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(Review Article)

A review of medicinal plants: Phytochemicals, molecular docking, and bioactive properties

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Abstract

The wide variety of bioactive substances found in medicinal plants has made them quite popular as of late. Several aspects of therapeutic plants are examined in this article. The basic concepts of phytochemicals are introduced, including where they come from, the roles they play in the body, and the latest methods for extracting them for use in nutraceuticals and functional foods. According to research shows that compared to conventional drugs, Apigenin and Alpha-Bisabolol exhibit far higher glide energy and docking scores. Cyperus scariosus and Parthenium hysterophorus are two examples of underappreciated plants whose nutritional and therapeutic potential, bioactive characteristics, and enzyme inhibitory powers are discussed. Molecular docking experiments are being conducted to see whether phytoconstituents can prevent diseases such as monkeypox, cardiovascular disease, epilepsy, and conjunctivitis; researchers are also investigating traditional therapies for COVID-19 and conjunctivitis. Adverse outcome pathways (AOP) and high-throughput techniques are two examples of modern methodological tools that have enhanced toxicological studies. The varied chemical compositions of primary and secondary metabolites have been the subject of qualitative and biochemical investigations that detail screening procedures. The paper concludes by discussing the bioactive features and their therapeutic uses, which include antimicrobial, cytotoxic, anti-inflammatory, and antiviral actions.

Keywords: Bioactive; Disease and disorders; Extraction; Molecular docking; Phytochemicals

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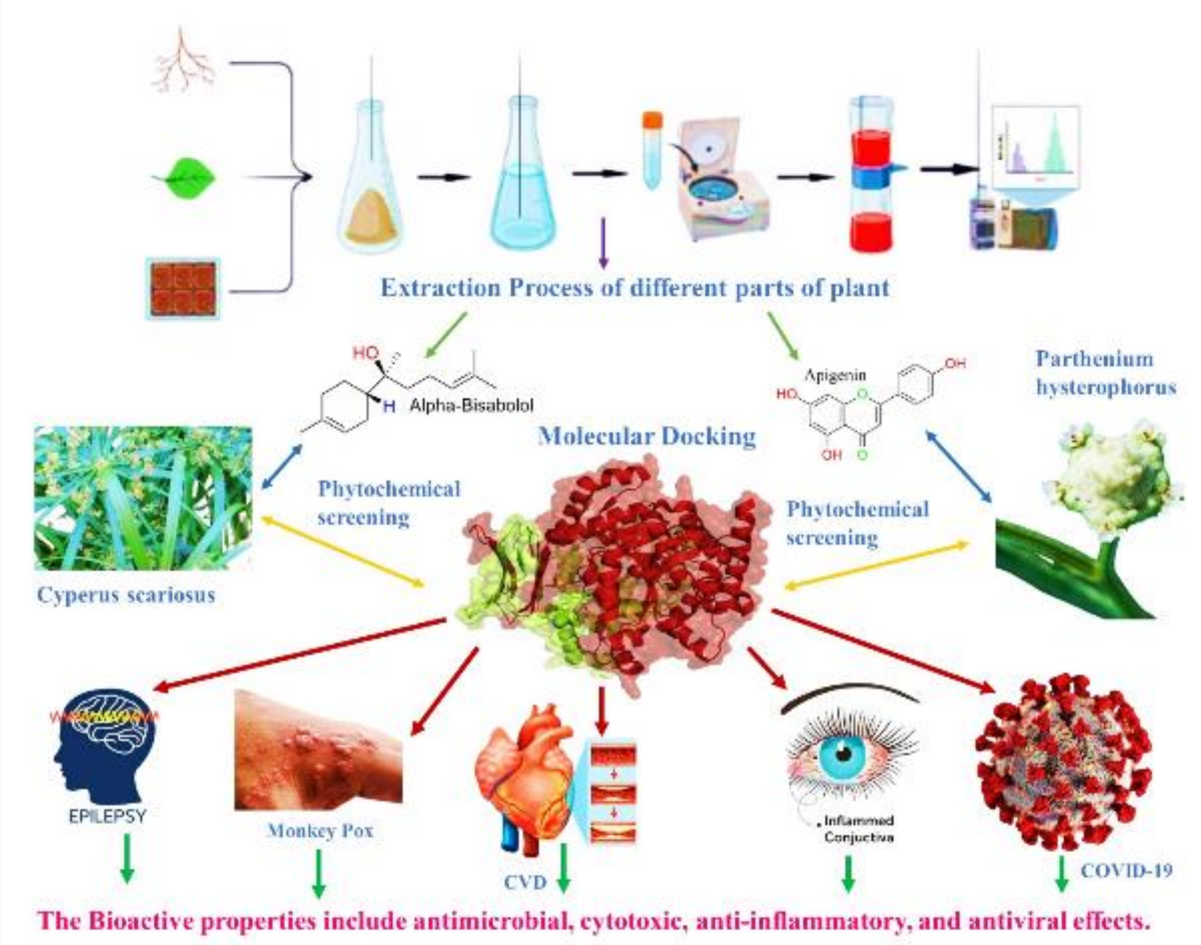
Graphical abstract



1. Introduction

1.1. Bioactive Substances and Medicinal Plants' Therapeutic Uses

The utilization of medicinal plants in medical research has a long-standing tradition in human civilization. The potential of these plants in modern medicine is immense, and their systematic investigation has become more advanced with the growth of science. An increasing number of individuals are becoming aware of the presence of bioactive compounds in medicinal plants, which have the potential to exert significant pharmacological effects. We all recognize the importance of plants. In recent years, there has been a growing recognition of the significance of plants as a viable source of alternative medicine. Numerous plant species possess the potential to be utilized as medicinal remedies. Generally, individuals have less difficulty in tolerating, and the pharmaceuticals derived from botanical sources are readily obtainable, inexpensive, secure, and efficacious. Of the numerous plants that have been utilized for therapeutic purposes for millennia, the ones that show the greatest potential as novel pharmaceuticals are those possessing antibacterial capabilities, anticancer agents, and antihepatotoxic compounds. According to the World Health Organisation, medicinal plants are regarded as the most efficacious source for a range of treatments. Approximately 80% of the population in developed countries is believed to utilize traditional medicine, often employing plant-derived substances for medicinal reasons. Further research is necessary to address the gaps in our understanding of the safety, effectiveness, and other important variables related to these plants [3]. Medicinal plants include a diverse range of bioactive compounds such as tannins, alkaloids, polysaccharides, terpenoids, steroids, and flavonoids. These chemicals have an impact on human physiology [4,5]. These compounds are synthesized by the metabolic processes of organisms, either as part of their primary or secondary metabolism. The function of secondary metabolites, despite their diverse chemical and taxonomic characteristics, remains unknown. These communities, including the medical, agricultural, veterinary, and scientific fields, extensively utilize them, among various others [6]. Based on in vitro studies, a wide range of phytochemicals have been found to suppress the growth of all types of bacteria [7]. Since ancient times, plant components have been utilized in phytomedicines. For instance, these characteristics can be observed in the roots, fruits, seeds, flowers, bark, or leaves [8]. Having knowledge of the chemical composition of plants is beneficial when attempting to synthesize intricate novel compounds [9,10,11]. Expanding research into medicinal plants is crucial for the development of new therapeutic prospects. This assessment will not only validate established usage but also explore novel applications, all with the objective of enhancing our understanding of the safety and efficacy of plant-derived compounds. By adopting this approach, we may effectively harness these natural resources to develop durable and effective healthcare solutions.

1.2. Advanced Extraction Methods, Phytochemical Sources, and Bioactivities for the Development of Functional Foods and Nutraceuticals

In recent years, there has been a significant increase in interest in studying the potential health benefits and applications of phytochemicals in functional foods and nutraceuticals. Gaining a deeper comprehension of the diverse functions and extraction methods of these compounds is essential for advancing our scientific knowledge and facilitating their practical applications in nutrition and health. Plants generate phytochemicals as a defensive measure. Various types of foods, including whole grains, fruits, vegetables, nuts, and herbs, are recognized to contain over a thousand distinct phytochemicals. Some notable phytochemicals include carotenoids, phytosterols, dietary fibers, polyphenols, isoprenoids, and saponins. The phytochemicals possess antioxidant capabilities, as well as antiviral, antiallergic, antispasmodic, antihelmintic, antibacterial, and antidiarrheal effects [12, 13]. They contribute to the regulation of gene transcription, enhance intercellular communication through gap junctions, boost immunity, and provide protection against lung and prostate cancers [14–18]. As translational research gains greater attention, functional meals have gotten increasingly intricate. Phytochemicals obtained from different plants are extensively utilized in the manufacturing of nutraceuticals and functional meals. Phytochemicals can exhibit varying affinities for solvents and resistances to temperature conditions. The selected solvent significantly impacts both the purity of the extracted phytochemical and its suitability for use in the manufacturing of food and nutraceutical products. Hydrogen, ethanol, glycerol, fatty acids/oils, acetic acid, ionic liquids, CO2, deep eutectic solvents, natural deep eutectic solvents (NADES), and various other chemicals are classified as green solvents. Additional instances of solvents are benzene, ethyl acetate, methyl acetate, chloroform, butanol, methanol, hexane, and cyclohexane [19]. Handling a material with incompatible solvents or subjecting it to excessive temperatures can potentially compromise its useful properties. The phytochemical's matrix is an essential factor that significantly impacts the efficacy of the extraction process. The performance of phytochemical extraction techniques is influenced by various parameters related to the matrix, such as matrix type, structure, pre-treatment, particle size, and solid-liquid ratios [20]. The production of superior commodities hinges on the extraction of phytochemicals from crops while preserving their inherent structure and characteristics. Hence, it is imperative to select the suitable phytochemical extraction technique. Common traditional procedures for extraction include maceration, percolation, decoction, reflux, and Soxhlet extraction. Some of the newer methods for extraction include pressurized liquid extraction (PLE), high hydrostatic pressure extraction (HHP), microwave-assisted extraction (MAE), ultrasound-assisted extraction (UAE), pulsed electric field extraction (PEF), vibro-cavitation extraction, vacuum-oscillating boiling conditions, mill extractions, rotary-pulsation apparatus (RPE), liquid gas extraction (LGS), enzyme-assisted extraction (EAE), supercritical fluid extraction (SFE), and natural deep eutectic solvent extraction (NADES) [19-21]. Conducting further research is crucial in order to enhance these extraction techniques and maximize the yield and efficacy of phytochemicals. If we enhance our understanding of the variables that impact extraction efficiency, we can optimize the utilization of these compounds in the production of superior nutraceutical and functional food items.

1.3. Comparisons and Specific Phytochemical Investigations

Researchers have shown significant interest in the possibilities of Cannabis sativa L. in both traditional medicine and modern industry. This plant, which has its origins in Central Asia, possesses a significant number of phytochemicals and also offers important cellulosic and woody fibers. The wide range of biological actions exhibited by this substance, especially its metabolites, have important consequences for the pharmaceutical and construction sectors. The herbaceous plant Cannabis sativa L., native to Central Asia, has been utilized by both traditional medicine and industrial. It contains a wide range of phytochemicals and is a highly valuable source of cellulosic and woody fibers. The plant's metabolites possess potent bioactivities on humans, making it highly valuable to the building and pharmaceutical sectors. Cannabinoids possess a diverse range of pharmacological effects on humans, with a particular focus on their intoxicating features, which has led to them being the chemical class that has received the most scrutiny from researchers. This work conducted a synthesis of the phytoconstituents Apigenin and Alpha-bisabolol. It then proved the presence of both saturated and unsaturated components in the phytoconstituents of Cannabis sativa L. using in silico screening utilizing (PDB ID: 6FYZ) and spectral characterisation using NMR (1H and 13C). The phytoconstituents apigenin and alpha-bisabolol, found in the flowers and leaves of the cannabis plant, demonstrated higher docking scores and gliding energies when compared to conventional drugs such as Levetiracetam. Due to its substantial anti-epileptic effectiveness observed in computer-based studies, the phytoconstituent of Cannabis sativa is a crucial source material for the advancement of novel medications aimed at treating epilepsy, seizures, and other neurological disorders and ailments [22]. Additional research is necessary to investigate the complete capabilities of these phytoconstituents in clinical environments. The study of the mechanisms by which Cannabis sativa L. works and improving the methods of extracting and synthesizing its compounds could lead to the creation of new therapeutic drugs. These drugs have the potential to significantly improve the treatment of neurological illnesses and make present pharmaceutical interventions more effective.

1.4. The Cyperus scariosus Leaf: A Nutritional and Medicinal Resource

Exploring neglected bioresources and developing solutions to recycle agro-waste are crucial for promoting sustainability and facilitating a circular economy. An example of a bioresource is Cyperus scariosus (CS), which has been extensively utilized in Indian medicine due to its medicinal characteristics. Although the roots of CS are highly valuable, the above-ground sections are frequently thrown as agricultural waste because to a lack of awareness regarding their possible applications. The lack of proper utilization of bioresources and a lack of knowledge on how to effectively repurpose this waste using a circular economy approach result in the generation of agro-waste. The widespread usage of Cyperus scariosus (CS) root in Indian medicine is due to its vital medicinal characteristics. The useless bioresource, referred to as CS aerials, is unfortunately disposed of as agricultural trash. Many individuals regard computer science as a nuisance due to their lack of knowledge. The ongoing inquiry into the possible medicinal and nutritional value of CS leaves as a food source is unprecedented. The nutritional and dietary value of the underutilized Cyperus scariosus R.Br. (CS) leaves was evaluated by measuring the plant's phytochemicals and metal ions using advanced HPLC and ICPOES technologies. The concentrations of cafeic acid, catechin, epicatechin, trans-p-coumaric acid, and transferulic acid, as determined by HPLC analysis, were 10.51, 276.15, 279.09, 70.53, and 36.83 μg/g, respectively. The GC-MS/MS data revealed the presence of fats such as linolenic acid, phytol, palmitic acid, and others. The analysis using Inductively Coupled Plasma Optical Emission Spectroscopy (ICPOES) detected notable concentrations of sodium (Na), potassium (K), calcium (Ca), copper (Cu), iron (Fe), magnesium (Mg), manganese (Mn), and zinc (Zn). Compared to the standard ($CaCO_3$), the CS leaves showed better antacid activity, with TPC and TFC levels of 17.933 mg GAE eq./g and 130.767 mg QCE eq./g, respectively, and an IC_{50} value of 2.78 mg/mL in the DPPH assay. The methanolic extract of CS leaves exhibited antimicrobial activity against Staphylococcus aureus (15 ± 2 mm), Pseudomonas aeruginosa (12 ± 2 mm), and Escherichia coli (10 ± 2 mm). The findings from the in vitro experiments on the antioxidant, antiacid, and antibacterial properties were validated by the in-silico tests. Moreover, computational investigations revealed that the CS leaves possessed anti-inflammatory and anti-cancer characteristics. The findings indicated that the unused part of CS possesses therapeutic properties, and that agricultural waste can be converted into a pharmaceutical substance that is effective for human use. Our investigation shown that CS leaves possess nutritional value, therapeutic importance, and potential use in the pharmaceutical industry, as well as in bio-valorization and environmental enhancement [23]. The findings have significant ramifications, indicating that other agricultural wastes may also be reassessed for their potential advantages. By incorporating these biological resources into the pharmaceutical sector, we may promote more environmentally friendly methods and increase the benefits obtained from agricultural operations. Additional investigation into the enhancement of extraction and usage techniques for these bioresources is imperative in order to fully exploit their capabilities.

1.5. Inhibition of enzymes related with Parthenium hysterophorus and the efficacy of phytochemicals

The investigation of phytochemicals and their possible therapeutic uses is an emerging area of inquiry that shows potential for the creation of novel pharmacological substances. Exploring the bioactivity of different plant extracts can result in the identification of new compounds that possess noteworthy therapeutic characteristics. The researchers discovered that many active phytochemicals, including as steroids, alkaloids, and terpenoids, were present in both the crude extracts and distinct fractions. The polar extracts and fractions contain phytochemical components that have strong enzyme inhibitory activity, specifically against urease, α-glucosidase, and phosphodiesterase. Furthermore, scientific research substantiates the soothing, anti-inflammatory, and pain-relieving characteristics of plants. Based on our research, it can be deduced that P. hysterophorus has the potential to provide pharmaceutical companies novel medication candidates that are both safer and more efficient in targeting enzymes such as urease, α-glucosidase, and phosphodiesterase. This has the potential to alleviate the economic burden on these sectors [24]. These findings emphasize the significance of conducting additional study on the phytochemical compositions of therapeutic plants. Through the process of isolating and identifying these bioactive chemicals, we can deepen our comprehension of their modes of action and therapeutic capabilities. This research not only enhances the progress of natural product chemistry but also provides practical advantages for the pharmaceutical sector in terms of generating economical and powerful treatments.

1.6. Analysis of the nutritional, medicinal, phytochemical composition, and bioactive efficacy of Mimosa pudica leaves

It is essential to investigate the untapped plant resources in order to uncover their medical and nutritional properties. This research is vital for promoting sustainable practices and creating novel therapeutic substances. The leaves of Mimosa pudica (MP) are an intriguing subject of research since they contain a diverse range of phytochemicals and exhibit bioactive capabilities. Overall, this examination of MP (Mimosa pudica) leaves was innovative. Aside from fatty acids and essential metal ions, it is nutritionally abundant because of the inclusion of phytochemicals like epicatechin and catechin. This study presents an assessment of the antioxidant properties, total phenolic content, and therapeutic potential of MP leaves. The nutritional value of MP leaves is evidenced by the presence of phenolic compounds (such as catechin and epicatechin), fatty acids, micronutrients (such as calcium, sodium, potassium, magnesium, iron, and zinc), and other nutrients. The methanolic extract of MP leaves, at a dosage of 100 mg/ml, exhibited inhibitory zones against the following bacteria: Staphylococcus aureus (15±2 mm), Escherichia coli (12±2 mm), Pseudomonas aeruginosa (8±2 mm), and Salmonella typhi (8±2 mm). The antioxidant, antiacid, and antibacterial properties observed in in vitro testing were confirmed through in silico study. Moreover, in silico studies revealed that MP leaves exhibited both anti-inflammatory and anti-cancer characteristics. This study showcased the conversion of agricultural waste into a very potent medicinal material and the utilization of the underutilized section of MP. Future research should be done to assess the therapeutic potential of MP leaves using toxicological and pharmacological tests [25]. These findings emphasize the need for additional research on the pharmacological and toxicological characteristics of MP leaves in order to completely understand their therapeutic capabilities. Through the optimization of extraction and utilization methods, we can enhance the benefits obtained from this bioresource that is now not fully utilized. This will have a positive impact on both the advancement of pharmaceuticals and the preservation of the environment.

2. Molecular Docking and Viral Inhibitory Studies

2.1. Monkeypox therapy linked to bioactive profile and molecular docking study

The quest for novel antiviral drugs is essential in addressing the rise of infectious diseases, especially those that provide substantial public health obstacles. In recent years, there has been significant interest in the possibility of natural compounds to serve as valuable sources for the development of new antiviral medications. Monkeypox is a zoonotic virus, meaning it may infect both humans and animals. It causes symptoms that are similar to, but less severe than, those caused by smallpox. Following the eradication of smallpox in 1980 and the subsequent discontinuation of smallpox immunization, monkeypox has emerged as the most significant orthopoxviral concern in public health. Considerable progress has been made in the advancement of novel antiviral treatments, with natural compounds serving as valuable reservoirs for potential and emerging antiviral therapeutics. This study employed molecular docking techniques to examine the potential of several biologically active compounds present in medicinal plants for the prevention of monkeypox. Maestro 12.8 was utilized for the docking experiment. Vernonia amygdalina del. contains phytoconstituents such as Luteolin, Luteolin-7-o- β-glucoside, Vernodalol, Vernolepin, and Vernodalin. These phytoconstituents are similar to the antiviral drug Tecovirimat (TPOXX). The results demonstrate the efficacy of this screening strategy, hence expediting the drug discovery process for emerging infectious diseases. The docking experiment with the PDB Id (6LUT) receptor revealed that various phytoconstituents screening compounds derived from medicinal plants, such as Luteolin (− 3.244), Luteolin-7-o-β-glucoside (− 2.357), Vernodalol (− 2.089), Vernolepin (− 1.757), and Vernodalin (-1.534), exhibited lower docking scores compared to the antiviral drug Tecovirimat (− 0.162). These findings indicate that these chemicals have the potential to prevent Monkeypox infection and could serve as a promising reservoir of novel antiviral medications that specifically target the Monkeypox virus [26]. These findings emphasize the significance of ongoing research on natural products for the identification of antiviral drugs. Through the utilization of sophisticated molecular docking techniques, scientists may more effectively discover promising phytochemicals, which may ultimately result in the creation of robust medicines for monkeypox and other developing viral dangers. Additional in vitro and in vivo investigations are required to authenticate the effectiveness and safety of these drugs, therefore opening up possibilities for novel treatment alternatives in combating viral infections.

2.2. The phytochemical impact of SARS-CoV-2 and its bioactive potency

The COVID-19 epidemic has resulted in unparalleled worldwide difficulties, affecting several facets of human existence. Gaining a thorough comprehension of the various and complex consequences of the pandemic is crucial in order to formulate comprehensive approaches to reduce its influence and enhance resilience in the event of future outbreaks. The COVID-19 pandemic has had a significant impact on various aspects of human life. The areas encompassed are health, the environment, the economy, education, and psychology. This narrative study explores the diverse impacts of COVID-19 on individuals and communities, while also examining the potential contribution of traditional medicine in mitigating the virus's transmission. The review explores the complex relationship between health and socioeconomic well-being, examining the symptoms, routes of transmission, and populations most susceptible to contracting COVID-19. Environmental implications such as changes in air quality, waste disposal concerns, and adjustments in energy usage are all subjects of examination. The text extensively discusses the mental health repercussions of the epidemic, such as increased distress and worry. Simultaneously, our inquiry thoroughly examines the precautions advocated by traditional medicine. This study also examines cultural activities like as steam inhalation and salt water gargling, as well as traditional medicines like herbal teas, decoctions, and plant secondary metabolites. Furthermore, the impact of lifestyle interventions, such as consuming well-balanced meals, employing stress reduction approaches, and utilizing traditional exercise methods, on overall health and the immune system is evaluated. This part provides a concise overview of the findings and presents a discerning assessment of the effectiveness of conventional preventive methods in light of the worldwide epidemic. This publication provides a comprehensive explanation of the cultural relevance and scientific foundation of these traditional practices. The outcomes of this analysis will facilitate the direction of future research and foster collaboration between conventional and alternative medicine, with the aim of enhancing preparedness for pandemics. This article examines the potential of traditional medicine in mitigating the consequences of COVID-19 and offers an in-depth review of the virus's significant influence on human existence. The significance of traditional medicine in fostering a robust and flexible reaction to forthcoming global health crises is further underscored [27]. These findings highlight the necessity of adopting an integrative healthcare approach that combines contemporary and traditional approaches. By promoting increased cooperation among diverse medical frameworks, we can bolster our ability to effectively address public health emergencies. Future research should prioritize the validation of the effectiveness of traditional treatments by thorough scientific investigations, to ensure their safety and benefits for widespread use.

2.3. Wide studies, Clinical presentations, and Treatment Options for Conjunctivitis

Comprehending and researching ocular disorders, specifically conjunctivitis, is crucial for the development of accurate diagnostic and treatment approaches. Conjunctivitis, sometimes referred to as "pink eye," is a widespread ailment that necessitates meticulous inspection in order to differentiate between its different forms and causes. Conjunctivitis refers to the inflammation of the membrane that covers the exposed sclera and borders the eyelids. The most prevalent reason for "red eye" is this. Conjunctivitis is a term that refers to a wide range of disorders that result in inflammation of the conjunctiva. Possible etiologies of hyperacute, acute, or chronic inflammations include both infectious and non-infectious factors. The term "red eye," also known as conjunctival injection, is a prevalent symptom of various eye illnesses and can make up to one percent of all visits to primary care physicians. These two symptoms can be utilized to diagnose "serious eye conditions," such as keratitis and anterior uveitis, in up to 59% of instances. Anisocoria and mild photophobia showed a significant connection with "serious eye conditions". Prior to commencing antibiotic treatment, it is advisable to get swabs from the discharge. Subsequently, the swabs are cultured in a regulated setting utilizing diverse growth media. Individuals who have weakened immune systems or suffer from chronic blepharitis should undergo fungal infection testing using Sabouraud agar plates. Individuals with a history of surgery or trauma may also experience advantages from anaerobic culture plates. Acute hemorrhagic conjunctivitis (AHC) is a highly contagious type of conjunctivitis caused by viral infections. The symptoms include a feeling of a foreign object in the eye, significant swelling of the eyelid, inflammation of the conjunctiva, bleeding beneath the conjunctiva, dilation of the blood vessels in the conjunctiva, and excessive bleeding. Neisseria gonorrhoeae is a common cause of hyperacute conjunctivitis, which can be transmitted through sexual activity can affect both adults and neonates. Ocular allergies can impact not only the cornea, conjunctiva, and eyelids, but also other parts of the eye. Leonardi et al. categorized ocular allergy disorders into three main types based on the underlying immunological mechanism that leads to the development of symptoms. Symptoms of viral conjunctivitis include red eyes, irritation, photophobia, burning, excessive tearing, and a quick start of a sensation as if a foreign object is present. Patients with bacterial conjunctivitis exhibit all of the aforementioned symptoms, as well as mucopurulent discharge and mattering of the eyelids upon awakening. Standard treatment for conjunctivitis involves measures to prevent exposure to allergens (such as pollen, animals, and dust mites), the use of artificial tears, adequate hand hygiene, the application of cold compresses, refraining from rubbing the eyes, and the use of a mild cleaner to eliminate debris and allergens [28]. Subsequent investigations should prioritize the study of the occurrence and distribution of conjunctivitis, the underlying mechanisms responsible for its many manifestations, and the creation of specific therapeutic interventions. Research on patient outcomes, the efficacy of various therapeutic strategies, and the possibility of resistance to conventional treatments is crucial. In addition, the investigation of novel diagnostic tools and preventive strategies can greatly improve patient care and alleviate the strain on healthcare systems.

2.4. Enhancing Immune System in Pregnant Women Amidst COVID-19: Insights from Ayurveda

As the COVID-19 epidemic has endured for the past four years, it has evolved from an immediate crisis to a long-lasting health problem. The current situation requires a thorough comprehension of its lasting consequences and the possible contribution of alternative medicine methods in handling and reducing its ramifications. Given that the SARS-CoV-2 virus (COVID-19) pandemic has persisted for four years, the illness is now classified as a chronic health issue rather than an emergency. Coronavirus type 2 is responsible for a diverse range of illnesses, one of which being COVID-19. India recorded a total of 195,123 fatalities and 2.8 million confirmed COVID-19 cases on April 26, 2021. Recently, this nation has had two surges of the virus. Common signs of the illness include fever, dry cough, and overall fatigue. However, these symptoms usually resolve after a few days. Nevertheless, in exceedingly uncommon instances, these symptoms may escalate to respiratory distress, organ failure, and ultimately mortality. Pregnant women have a higher likelihood of contracting COVID-19 and may experience more severe symptoms compared to the general population, as stated by the World Health Organization. This can be attributed to their weakened immune system and the alterations in their physiological responses. Additionally, there is an increased likelihood of experiencing premature childbirth. In order to protect individuals who are at risk from the coronavirus, further precautions need to be implemented. Regrettably, there is yet no COVID-19 drug deemed suitable for administration to pregnant women. Across the world, individuals are focusing on strategies to mitigate issues. The current COVID-19 pandemic underscores the urgent requirement for enhancing the immune system; Ayurvedic methods that fulfill this purpose have gained significant attention in recent weeks. This website provides comprehensive information on a wide range of Rasayana drugs, including both compound and single formulations, as well as preventive measures. The main objectives of this study are to explore Ayurvedic methods for regulating the immune system, promoting health, and preventing diseases. Additionally, the study aims to gain insights into the Ayurvedic perspective on COVID-19 during pregnancy. Ayurvedic interventions can enhance the immunity of pregnant women and successfully mitigate the transmission of COVID-19, hence reducing the worldwide illness burden [29]. This study highlights the importance of combining traditional medicine methods with modern medical procedures to improve overall health outcomes during the epidemic. Examining the impact of Ayurvedic practices on enhancing immunity, particularly among susceptible groups such as pregnant women, can provide significant knowledge on supplementary approaches for preventing and managing diseases. Subsequent studies should investigate the effectiveness of these conventional methods, their incorporation into conventional healthcare, and their influence on public health in the context of ongoing and future health emergencies.

2.5. Ciprofloxacin, a novel antibacterial medicine, has been found to be effective through in-silico study

Quinolone derivatives, especially ciprofloxacin, have shown remarkable antibacterial properties in the continuous search for effective antibacterial medicines. Ciprofloxacin, belonging to the quinolone category, possesses structural resemblances to nalidixic acid and demonstrates strong biological efficacy. An essential element in improving the effectiveness of quinolones is their ability to interact with metal ions by forming chelates. Quinolones can function as ligands in three different ways: unidentate, bidentate, and bridging. The biological activity of quinolones is greatly enhanced by the presence of certain transition metals, including Ni^{2+}, Co^{2+}, Ca^{2+}, Zn^{2+}, Ag^{2+}, Au^{2+}, Mn^{2+}, Mg^{2+}, and Fe^{2+}. This study investigated the potential of ciprofloxacin derivatives that contain silver ions. We compared their effectiveness with two mainstream medications, norfloxacin and ciprofloxacin, using in-silico docking studies (PDB ID: 2XCT). The study centered on the ciprofloxacin analogue (L1) that was combined with silver ions. The docking scores and glide energies indicated that the silver metal complex of the ciprofloxacin analogue displayed a higher binding affinity in comparison to both norfloxacin and ciprofloxacin. The encouraging in-silico results emphasize the potential of this innovative silver-based ciprofloxacin derivative as a valuable resource for future antibacterial medicines. The extensive efficacy displayed against a wide range of microorganisms indicates that it has the potential to be a valuable asset in the collection of medications designed to combat bacterial and fungal diseases [30]. This study enhances the progress of improved antibacterial treatments by incorporating metal ions into quinolone structures. It also opens up opportunities for future investigations on metal-based quinolone derivatives and their therapeutic uses. Future research should prioritize the validation of these computer-generated results by conducting experimental trials to evaluate the therapeutic significance and effectiveness of these innovative drugs.

3. Toxicological and Methodological Advances

3.1. Improving Embryo Implantation During Freeze-Thaw Embryo Transfer Cycles: The Role of Human Chorionic Gonadotropin

A comprehensive knowledge of the hormonal cycles associated with embryo implantation and pregnancy is essential for enhancing assisted reproductive technologies in the field of reproductive medicine. A crucial differentiation between natural and artificially manufactured cycles lies in the absence of the luteinizing hormone (LH) peak in artificial cycles. The absence of an LH peak generates inquiries regarding the optimization of hormonal assistance for embryo implantation. Given the identification of LH/hCG receptors in the human endometrium and the evidence showing that human chorionic gonadotropin (hCG) might enhance embryo implantation, investigating methods to activate these receptors could have important clinical advantages. This review study examines the function of human chorionic gonadotropin in promoting the change in the endometrium from a non-secretory state to a secretory state during frozen-thawed embryo transfer cycles. This work seeks to advance our comprehension of how to boost implantation outcomes in assisted reproductive settings by investigating the impact of hCG on the endometrial lining and its ability to compensate for the absence of an LH peak in artificial cycles [31]. The results of this review have consequences for enhancing treatment regimens and enhancing the rates of success for embryo transfers. Future research should prioritize gaining a deeper understanding of the processes by which hCG affects endometrial receptivity and devising methods to incorporate this information into clinical practice.

3.2. Possible Diagnostic Biomarkers for Recurrent Implantation Failure: The Function of KIR and LILR Variants and Their Ligands

Numerous individuals experiencing difficulty in conceiving sometimes postpone parenthood due to the significant social and economic challenges resulting from reproductive failure. The demand for assisted reproductive technologies (ART) increases as the natural capacity to conceive and sustain a pregnancy decreases with advancing age. Approximately 10% of patients undergoing in vitro fertilisation (IVF) may experience recurrent implantation failure (RIF), a syndrome characterised by the repeated failure of embryos to successfully implant after many transfers. Endometriosis, uterine fibroids, hydrosalpinx, and endometrial polyps are gynaecologic diseases that can cause recurrent implantation failure (RIF). Additional factors may include uterine dysfunction, immunological complications during implantation, and compromised gamete quality. Another concern associated with Assisted Reproductive Technology (ART) operations is the potential for implantation failure. Recent study has focused on the role of natural killer (NK) cells in both normal and abnormal pregnancies, due to their significant presence in the endometrium and their interactions with extravillous trophoblast cells during early pregnancy. Regulating immune responses at the interface between the mother and foetus is an essential role of NK cells, particularly CD56 bright cells. Trophoblasts establish communication with killer immunoglobulin-like receptors (KIRs), which are specific molecules belonging to the HLA class I. The outcome of this interaction may result in either an increase or decrease in NK cell activity, production of soluble factors, and cytotoxicity. Moreover, the families of immunoglobulin-like transcript (ILT) and leukocyte immunoglobulin-like receptor (LILR) are present in human placentas. It should be noted that stromal cells and smooth muscle layers that surround arteries both possess LILRB1 (ILT2) and LILRB2 (ILT4), respectively. This study examines the possible diagnostic biomarkers for vulnerability to reproductive immunological failure (RIF), which could be genetic variations in KIR, LILRB, and their ligands (HLA-C, HLA-G). A comprehensive study of these genetic factors [32] could provide valuable insights into the causes of implantation failure and offer direction for developing targeted medicines to enhance the outcomes of assisted reproductive technology (ART). The findings of this study have the potential to enhance the efficacy of assisted reproductive technology (ART) by providing insights into more accurate diagnosis and treatment of patients in the field of reproductive medicine.

3.3. Characteristics of Mangifera Indica genotypes related to phytonutrient content and antioxidant activity

Mangoes, scientifically known as Mangifera indica L., are widely recognised as one of the most renowned tropical fruits worldwide. They belong to the Anacardiaceae family. These fruits are well-known for their abundant and diverse range of nutrients, such as vital vitamins, carotenoids, polyphenols, amino acids, potassium, copper, and omega-3 and omega-6 fatty acids. Gallic acid is the predominant phenolic component found in mango mesocarp. In addition, mangoes also contain significant amounts of other essential phenolic compounds, including gallotannins, quercetin, isoquercetin, ellagic acid, and β-glucogallin. Recent research indicates that extracts derived from Mangifera indica exhibit promising therapeutic capabilities, such as immuno-modulatory, anti-inflammatory, analgesic, antiviral, and antibacterial activities. In order to examine these characteristics, scientists gathered and examined samples from a total of eighty-one mango trees, which represented eighteen distinct genotypes of the M. indica species. The study aimed to assess the antioxidant activity, total phenolic content, physicochemical properties, and high-performance thin-layer chromatography (HPTLC) profiles of the mango extracts. This in-depth investigation seeks to clarify the potential of mangoes and their extracts to have a positive impact on health. The findings could pave the way for the creation of functional foods or nutraceuticals that offer significant health benefits. An in-depth comprehension of the differences between various genotypes and their corresponding bioactive components will provide significant knowledge regarding the use of mangoes in health and wellness applications [33].

3.4. Biological indications, phyto-pharmacognostic evaluation of Gloriosa superba L. and Epimedium sagittatum, and profiling

An extensive analysis of the medicinal plants Epimedium sagittatum and Gloriosa superba L. has been conducted by pharmacognostic evaluation. This work rigorously investigates a range of physical-chemical factors, such as ash and extractive levels, using fluorescence techniques. In addition, we have undertaken a thorough examination of the thick layer chromatographic behaviour of several extracts and performed an initial phytochemical analysis. Both Gloriosa superba L. and Epimedium sagittatum are known to have a diverse array of advantageous benefits. The benefits of this substance encompass its anti-inflammatory qualities, ability to prevent cancer, capacity to alleviate symptoms of Parkinson's disease, adaptogenic effects, ability to reduce body temperature, actions against obesity, antibacterial activity, and protection of the liver. Furthermore, the study investigates additional possible advantages such as hypolipidemia, immunomodulation, cardiovascular protection, augmentation of sexual behaviour, and consequences for tolerance and reliance. The wide-ranging medicinal possibilities of these plants are extremely promising and emphasise the necessity for additional investigation. The encouraging findings from this study indicate that Gloriosa superba L. and Epimedium sagittatum should undergo comprehensive clinical trials to confirm their effectiveness and explore any other potential therapeutic qualities. These investigations have the potential to result in the creation of new medicines for various illnesses, therefore broadening the range of medicinal uses for these plants [34].

3.5. Experimenting with ligand-receptor complex prediction and basic molecular docking applications

Molecular docking is a crucial computational method employed to forecast the arrangement and strength of binding between ligands and receptors. This approach is crucial in the field of drug discovery and development, as it enables researchers to simulate and analyse the interactions between tiny molecules (ligands) and biological targets (receptors). The main objective of molecular docking is to precisely forecast the binding conformation of the ligand within the active region of the receptor. The docking procedure consists of two essential steps. The initial stage involves sampling, during which various conformations of the ligand are examined within the active region of the receptor. This process entails the generation and evaluation of several ligand orientations and conformations in order to discover the ones that effectively match the binding site of the receptor. In the second stage, these conformations are evaluated and ranked based on a score system that estimates their binding affinity and stability. The success of this technique depends on the precision of the sampling algorithms and the dependability of the scoring systems. Sampling algorithms strive to accurately replicate the experimental binding mode of the ligand, with the objective of discovering the most advantageous conformation. The scoring system subsequently arranges these conformations in a hierarchical order, with the desired binding mode seen in the experiment being ideally positioned as the highest-ranked answer. This summary offers a brief and clear explanation of the core principles of docking theory, emphasising the interconnectedness of the sampling and ranking stages [35]. Through comprehension of these fundamental principles, researchers can more effectively analyse docking outcomes and improve the development of novel medicinal medicines.

3.6. Lycopersicum solanum Plant compounds exhibited by L. that are effective docking ligand receptor predictors

Parkinson's disease is a neurological ailment that worsens over time and is characterised by the deterioration of neurones that produce dopamine. This deterioration causes a variety of symptoms, both related to movement and unrelated to movement. There is a growing emphasis on natural compounds in the hunt for effective treatment agents to slow down the evolution of Parkinson's disease and alleviate its symptoms. Tomatoes (Solanum lycopersicum L.) have been identified as a source of phytoconstituents that may possess anti-inflammatory and neuroprotective qualities. The objective of this study is to investigate the therapeutic properties of phytoconstituents derived from Solanum lycopersicum L. in relation to Parkinson's disease through the use of molecular docking analysis. Molecular docking is an algorithmic method employed to forecast the binding interactions between diminutive molecules and target proteins. Through the analysis of the interactions between these phytoconstituents and crucial protein targets linked to Parkinson's disease, our objective is to pinpoint potential candidates that warrant further examination. The study will utilise sophisticated computational techniques to analyse the strength of attraction and interactions between phytoconstituents produced from tomatoes and these crucial proteins. The results of this study may offer fresh perspectives on possible therapy strategies and the creation of drugs for Parkinson's disease, potentially resulting in innovative treatments that utilise the neuroprotective characteristics of natural compounds [36].

3.7. Dacus carota bioactive potency with characterization, profiling and CVD potential

Cardiovascular disease (CVD) continues to be a major worldwide health issue, leading to continued investigation of new therapeutic approaches. This research publication examines the possible advantages of phytochemicals obtained from Daucus carota, also known as carrots, in assessing and controlling cardiovascular disease (CVD). Carrots have a variety of phytoconstituents, and this study specifically examines three important markers: p-hydroxybenzoic acid, caffeic acid, and chlorogenic acid. The markers were found and measured utilising a comprehensive process that involves analysing their spectrum properties using 1H and 13C NMR spectroscopy and quantifying them by High-Performance Thin-Layer Chromatography (HPTLC). The spectrum analysis verified the existence of both saturated and unsaturated molecules in these phytochemicals. In order to evaluate their therapeutic potential, the three discovered phytoconstituents underwent in-silico screening utilising the protein structure (PDB ID: 5JAD). The molecular docking simulations demonstrated that these phytochemicals displayed higher docking scores and lower glide energies in comparison to traditional cardiovascular medicines such as Felodipine. These findings indicate that the chemical components found in carrot roots may provide improved protection for the heart. The research highlights the significance of different methodological factors, such as sample collection, identification, and preparation, along with the use of modern analytical techniques like HPTLC, TLC, NMR spectroscopy, and molecular docking investigations. The results emphasise the encouraging cardioprotective characteristics of the phytochemicals discovered in Daucus carota, emphasising their potential as prospects for the creation of novel anti-cardiovascular disease (CVD) and anti-congestive heart failure (CHF) medications. To completely understand the therapeutic potential of varietal differences, optimise extraction procedures, and evaluate synergistic effects, further research is suggested. This research will also help progress the development of effective medicines for cardiac illnesses [37].

4. Qualitative and Biochemical Analysis Techniques

4.1. Phytochemical Screening

This technique involves the analysis of specific chemical constituents present or absent in a plant. The preliminary phytochemical screening was conducted using the established techniques outlined in the publications of Sofowara (1993) [38], Savithramma et al. (2011) [39], Rasal (2005) [40], and Kokate (2003) [41]. Chemical tests were performed to confirm the presence of specific compounds.

4.2. Qualitative Analysis of Primary Metabolites [38-42]

Carbohydrate Assessment: 1. Benedict's Test: Following the filtration of the solution, precisely 0.5 millilitres of Benedict's reagent were introduced to it. The components were heated in a bain-marie until they reached the boiling point, which occurred in around two minutes. An unmistakable red precipitate confirms the existence of sugar. To perform Molisch's test, combine 2 millilitres of crude extract with 2 millilitres of Molisch's reagent. Vigorously agitate the ingredients to thoroughly combine. The third step involved dispersing 2 millilitres of concentrated H_2SO_4 down the edge of the test tube. The observation of a violet ring during the interphase facilitated the identification of carbs. The user did not provide any text. A To test for proteins, a solution was prepared by combining 1.1 ml of the plant sample with 1 ml of 40% sodium hydroxide. A minute quantity of copper sulphate was carefully poured onto the edges of the test tubes. Proteins become evident as the fluid changes colour to a pinkish or violet hue. A mixture of two millilitres of crude extract with Millon's reagent resulted in the formation of a white precipitate, which became red upon gentle heating, thereby indicating the presence of protein. The fatty acid test involved the mixing of 0.5 millilitres of the extract with 5 millilitres of ether. The paper was desiccated after the extract was allowed to evaporate on filter paper. The transparency of filter paper is a reliable measure of the concentration of fatty acids. Resins undergo the precipitation test to evaluate their performance in terms of binding agents, gums, stable lipids, and oils. By utilising a volume of fifteen millilitres of ethanol with a concentration of 95%, the extraction process was performed on half a gramme of the extract. Place the beverage extract in a beaker and then add 20 mL of distilled water. To determine the amount of fixed oils and fats, create a solution by combining 1 millilitre of extract, a little amount of 0.5 N alcoholic potassium hydroxide, and one drop of phenolphthalein. Allow the mixture to gently cook for a minimum of 90 minutes in a water bath. The existence of rendered fats and oils is deduced from the soap-making process or from the neutralisation of acids. Combine 25 millilitres of pure alcohol with 10 millilitres of water and mix consistently to identify any gums and mucilage present. After collecting the precipitate, allow it to dry naturally. Pay attention to the presence of carbohydrates and swelling characteristics in the precipitate.

5. Bioactive Properties and Functional Studies

5.1. Bioactive Properties

The wide variety of fruits found worldwide is widely acknowledged for their significant health advantages, which include supplying vital nutrients like fibre, vitamins, minerals, and phytochemicals, depicted in Figure 2: Origin of Bioactive. It is essential to consume a certain quantity of fruits in order to uphold good health and prevent a range of illnesses. Inadequate fruit consumption has been associated with several health problems, such as obesity, cancer, cardiovascular disease, and chronic illnesses [43, 44]. Australia boasts a diverse range of plant species, numbering over 25,000, out of which over 2,000 are used for human food. A small number of these plants are also exported globally [45]. Native fruits are particularly notable for their distinct flavours and nutritional compositions. The fruits listed, such as bush tomato, Davidson's plum, Kakadu plum, lemon aspen, pepper berries, quandong, and riberry, can be found in many locations of Australia throughout the year, including both desert and damp areas. They have recently garnered attention in the Australian market and have made a substantial contribution to the country's economy [46]. The commercialisation of Australian native fruits encounters obstacles in meeting the demands of both domestic and international markets, despite their considerable potential. This has led to a progressive growth of the indigenous food sector [47]. Nevertheless, these fruits are acknowledged as a valuable reservoir of bioactive substances that have been proven to possess anti-inflammatory, antidiabetic, antioxidant, and antibacterial characteristics [48].The growing public fascination with plant-based goods is fuelled by accumulating evidence of their advantageous impact on health. The phytochemicals obtained from these fruits provide potential alternatives to manufactured drugs because of their diverse bioactive capabilities, such as enhancing plant health and demonstrating effectiveness against bacterial infections and different diseases. This highlights the significance of conducting additional study on these indigenous fruits in order to fully exploit their potential for promoting good health and to facilitate the expansion of the local food sector [49].

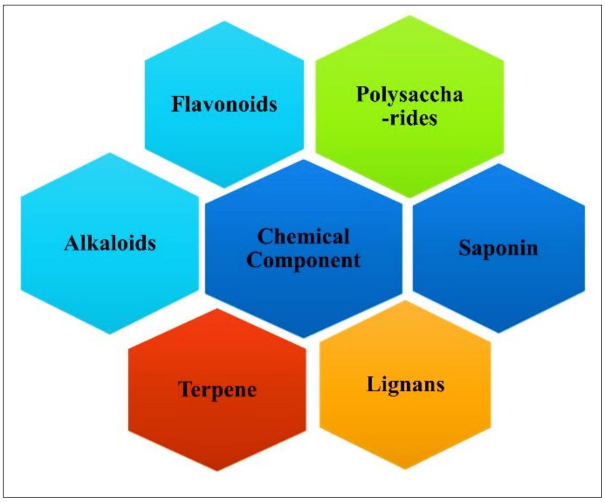


Figure 2 Origin of Bioactive

5.2. Mechanism for Free Radical Trapping Demonstrating Antioxidant Activity

Oxidative stress, which refers to an unevenness between free radicals and antioxidants, has been linked to the emergence of many health ailments, such as respiratory diseases, malignancies, ageing, and other disorders [48]. During cellular oxygen metabolism, free radicals such as hydroxyl, superoxide, nitric oxide, hydroperoxyl, nitrogen dioxide, and lipid peroxyl radicals are generated [49]. If these reactive species are not neutralised by antioxidants, they can cause substantial damage. As a result, the assessment of antioxidant activity in plants and their derivatives has become an essential field of study. Novel approaches in testing antioxidant activity now encompass hydrogen atom transfer (HAT) and single electron transfer (SET) assays, which are crucial for assessing the potential of different substances. SET assays, such as the total phenolic content (TPC) utilising Folin-Ciocalteu reagent, ferric reducing antioxidant power (FRAP), and cupric antioxidant capacity (CUPRAC), evaluate the potential of an antioxidant to give away an electron and decrease the levels of metal ions or radicals. On the other hand, HAT tests, such as ORAC, TRAP, and TOSC, evaluate the potential of antioxidants to transfer hydrogen atoms and neutralise radicals [49]. In addition, the Trolox equivalent antioxidant capacity (TEAC) and the 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging capacity assay, which integrate SET and HAT methodologies, provide a thorough understanding of antioxidant capacities. Although the TPC, FRAP, and DPPH assays are commonly employed because of their simplicity, cost-effectiveness, and ease of implementation, they do not distinguish between hydrophilic and lipophilic compounds [48,49]. In order to address this constraint, researchers are advised to utilise various approaches to conduct a comprehensive assessment of antioxidant activity, as recommended by the study conducted by Chaves [50]. Within the Proteaceae family, multiple investigations have revealed inconclusive findings regarding antioxidant activity. These discrepancies may arise from variations in the solvents used for extraction, the provenance of the plants, and the methodologies employed. As an example, the extract of O. grandiflora leaves from Ecuador, which was dissolved in water and ethanol, showed an IC50 value of 6.69 ± 1.39 μg/mL. In comparison, the extract dissolved in pure ethanol had an IC50 value of 292.37 ± 9.37 μg/mL [52]. This variance emphasises the influence of solvent selection on the measurement of antioxidant activity. Similarly, other DPPH experiments conducted on O. grandiflora flowers yielded inconsistent outcomes, with IC50 values varying from 14.39 ± 1.43 μg/mL to 955.23 ± 0.25 μg/mL [53]. Roupala paulensis, a species within the Proteaceae family, exhibits the highest total phenolic (TP) content of 24.27 ± 0.76 g GAE/100 g. However, its ability to scavenge DPPH radicals did not increase, potentially because the assay is sensitive to variables such as Lewis bases, light, and solvents [54]. Hakea terminalis, with an IC50 value of 156.9 mg/mL in the DPPH experiment, exhibited significant antioxidant activity, particularly in the stem of the plant [55]. Only a limited number of native Australian fruits, such as

Hakea sericea, Hakea salicifolia, and Phyllocladus linearis, have been examined for their antioxidant and antibacterial properties. It is worth mentioning that the fruit of Hakea sericea has significantly higher quantities of ellagic acid (3700 ± 60 mg/100 g DW) compared to other native Australian species [56-63]. The high ellagic acid concentration of this fruit is directly related to its notable antioxidant activity, as demonstrated by its higher total phenolic content (TPC) and ferric reducing antioxidant power (FRAP) values compared to bush tomato and other indigenous fruits. Nevertheless, there are differences in antioxidant activity between pepper berries from Tasmania and Brisbane, suggesting that environmental factors and growing conditions have a substantial impact on the functional and nutritional properties of these fruits [64, 65, 66].

5.3. In vitro antimicrobial efficacy against commonly used and reference medications as well as certain bacteria, such as Escherichia coli

Foodborne infections present substantial hazards to human health, resulting in a range of illnesses and epidemics. The New South Wales Food Authority has identified Bacillus, Salmonella, Campylobacter, Escherichia, Staphylococcus, and Listeria spp. as the most prevalent offenders. For example, infections induced by Staphylococcus aureus can lead to symptoms such as nausea, vomiting, and stomach pain occurring within a timeframe of 30 minutes to 8 hours after being exposed. While antibiotics have played a crucial role in treating these diseases, their extensive usage has resulted in the development of antibiotic-resistant bacteria, which poses a significant obstacle for modern medicine. This has stimulated the pursuit of novel antimicrobial compounds, specifically those obtained from natural sources. For a while now, researchers have been studying natural products to uncover their possible medicinal characteristics, particularly their ability to fight against bacteria. Notable examples of plants that have showed promise in this area include Terminalia carpentariae [68], Terminalia ferdinandiana [69], Acacia floribunda [70], Macadamia integrifolia [71], and Hakea sericea [72]. In order to evaluate the effectiveness of antimicrobial agents, various standardised techniques are utilised, with dilution and diffusion assays being the prevailing methods. Additional methods encompass bioautography, time-kill tests, ATP bioluminescence experiments, and flow cytofluorometric procedures. Nevertheless, these sophisticated techniques typically necessitate specialised apparatus and rigorous statistical examination, rendering them less accessible in comparison to conventional procedures.The agar disc diffusion and well diffusion tests are officially recognised procedures for assessing antibiotic susceptibility. However, these approaches fail to differentiate between the bactericidal and bacteriostatic effects [73]. Dilution procedures are employed to ascertain the minimum inhibitory concentration (MIC), which refers to the lowest concentration of an antimicrobial agent that effectively prevents observable microbial growth. The minimum bactericidal concentration (MBC) or minimum fungicidal concentration (MFC) is a measure of the lowest concentration needed to effectively kill 99% of microorganisms. Various dye reagents, including resazurin, 2,3,5-triphenyltetrazolium chloride (TTC), and 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide (MTT), have been studied to improve the precision of visual evaluations.The antibacterial characteristics of the Proteaceae family, which includes taxa such as Grevillea, Hakea, and Protea, have been thoroughly investigated. Studies reveal that individuals belonging to this family demonstrate substantial antibacterial activity against a variety of diseases. The fruit of Macadamia integrifolia exhibits significant antibacterial properties against Escherichia coli, with a minimum inhibitory concentration (MIC) of 5.3 μg/mL [71]. This surpasses other species with higher MIC values, such as >100 μg/mL [76], 31.125 ± 0.2 μg/mL in Embothrium coccineum leaves [77], and 156 μg/mL in Darlingia darlingiana bark [78]. Similarly, the stem of Roupala brasiliensis demonstrates strong antimicrobial activity against Staphylococcus aureus, with a minimum inhibitory concentration (MIC) of 15.6 μg/mL [79]. Additionally, the aerial portions of Grevillea avellana showed significant antibacterial activity against Pseudomonas aeruginosa, with a MIC of 64 μg/mL [80]. Furthermore, the selection of a solvent for extraction can have a substantial impact on the antibacterial effectiveness of plant extracts. Embothrium coccineum leaves were subjected to extraction using different solvents, resulting in variable minimum inhibitory concentration (MIC) values against E. coli. The MIC values were 250 μg/mL with hexane, 31.125 μg/mL with dichloromethane, 125 μg/mL with ethyl acetate, and 250 μg/mL with ethanol [77]. In addition, the leaves of Macadamia integrifolia showed varying minimum inhibitory concentration (MIC) values depending on where they were collected. The MIC values ranged from 2790 μg/mL at Mt. Coot-tha to 2.4 μg/mL at the Logan campus of Griffith University [71, 82]. These differences highlight the influence of environmental influences on the bioactive characteristics of plants. Gaining a comprehensive understanding of these aspects is essential for maximising the efficiency of the development of plant-derived antibacterial drugs.

5.4. Comparing conventional medicine-based cytotoxicity with cancer line assessments

Cancer continues to be a highly significant worldwide health issue, with its influence steadily increasing in recent times. The World Health Organisation (WHO) reported a significant increase in cancer-related fatalities from around 4 million in 2014 to 10 million in 2018 [83]. Due to the increasing occurrence and death rates, there is a pressing requirement for the creation of efficient anticancer treatments. It is worth mentioning that the natural world has provided a significant number of chemicals that have the ability to fight against cancer. More than three thousand plant species have been discovered as sources of useful substances that can combat cancer, making up almost 60% of all natural goods

[84]. Extensive research is conducted in the development of anticancer medications to investigate the cytotoxic effects of different substances. Cytotoxicity study investigates the impact of these chemicals on cell growth, damage, and reproduction in controlled laboratory settings. Cytotoxicity assays in modern research are commonly categorised into four types: dye exclusion, colorimetric, fluorometric, and luminometric [85]. The methyl thiazolyl tetrazolium (MTT) assay is a commonly employed colorimetric technique for evaluating cell proliferation. Nevertheless, the MTT assay has drawbacks due to its high sensitivity and susceptibility to interference from compounds like kaempferol and (-)-epigallocatechin-3-gallate, which can hinder the conversion of MTT to formazan [86]. The investigation into the cytotoxic characteristics of plant chemicals derived from the Proteaceae family has shown significant potential. Roughly 50% of the studies on the toxicity of Proteaceae species have concentrated on chemicals that have also been examined in other plant families. For example, 2-methoxyjuglone, which is present in different species within the Juglandaceae, Sterculiaceae, and Proteaceae families, has demonstrated varying levels of cytotoxicity. One study found that the IC50 value against HepG2 cells was 2.2 μg/mL. However, the cytotoxicity of 2-methoxyjuglone isolated from L. hirsuta leaves was weaker in comparison, with an IC50 value of 3.8 μg/mL [87, 88]. Furthermore, 2-methoxyjuglone has shown promising anticancer activity in laboratory studies against many types of human cancer cells, such as breast cancer, colon adenocarcinoma, and hepatocellular carcinoma cells [90]. Graviquinone, obtained from G. robusta, is a remarkable chemical that has demonstrated substantial cytotoxic properties against many cancer cell lines. Graviquinone demonstrates IC50 values of 15.0 ± 3.0 μM against MCF-7 cells, 10.8 ± 2.3 μM against NCI-H460 cells, and 5.9 ± 0.1 μM against SF-268 cells [89]. The cytotoxic effects of this substance are observed in several types of cells, such as thymic lymphoma, lung tumours, immortalised cells, and squamous cell carcinoma. The concentration required to inhibit 50% of cell growth (IC50) ranges from 0.03 to 11.83 μM [91]. These findings indicate that graviquinone has significant promise as a cytotoxic agent for the treatment of different types of tumours. In addition, G. robusta contains methyl 2,5-dihydroxycinnamate, a chemical that is also present in other plants such as Murraya paniculate leaves [93] and Philadelphus coronaries branches [92]. These plants have shown anticancer properties. Hydroquinone obtained from H. lobata leaves has demonstrated the ability to suppress the growth of the MGC-803 and HEEC cell lines. The IC50 values for these inhibitory effects were measured at 11.3 ± 2.1 and 19.4 ± 1.9 μg/mL, respectively [94]. The occurrence of this compound in both marine and terrestrial plant species highlights its significance in investigations on cytotoxicity and antioxidant activity [95–97]. These findings collectively emphasise the potential of natural plant chemicals as valuable sources of new anticancer medicines and emphasise the significance of ongoing research in this sector.

5.5. Inhibition of Inflammation (via the Prokinase pathway)

Inflammation is an essential biological reaction that safeguards the body against detrimental stimuli, such as viruses or injuries. It is defined by a variety of symptoms, such as erythema, oedema, discomfort, and impaired functionality. Inflammation can be categorised into two distinct types: acute and chronic. Although acute inflammation serves as a defence mechanism, persistent inflammation can exacerbate a range of health problems and disorders. Chronic inflammatory disorders, such as asthma, can have a substantial impact on health and quality of life [98]. Contemporary therapies for inflammation frequently utilise artificial medications, such as nonsteroidal anti-inflammatory medicines (NSAIDs) and corticosteroids. Nevertheless, these drugs might cause substantial detrimental consequences, such as gastrointestinal complications such bleeding and ulcers [98, 99]. Consequently, there is an increasing curiosity in investigating plant-derived anti-inflammatory substances that may provide effectiveness with reduced adverse effects. Aboriginal peoples have long been aware of the anti-inflammatory characteristics of several plants, including those in the Eucalyptus species. They utilise these plants for their therapeutic advantages [100]. Within the realm of contemporary research, the evaluation of anti-inflammatory action involves many approaches, such as the suppression of nitric oxide (NO), cyclooxygenase-1 and -2 (COX-1/2), xanthine oxidase (XO), lipoxygenase (LOX), and tumour necrosis factor-alpha (TNF-α) [101-102]. The anti-inflammatory capabilities of the Proteaceae family have been extensively researched. Studies have shown that several species of Proteaceae demonstrate variable levels of anti-inflammatory properties. As an illustration, the roots of Hakea terminalis, a species belonging to the Proteaceae family, have demonstrated the most potent anti-inflammatory action. The IC50 value, a measure of effectiveness, was determined to be 11.98 ± 0.71 μg/mL [102]. Animal models such as chicks, pigs, and rats have been used to assess the anti-inflammatory properties of Proteaceae species. However, comparing the results of different studies is difficult because of differences in the models and methods used. The influence of extraction procedures, solvents, and sample processing on bioactivity is very substantial. For example, extracts from P. simplex show different rates of inhibition according on the solvent used [103], while investigations on G. avellana have shown that roasting methods can change the level of inhibition activity [104]. Hence, it is imperative to take into account these parameters when designing future research in order to precisely evaluate bioactivity. Although there has been some progress, there is still insufficient study especially investigating the anti-inflammatory potential of phytochemicals in Proteaceae species. One instance is bisresorcinol, which has been discovered in the trunk of Hakea terminalis. It has shown significant anti-inflammatory effects in RAW 264.7 cells and possesses anti-aging capabilities [105]. Furthermore, oleanolic acid, a chemical molecule found in several species of Proteaceae, has undergone thorough examination and analysis due to its significant anti-inflammatory properties [108, 109]. Presently, the primary emphasis of research has been on leaves, flowers, stems, roots, and other components of the Proteaceae family, while the investigation of fruits has been limited. By including a wider variety of plant materials into study, a more thorough understanding of their anti-inflammatory capabilities can be obtained, therefore filling in current gaps in knowledge. Additional research is advised to examine the complete range of anti-inflammatory substances found in the Proteaceae family and other plant sources.

5.6. Antiviral Activity (Host genomic mechanism)

The occurrence and dissemination of pandemics pose a recurring obstacle in human health as a result of the genetic diversity of viruses. Although numerous antiviral treatments have been developed, traditional therapies still have drawbacks, such as low effectiveness and the emergence of virus resistance. This has sparked a growing curiosity in investigating alternative therapies, specifically chemicals derived from plants, for the purpose of controlling viral infections. Historical research has revealed approximately 100 plant species that possess potential antiviral capabilities. These studies have primarily concentrated on viruses such as herpes simplex virus (HSV), human immunodeficiency virus (HIV), influenza virus, and hepatitis C virus (HCV) [110]. The Proteaceae family has been a subject of particular interest when studying plant groups for their antiviral activities. Preliminary studies have shown that some species in this family possess antiviral capabilities. Conospermum incurvum has demonstrated the capacity to hinder HIV-1RF, therefore safeguarding the T4-lymphoblastoid cell line. The activity has been ascribed to a compound called conocurvone, which is a naphthoquinone derivative discovered in C. incurvum [111]. Furthermore, the bark extracts of Darlingia darlingiana and Banksia bleasdalei have demonstrated promising action against HSV [113]. However, Hakea saligna, although it is used in traditional medicine, has not demonstrated notable antiviral effects against the Ranikhet sickness virus at a lethal dose (LD50) value of greater than 1000 mg/kg [112]. In addition, there is no evidence of antiviral properties in the leaves of Lomatia ferruginea against HSV and HIV, or in the barks of Banksia integrifolia, Cardwellia sublimis, and Buckinghamia celsissima against HSV. While certain Proteaceae plants have demonstrated potential in suppressing specific viruses, the extent of research in this field is still restricted. Presently, the antiviral properties of Proteaceae plants have been mostly recorded in relation to their effectiveness against HIV, HSV, and Ranikhet sickness virus. This is in contrast to the abundance of data available on other bioactive qualities of these plants. Additional comprehensive investigations are required to improve our comprehension of the antiviral capabilities of Proteaceae species. By broadening the scope of research to encompass a wider array of viral targets and conducting thorough investigations into other members of the Proteaceae family, it is possible to uncover further therapeutic opportunities and make significant contributions towards the advancement of novel antiviral medicines.

6. Conclusion

Medicinal plants offer a potential pathway for discovering new drugs and developing treatments. They include a variety of bioactive substances that can be extracted and utilised using modern techniques such as molecular docking and biochemical screening. Combining traditional knowledge with current scientific methodologies improves our comprehension of the therapeutic and nutritional advantages they offer. Future research should prioritise the investigation of the underlying processes by which certain substances exert their effects, as well as the implementation of robust clinical trials. Additionally, it is important to explore how different phytochemicals interact with each other in order to maximise their combined therapeutic benefits.

6.1. Future Directions

The future directions involve a holistic approach to advancing the comprehension and implementation of medicinal plants in healthcare. Validating in vitro findings with in vivo investigations is essential to verify the bioactivity and safety characteristics of bioactive chemicals found through screening techniques. Furthermore, investigating the combined effects of phytochemical combinations shows potential for creating innovative therapeutic uses that take advantage of the complementary actions of various chemicals found in plant extracts. The importance of sustainability necessitates the exploration and implementation of extraction techniques that minimise harm to the environment while maximising the amount and quality of bioactive extracts. Pharmacokinetic studies are necessary to understand how these substances are absorbed and processed in the human body, providing valuable information for determining the most effective dosage and treatment techniques. Interdisciplinary collaboration is crucial for effectively using technical breakthroughs in drug delivery systems and personalised treatment. It enables the transformation of scientific findings into practical healthcare solutions that fully harness the potential of medicinal plants. Collectively, these endeavours will promote the incorporation of plant-derived treatments into conventional medicine, effectively tackling existing healthcare obstacles through inventive and environmentally-friendly remedies.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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