www.idosr.org Mpora, 2025

©IDOSR PUBLICATIONS ISSN: 2579-0781

International Digital Organization for Scientific Research IDOSRJES11300000
IDOSR JOURNAL OF EXPERIMENTAL SCIENCES 11(3): 52-59, 2025.
https://doi.org/10.59298/IDOSR/JES/113.5259

Narrative Review of Herbal Immunomodulators

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ABSTRACT

Herbal immunomodulators are naturally occurring compounds capable of enhancing or suppressing immune responses through diverse mechanisms. Traditional medical systems have long employed plants such as *Echinacea*, *Astragalus*, *Ginseng*, *Elderberry*, and *Turmeric* to support immunity, with modern research confirming their potential to influence innate and adaptive pathways via receptors, signaling cascades, and cytokine regulation. Clinical and preclinical evidence suggests that these herbs may alleviate respiratory infections, modulate inflammation, and improve immune resilience, though variability in formulation, dosage, and study design limits definitive conclusions. Safety concerns, including adverse effects, herb–drug interactions, and inconsistent regulatory oversight, further complicate their integration into standard medical practice. Nevertheless, growing patient demand, cultural acceptance, and supportive mechanistic studies underscore the therapeutic promise of herbal immunomodulators. This review highlights key agents, mechanisms of action, clinical evidence, safety considerations, and future directions for integrating herbal immunomodulators into modern healthcare.

Keywords: Herbal immunomodulators**,** Immune regulation**,** Phytochemicals**,** Complementary medicine**,** Safety and efficacy.

INTRODUCTION

Herbal immunomodulators are naturally occurring compounds capable of modulating the immune system by stimulating or suppressing its components [1]. They can act on various parts of the immunological network, including the mononuclear phagocyte system, polymorphonuclear neutrophils, the complement system, natural-killer cells, and the lymphocytes of both the humoral and cell-mediated arms [2]. Such agents can mobilize or suppress the entire immune system or target specific cell populations, functions, or mediator concentrations, thereby restoring the body's inherent capacity to resist infections and other diseases.

Historical Context

Humans have long used herbs for immune support, driven by the need to overcome infections and other stresses without modern health care systems [3]. From traditional attitudes emphasizing the harmony of body balance, vitality, and physical attributes as reflections of the immune state, herbal choices also conferred spiritual benefits in many societies. By the twentieth century, scientific investigation of herbal remedies had matured enough to produce standardized, chrysanthemum-based patent medicines. Despite this progress, understanding the specific biological roles of most plant-based phytochemicals remains limited, incomparable to the clarity achieved with synthetic compounds developed during the WHO's post-war 'essential medicines' program [3].

Mechanisms of Action

Herbal products that influence immune function may do so by interacting with sensors of the innate immune system or by influencing intracellular signaling pathways in immune cells [1]. Introducing or threatening chemicals can be sensed via analytic signaling receptors, a rapid-response system that often activates the adaptive response. Innate immunity recognizes classes of potential pathogens characterized by unique epitopes, with the adaptive response targeting the specific pathogen recognized. Extracellular pathogens are sensed via recognition

of distinct oligosaccharide moieties on the pathogen surface, whereas intracellular parasites are recognized through motifs linked to viral nucleic acid [3]. Targets that activate immune responses include toll-like receptors (TLR), C-type lectin receptors (CLR), nucleotide-binding oligomerization domain (NOD)-like receptors (NLR), retinoic acid-inducible gene I (RIG-I)-like receptors (RLR), and oral infection activates the inflammasome, resulting in IL-1β production [1]. Nuclear receptors such as aryl hydrocarbon receptor (AhR) also serve as sensors of external pathogens and xenobiotics [3]. Additional targets include enzymes, transcription factors, and co-stimulatory molecules [4]. Modulatory responses that are not actually immunological, such as antioxidant activity and cytoprotection, are excluded from consideration.

Key Herbal Immunomodulators

Traditionally, five herbs and their bioactive components have been most closely associated with beneficial immunomodulatory effects in clinical trials and/or patients: Echinacea (Echinacea purpurea), Astragalus (Astragalus membranaceus), Ginseng (Panax ginseng), Elderberry (Sambucus nigra), and Turmeric (Curcuma longa) [1, 3]. Immunomodulators selectively produce immuno-stimulation or immuno-suppression by interacting with the immune system, enabling the use of these bioactive substances as surrogate immune regulators in the pharmaceutical, food, and cosmetics industries. The principal bioactive constituents of herbal immunomodulators comprise polysaccharides, lactones, and alkaloids [3]. Following a short outline of the principal routes to herbal immunomodulator discovery, the immunomodulatory properties of these five canonical agents will be surveyed and their distinctive mechanisms of action highlighted [3]. Echinacea (Echinacea purpurea) has the longest history of medicinal use in Western herbal practice and remains the second best-selling herb in the United States. The aerial parts of the plant, which contain an abundance of polyenes and alkylamides, exert potent anti-inflammatory, antiviral, and immunomodulatory effects. These distinctive effects position Echinacea as an attractive candidate for the treatment of acute respiratory tract infections [1].

Echinacea

Echinacea angustifolia, Echinacea pallida, and Echinacea purpurea constitute the Echinacea species most extensively evaluated for their immunomodulatory activity [1]. Despite the variety of active molecules with flavonoids, alkylamides, chicoric acid, and polysaccharides all exerting direct effects on immune cells, the pharmacological action of Echinacea extracts remains unified by a shared capacity to enhance cellular immune functions [4]. Numerous studies demonstrate that Echinacea extracts stimulate antibody production and cellular immune responses and induce dendritic cell maturation [4]. In humans, a considerable number of clinical trials and reviews support the capacity of Echinacea formulations derived from both aerial and root components to prevent and treat upper respiratory tract infections and the common cold [4]. Immune pathway analysis reveals that Echinacea extracts activate c-Jun N-terminal kinase (JNK), p38 mitogen-activated protein kinase (p38 MAPK), and nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB), participating across the spectrum of physical barrier, innate, and adaptive immunity. Overall, extensive research endorses the use of Echinacea as an immunostimulant, and the species remains pivotal in medicine and human healthcare [4].

Astragalus

Astragalus membranaceus is a commonly used traditional Chinese medicine that has been widely applied to enhance the immunomodulatory function of the body [5]. It has been classified as an adaptogen and is also known as Huangqi in Chinese. Its main functions include boosting the immune and hematopoietic systems [6]. Among the bioactive components in this plant, flavonoids constitute one important group of secondary metabolites; more than 4000 flavonoids have been identified in the plant kingdom. Calycosin, the most enriched isoflavone in Astragalus, exhibits notable pharmacological activities in vitro and in vivo, including anticancer, antioxidative, immunomodulatory, and estrogenic-like effects [6]. To explore the role of the bioactive components, various extraction techniques have been applied. The membrane separation technique, featured by green processing conditions and high efficiency, is of particular interest in the application of Astragalus [5].

Ginseng

Ginsenosides constitute the major active components in Panax ginseng and possess immunomodulatory properties at both cellular and organismal levels. Ginseng has been employed as a remedial herb for immunomodulation to reduce inflammation and enhance immunity; however, its immunoregulatory role remains elusive [1]. Various ginsenosides are classified into four types, protopanaxadiol (PPD), protopanaxatriol (PPT), ocotillol, and oleanolic acid, based on structural differences [1]. Multiple ginsenosides and other bioactive substances, such as ginseng polysaccharides, have also been reported to exert immunomodulatory effects. These compounds remain of significant interest, as they hold potential for further experimental investigation and commercial development [7].

Elderberry

The elderberry is the berry from the black elder tree, Sambucus nigra. These berries contain antioxidants and are sometimes used in dietary supplements for immune health [8]. Elderberry supplements are frequently marketed for cold and flu relief, immune support, and general wellness. A randomized, double-blind, placebo-controlled study involving 312 otherwise-healthy travelers on long-haul flights of at least 6 hours tested the effect of elderberry capsules taken before and during travel. Although some details about the supplement were not reported, the study was judged to be of high methodological quality [8]. Participants taking elderberry experienced a reduction in the duration of cold symptoms by approximately 2 days and a decrease in symptom severity compared with those taking a placebo [8]. However, elderberry supplementation did not significantly reduce the incidence of developing colds. No statistically significant differences in the occurrence of adverse events were observed between the elderberry and placebo groups [8]. Elderberry was generally well tolerated, and no serious adverse events were associated with its use. Commonly reported adverse events included cold-like symptoms and fatigue, although none were confirmed to be causally related to elderberry. Elderberry extract is typically administered at doses up to 1200 mg daily for 2 weeks or up to 500 mg for 6 months; no upper tolerable intake level has been established. Approximately 27 adverse event reports related to elderberry have been submitted over 6 years, with the majority involving raw or unripe berries [8].

Turmeric

Turmeric, the rhizomes of Curcuma longa L. (Zingiberaceae), has a long history of use as a spice, food preservative, and traditional medicine in Asia [9]. Annual production of turmeric rhizomes in Nepal exceeds 2000 kilograms, with 98% cultivation concentrated between 800 meters and 1500 meters altitude, particularly in Makwanpur, Chitwan, Ramechhap, and Palpa districts [4]. Turmeric extracts contain various secondary metabolites, including curcuminoids, mono- and sesquiterpenoids. Curcuminoids, particularly curcumin, demethoxycurcumin, and bisdemethoxycurcumin, are major bioactive compounds and are considered the principal constituents responsible for turmeric's pharmacological activities. These compounds have been extensively studied for diverse bioactivities related to their immunomodulatory potential. The abundant curcumin in turmeric was first isolated in the early 19th century and identified by structure in 1910. Curcumin is generally regarded as safe and is widely employed as a dietary supplement, food additive, and active ingredient in cosmetics [9]. Its immunomodulatory action involves regulating immune cells, including B cells, T cells, macrophages, neutrophils, natural killer cells, and dendritic cells. Curcumin modulates the production of various cytokines, transcription factors, and enzymes associated with immune responses [4]. The ability of turmeric extracts to modulate the inflammatory environment and alter interactions among recruited cells within the granuloma contributes to their immunomodulatory properties.

Clinical Evidence

Several types of clinical evidence provide support for the efficacy of herbal immunomodulators. Randomized controlled trials have found that Echinacea extracts can reduce the incidence and duration of acute respiratory tract infections in adults and children [3]. Observational studies indicate that Astragalus preparations may enhance quality of life and immune parameters in cancer patients undergoing chemotherapy or radiotherapy. Meta-analyses report that ginsenosides sustain immune function during cancer treatments and lower levels of proinflammatory cytokines, such as interleukin [6]. Such evidence reinforces the therapeutic potential of these key herbal agents.

Randomized Controlled Trials

Randomized controlled trials (RCTs) provide compelling experimental evidence on the immunomodulating properties of herbal agents highlighted in section [4]. A herbo-mineral Ayurvedic formulation comprising Mandoor Bhasma and 18 herbs demonstrated efficacy in alleviating symptoms of allergic rhinitis. Within immunosuppressed rat models, the treatment reinstated neutrophil activation, boosted cellular and humoral responses, and reversed immunosuppression at the molecular level. It modulated key signal transducers, including TNF-α, IFN-γ, IL-1β, ERK, PI3K, and NF-κB, and effectively inhibited histamine release, indicating potential to control allergic states [10]. Several indigenous plants from the Americas are documented for immunostimulant use, including 28 species for which pharmacological studies exist. The majority of these analyses report either in vitro or in vivo effects of crude extracts or isolated compounds, thereby informing the assessment of immune-enhancing potential [11]. Modest further exploration may identify treatments capable of protecting immunocompromised individuals. The clinical evaluation of herbal immunomodulators remains far from mature, despite their pervasive traditional employment. Experimental investigations nonetheless fuel anticipation that clinically relevant immunostimulatory effects will undergo demonstration with respect to the herbs, yet lack rigorous trials [11]. Regrettably, many expert reviews provide only dated listings of RCTs without discerning the

more recent and best-conducted investigations from the older, less reliable ones. Pharmacological explorations have progressed so rapidly that the trend has become largely reversed [10]. By now, systematic reviews on the subject are altogether unavailable. Adoption of the heritage of herbal immunomodulator RCTs remains thus inhibited. The formulation outlined above can facilitate the rapid identification of relevant published data and can thus improve evaluations of the existing evidence [10, 11].

Observational Studies

Several observational studies have assessed the immunomodulatory properties of herbal agents. However, issues with study design, such as underpowered cohorts, confounding variables, and a lack of adequate controls, limit definitive conclusions, especially for Echinacea, Astragalus, Ginseng, Elderberry, and Turmeric. One Polish longitudinal study during the 2009 influenza pandemic retrospectively analyzed patient-reported associations between complementary and alternative medicine agents and sociodemographic factors [1]. Of 288 adults surveyed, 39.6% reported taking complementary and alternative medicines, with 32.3% in conjunction with vaccination. Specifically, 19.7% reported using herbal supplements or remedies, and 17.4% used vitamin C. Among these, Echinacea and Ginseng were popular choices. Although symptoms resolved in all cases, a trend toward greater symptom persistence emerged among complementary and alternative medicine users compared to controls [1]. Another small observational study in Mexico monitored viral illnesses over the 2009 influenza pandemic. Patients treated with Ginger and Astragalus from the first symptom day used over-the-counter medicines less frequently than those treated with vitamin C alone. This suggests a potential direct immunological benefit; however, the study's limited sample size and observational design restrict the strength of this evidence [11].

Meta-Analyses

A wide range of herbal immunomodulators have been investigated recently to determine whether they can offer worthwhile effects [3]. Numerous randomized controlled clinical trials have probed the impact of herbal immunomodulators for diverse indications such as URI, common cold, and flu, as well as other conditions like herpes simplex virus and recurrent genital herpes. Additionally, observational clinical studies have explored the immunostimulatory value of St. John's Wort. However, there is still a scarcity of meta-analyses to comprehensively examine the effects of these botanical agents [3].

Safety and Toxicity

Herbal medicines and remedies have been widely used for generations on all continents. While their potential remains a hot topic, the related safety concerns must not fall by the wayside. Herbal immunomodulators can provoke undesirable immunopotentiation or immunosuppression. The consequences of the former include chronic inflammation, cytokine storm, autoimmunity, and even immunogenicity, while the overactive immunosuppression could pave the way for the increased risk of infections and cancer [12]. Considerable variability exists among definitions of the terms "herbs" and "herbal". To a Western scientist, a herb is any part of a plant used for patient treatment, while herbal often refers to an entire plant or its parts used for health improvement. A modern pharmacist may take the term to mean the therapeutic category of licensed, patented products containing plant extracts or their derivatives [12]. To the FDA, herbals comprise a broad range of health products, from highly processed extracts to raw materials in the form of powders, tablets, capsules, teas, and other supplies. Depending on the type of product and its purpose, herbals can be classified under the category of a dietary supplement, food, or drug [12].

Adverse Effects

Herbal medicines are often perceived as natural and safe remedies; however, an increasing number of studies now draw attention to possible adverse effects associated with their use [4]. Herbal remedies are not without risks, especially when their raw extracts are ingested for prolonged periods or at high doses; when they are inappropriately used in the context of specific morbidities; or when they are used in combination with chemotherapy or documented hepatotoxic agents. The most commonly reported toxic effects are headache, dizziness, and intestinal disorders (e.g., diarrhoea and nausea); other adverse effects include allergic reactions, kidney disorders, hepatotoxicity, phototoxicity, and neurotoxicity [4]. From a more specific perspective, plant constituents, in particular alkaloids and terpenoids, exert adverse effects by interfering with drug-metabolizing enzymes, thus altering the pharmacokinetics of associated drugs and increasing their adverse effects. Furthermore, pharmacodynamic interactions of coordinated drugs with the same target or with targets belonging to the same signalling cascade may produce unpredictable adverse outcomes. It is well established that patients commonly do not report the use of herbs or other supplements to their medical doctor, placing them at risk for potentially hazardous interactions with ongoing therapies. To date, clinical trials do not provide data for serious adverse effects linked to the oral administration of herbal medicines; however, this finding should be contextualised within the short treatment regime and restricted follow-up used in investigated trials [4]. The use of herbal agents in

patients with autoimmune diseases is not recommended because of their potential to intensify the immune response [3].

Drug Interactions

Drug interactions, substantial increases or reductions in drug exposures may result in toxicity or therapeutic failure. The potential of an herbal preparation or a herbal constituent to increase plasma concentration of a concomitant drug through inhibition of a cytochrome P450 (CYP) enzyme can be readily estimated by a simple in vitro determination of the IC50 or Ki value, coupled with measurement of aqueous solubility or the discounting of mechanistic information [2]. When done carefully, this procedure can yield order-of-magnitude estimates that distinguish among ingredients that are likely to result in a significant interaction, those with solely a moderate effect, and those with a negligible potential for interaction. Herbal preparations also exhibit a broad range of induction effects, and many induce multiple enzymes and transporters. Prediction of induction-derived changes in plasma concentrations is in its infancy, but inhibition and induction of P-glycoprotein (P-gp) and other transporters can contribute to alterations of systemic drug exposure and need to be considered. Phase II enzyme and transporter effects also have to be assessed. The failure to seek substantial reductions in anticancer drug plasma concentrations during clinical trials with St John's Wort has contributed to much avoidable patient suffering [4]. A variety of other therapeutic regimens are the subjects of current concern, including protease inhibitors, immunosuppressants, statins, benzodiazepines, anti-arrhythmic drugs, and beta blockers. The initial, and by far dominant, focus is on the potential for herbal constituents to reduce therapeutic efficacy, because medical practitioners and patients are generally unaware that herbal intake might carry any potential for adverse consequences [3].

Regulatory Considerations

Regulatory frameworks for herbal medicines largely remain disjointed from those of conventional Western drugs, often adapting standards for chemical entities in a manner that allows herbal products to circumvent stringent pharmaceutical regulations [1]. For instance, the U.S. Food and Drug Administration applies less rigorous criteria to herbal preparations than to pharmaceutical drugs. Similarly, the European Medicines Agency enforces distinct registration protocols aligned with the 2004 Traditional Herbal Medicinal Products Directive (Directive 2004/24/EC). Consequently, many herbal products are marketed with incomplete identification, lacking essential information on safety, efficacy, dose, and interactions. Overall, systemic investigation of the immunomodulatory effects of herbal medicines in global markets remains scarce and fragmented despite the widespread and increasing use of over-the-counter herbal immunomodulators in several countries [3].

Future Directions in Research

Herbal immunomodulators have long captivated researchers for their immune-boosting potential. Global prospects for their discovery benefit from understanding the wealth of traditional herbal systems and their rich medicinal chemistry [1]. Although unresolved questions remain, mechanisms and examples outlined in this review spotlight avenues for research that could generate potent herbal immunostimulants [4]. Medicinal herbs often combine sterols, lactones, saponins, terpenoids, phenolics, alkaloids, polypeptides, oligo- and polysaccharides, and essential oils in particular proportions [3]. Pathogen recognition receptor agonists polyphenols, arabinogalactan proteins, acemannan, β-glucans, and sulphated polysaccharides, evoke general immunostimulatory responses. Compounds capable of conferring high degrees of organ-specific immune modulation, such as andrographolide, deoxymatricarin, and palmatine, must be sought [3, 4].

Cultural Perspectives on Herbal Use

The perception of herbal immunomodulators varies significantly across cultures and historical periods. Some medicinal plants and their extracts are highly valued, while others may be feared or viewed as inferior to pharmaceutical products, regardless of documented protective benefits [3]. Traditional beliefs about the conditions that favor the proliferation of certain microbial groups also show cultural variation; for example, in many Western traditions, brown, red, or black colours are associated with infection or decay, whereas in traditional Chinese medicine, green or blue hues may indicate harmful microbial activity [1]. Despite these variations in perception, there is a well-documented relationship between certain cultures and specific medicinal plants [3].

Comparison with Conventional Immunomodulators

The immune response regulates homeostasis, limits tissue damage, and prevents infections by micro- or macroscopic invaders, toxin molecules, or malignant cells. Immunomodulators, which influence the immune response, can either stimulate or suppress immune function [1]. Herbal immunomodulators are known to either promote or normalize the body's physiological functioning or to prevent and cure tissue damage caused by physical, chemical, or infectious agents. When the immune response has been suppressed by drugs, hereditary

diseases, or environmental hazards such as pollution, immunomodulatory herbs may prove to be an attractive and comparatively safer alternative to conventional synthetic substances [1]. Standard immunomodulators are synthetic substances that affect the immune system. Cyclosporin A, tacrolimus (FK506), azathioprine, cyclophosphamide, and methotrexate have all been used as immunosuppressants and are beneficial for organ-transplant patients or individuals with autoimmune diseases. While their immunosuppressive properties are usually beneficial, these compounds exhibit side effects that include allergy, kidney damage, hepatotoxicity, febrile neutropenia, hypertension, and vomiting [1]. In contrast, immunostimulants based on Levamisole, Isoprinosine, and Lysozyme tend to be appliances rather than medications. Although they have immunostimulatory powers, the necessary pharmacokinetics and pharmacodynamics have not been established, and are often surpassed by the efficacy of naturally occurring components extracted from medicinal plants and their derivatives. Table 1 aggregates data on the safety, toxicity, and efficacy of these and similar substances with a focus on five well-studied herbs. These range from curative, supportive, to prophylactic immunostimulatory effects [3].

Patient Perspectives and Acceptance

In recent years, there has been increased interest in the use of herbal immunomodulators as complementary and alternative medicines as patients seek more natural and holistic approaches to health [1]. Surveys indicate that a significant proportion of patients taking conventional medicines also use herbal remedies, although the level of open disclosure to physicians and the reasons for not doing so remain unclear. Other factors influencing the choice to use herbal agents include the perception of immune enhancement and disease prevention, financial considerations, and a preference for natural treatments. Herbal medicines are widely used from the early years of life and during pregnancy despite limited safety data [10]. The diversity of opinions regarding herbal immunomodulator use and the lack of uniform terminology may contribute to variations in patient acceptance and compliance. Further in-depth studies are necessary to understand patient perspectives and choices regarding these agents [4].

Ethical Considerations

The expansion in the use of herbal supplements has resulted in increased interest in the immune system regulatory properties of traditional medicinal plants [1]. Despite the extensive literature documenting the effects of herbal immunomodulators on immune responses, there remain considerable gaps in knowledge about their mechanisms of action and clinical applications. Although herbs can modify pathogenic processes at multiple regulatory levels, elucidating these mechanisms requires further investigation [1]. Increased understanding of the underlying functions of herbal immunomodulators will facilitate the development of novel therapeutic agents with higher efficacy and fewer side effects. Such research could also provide new tools for exploring immune mechanisms and complementary therapies to enhance both conventional and alternative treatment approaches [1]. Herbal remedies have been used for thousands of years to treat and prevent various health problems. Investigation into herbal biological activity and phytotherapy had a significant impact on the development of scientific medicine in the last century [1]. With the advances of allopathic medicine and immunological research, herbal medicines were somewhat overlooked in the biomedical community. However, recent immunological studies clearly indicate that many medicinal plants exert immunomodulatory effects and provide scientific support for traditional belief systems [1]. The immunomodulating properties of medicinal plants are actively studied, and several commercial products available in different countries are based on these properties. Plants provide a large reservoir of chemically diverse compounds and formulation possibilities, offering new opportunities in immunomodulatory drug discovery [1].

Methodological Challenges in Herbal Research

One of the primary challenges in evaluating clinical research on herbal immunomodulators is the robustness of study designs. If reports have advocated insufficiently rigorous trial designs that may compromise the reliability of findings, the issue of design rigor remains a crucial concern [1]. Although various choices exist for study design, such as randomized placebo-controlled trials or open-label studies, the preference for randomized placebo-controlled designs reflects their superior standard, especially for studying efficacy [1]. Good quality randomized controlled trials reveal positive evidence for herbal immunomodulators, whereas other study designs frequently produce inconsistent results. Corroborative evidence arises from observational studies and meta-analyses that also demonstrate positive utility. Studies focusing on Echinacea consistently produce uniformly positive evidence, whereas more heterogeneity characterizes investigations of Astragalus or ginseng [4]. Additional methodological difficulties arise from the lack of consensus on standardized methodologies for assessing immunomodulatory properties and the considerable variability inherent in herbal preparations. This variability, pronounced among popular immunomodulators such as Echinacea, Astragalus, and ginseng, complicates the support of claims by a universally accepted mechanism of action and should be addressed before embarking on clinical studies [4].

Integration into Modern Medicine

Modern medicine incorporates herbal immunomodulators as complementary therapies to conventional treatments. A large segment of the global population depends primarily on herbal medicines, with recent surveys indicating steady growth in the use of botanical-based medicines as prophylactic and health supplements worldwide [1, 2]. Interest in herbal immunomodulators as immune-enhancing agents is robust and increasing. Several plant species with a concentration on Indian medicinal plants have been explored for their implied immunomodulating abilities [1]. There is an urgent need to investigate and document the potential of plants that are believed to boost the body's natural defenses and treat chronic and infectious diseases to develop potent drug candidates for selective immunomodulation with minimal side effects. Semi-synthetic and synthetic methods may be used to improve the bioavailability and selectivity of herbal immunomodulators [2].

Case Studies

The immunomodulatory efficacy of herbal formulations manifests compellingly in a herbo-mineral Ayurvedic preparation, IMMBO, which integrates Mandoor Bhasma with 18 selected herbs. Clinical observations denote IMMBO's efficacy in managing allergic rhinitis, an immunological disorder characterized by histamine-mediated hypersensitivity [10]. In a spectrum of experimental protocols employing immunosuppressed rats, the formulation restores neutrophil activation and enhances both cellular and humoral immune responses. Molecular investigations reveal that IMMBO counteracts immunosuppressive agents, selectively modulating critical signaling mediators such as TNF-α, IFN-γ, IL-1β, ERK, PI3K, and NF-κB, thereby implicating a multifaceted mechanism of immune regulation. The capacity to inhibit histamine release further underscores its potential in attenuating allergic manifestations. Despite these insights, the comprehensive mechanistic architecture of IMMBO's action remains to be elucidated, warranting dedicated pharmacological scrutiny [10]. Among natural immunomodulators, Echinacea stands as a paradigmatic example. The genus comprises nine herbaceous species endemic to North America, with E. purpurea, E. angustifolia, and E. pallida enjoying long-standing ethnomedicinal utilization against respiratory infections and inflammatory conditions, ranging from cold and cough to bronchitis and oropharyngeal inflammations [10]. The marketplace offers a variety of formulations, including fresh and dried aerial parts, rhizomes, roots, and alcoholic extracts, often in polyherbal combinations. Echinacea remains among the top-selling botanicals in the U.S. and Europe. Phytochemical investigations attribute its immunomodulatory prowess primarily to alkamides and caffeic acid derivatives, which collectively stimulate macrophage phagocytosis and natural killer cell activity, positioning the species as a potent immune promoter [4]. Clinical trials, however, prompt cautious interpretation due to the absence of standardization and variable quality; nonetheless, certain E. purpurea preparations demonstrate statistically significant reductions in the severity and duration of cold symptoms [10].

Global Usage Patterns

Several population surveys of herbal medicine usage have been published in recent years that have an important bearing on the increasing commercial importance of herbal/specialty products. In the USA, about 30–50 % of the general population has used at least one form of alternative or complementary medicine either once or regularly [10]. In the United Kingdom (UK), the prevalence was a staggering 71.4 % in the year 2000, and was predicted in 2005 to surpass 70 million individual visits a year at an annual cost of £390 million. Worldwide usage of herbal medicine was clearly benefited by Governmental initiatives supportive of research and commercialization in China, Japan, and South Korea [10]. These Government-sponsored schemes have encouraged the development of herbal products for everyday use in these countries. This has been accompanied by complementary usage, usually under the combined supervision of a Western-trained medicine practitioner and a traditional medicine expert. Particular value is now assigned to those herbal medicines that have been subject to extensive scientific research, while high-tech industrial non-traditional herbal products are usually the most acceptable [11, 12].

CONCLUSION

Herbal immunomodulators represent a dynamic interface between traditional medicine and modern immunology, offering both opportunities and challenges in clinical application. Evidence supports their ability to influence key immune pathways, reduce infection severity, and enhance resilience, particularly with well-studied agents such as *Echinacea*, *Astragalus*, *Ginseng*, *Elderberry*, and *Turmeric*. However, the therapeutic utility of these botanicals remains constrained by inconsistent study designs, lack of standardized preparations, safety concerns, and regulatory gaps. Herb–drug interactions and risks of immune overstimulation or suppression require careful clinical consideration, particularly in vulnerable populations. Despite these limitations, herbal immunomodulators hold substantial promise as complementary or adjunctive therapies when integrated with conventional medicine. Advancing this field will require rigorous clinical trials, standardized quality control, and mechanistic studies to

establish safety, efficacy, and therapeutic relevance. With thoughtful integration, these botanicals could provide safer, more accessible options for immune modulation and global health improvement.

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CITE AS: Mpora Kakwanzi Evelyn (2025). Narrative Review of Herbal Immunomodulators. IDOSR JOURNAL OF EXPERIMENTAL SCIENCES 11(3): 52-59.
https://doi.org/10.59298/IDOSR/JES/113.5259