *et al.,* 2022).

13. Conclusion

Ayurvedic phytomedicines are the connection between ancient knowledge and modern biomedical science, providing a holistic philosophy of health with current trends in personalized and preventive medicine. The history of over 5000 years, Ayurveda offers a treasure trove of plant-based medicines by current research for their anti-inflammatory, antioxidant, hepatoprotective, antidiabetic, and cardioprotective effects. The incorporation of sophisticated analytical methods HPLC, MS, NMR, and metabolomics has facilitated the purification and characterization of bioactive molecules such as curcumin, withanolides, and boswellic acids and has their modes of action at the molecular level. The standardization, bioavailability, regulatory harmonization, and clinical demonstration of nanotechnology, omics technologies, and computer-aided drug discovery are overcoming these limitations, and the efficacy and worldwide of Ayurvedic products are increased. Multidisciplinary convergence of traditional knowledge with advanced science is the future for Ayurvedic phytomedicines in sustainable, evidence-based therapies for lifestyle and chronic diseases. The quality control, intellectual property, and clinical trial design, Ayurveda can shift from an alternative to a contemporary pharmacotherapeutics. The integration of Ayurveda with biomedical innovations has the potential for drug development, providing safer, multi-targeted, and major responses to global health issues.

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ISBN: 978-81-977907-4-4