



Advanced approaches to immunomodulation in clinical practice: Analysis of dietary supplements and medicines

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Abstract. The purpose of the study was to establish the immunomodulatory properties of herbal remedies and the prospects for their clinical implementation. The methodology was based on a theoretical and analytical generalisation of literature data on the immunomodulatory properties of preparations “Immunormalin”, “Immunal”, Asian ginseng, *Ginkgo biloba*, common marigold, and shiitake mushrooms. The results of the analysis showed that “Immunormalin” was marked by a wide range of mechanisms, combining antioxidant, anti-inflammatory, prebiotic, and sedative effects, which simultaneously covered immune, metabolic, and neuroendocrine pathways. This multifactorial nature distinguished it from more highly specialised products and determined a special position among nutraceuticals. In contrast, “Immunal”, created based on *Echinacea purpurea*, demonstrated a directed immunomodulatory mechanism through the activation of macrophages and T-lymphocytes, which made it mainly effective in the prevention of respiratory infections. Asian ginseng combined the properties of an adaptogen and an immunomodulator, causing increased resistance of the body to infections and the formation of antitumour potential. *Ginkgo biloba*, sharing an antioxidant and anti-inflammatory effect with ginseng, had an additional vascular-regulating effect, which expanded its use in chronic pathologies and complex therapy of metabolic syndromes. *Calendula officinalis* showed the most pronounced anti-inflammatory profile among the compared agents, since it suppressed the production of pro-inflammatory cytokines and stimulated the secretion of anti-inflammatory mediators, which reduced the risk of tissue damage in long-term inflammatory processes. Shiitake mushrooms, due to their beta-glucan content, acted as natural adjuvants, enhancing the cellular immune response and combining antiviral and antitumour activity. Generalisation of the results showed that natural immunomodulators have a common antioxidant effect, but differ in multifactorial and clinical orientation, which determines the need for standardisation and differentiated use. The results obtained can be used by clinicians, pharmacologists and researchers in the field of evidence-based herbal medicine to optimise the selection of immunomodulatory agents and develop standardised approaches to their use

Keywords: inflammatory process; cytokines; macrophages; lymphocytes; interleukins; bioactive compounds; infections

✦ INTRODUCTION

Infectious diseases and complications that occur against the background of immune dysfunction in patients with chronic pathologies substantiate the need to find new approaches to immune correction. Immune insufficiency is accompanied

by a tendency to severe infections, a decrease in the effectiveness of immunoprophylaxis, and the development of prolonged inflammatory processes. Attention is paid to the use of phytopreparations and nutraceuticals that contain

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biologically active polysaccharides, saponins, and phenolic compounds that can modify cytokine regulation, activate macrophages and natural killer cells (NK cells) and maintain antioxidant balance. Such drugs are considered as an auxiliary component of complex therapy aimed at strengthening the immune response and preventing complications that occur due to weakened immune reactivity.

Phytopreparations were considered an important component of immunocorrection, as they combined the ability to influence cellular mechanisms of immunity with a relatively low level of toxicity. Administration of plant complexes has been shown to alter interleukin (IL) secretion and macrophage activity, as noted by I. Bielenichev *et al.* [1], and these effects were considered as the basis for integrating herbal remedies into complex therapeutic regimens. The researchers also noted that such approaches created conditions for personalising immune support depending on the clinical context. Generalisation by C. Burlou-Nagy *et al.* [2] showed that multicomponent phytopreparations stimulated phagocytic activity and cytokine production, which provided an increase in innate and adaptive responses. The researchers further emphasised that it was the multi-factorial nature of the action that opened up opportunities for their use in preventive strategies. Review by J.A. Valdés-González *et al.* [3] summarised the pharmacological properties of polysaccharides and ginsenosides that modified inflammatory cascades and activated the antitumour immune response. These results were interpreted as confirming the role of plant metabolites in supporting the body in cancer and inflammatory processes.

Plant bioactive complexes have a multi-vector effect on the immune system, activating cells of innate and adaptive immunity and regulating cytokine balance. It was found that polysaccharides of Asian ginseng (*Panax ginseng*) modified the function of macrophages and T-lymphocytes, altering IL secretion and stimulating proliferation, as reported by Y. Hu *et al.* [4]. These results demonstrated the potential of ginseng as a basis for the development of standardised immunotherapy drugs. Systematic analysis performed by N. Mohamed [5] combined data on polysaccharides of various medicinal plants and showed their ability to comprehensively affect immune regulation. The researcher also emphasised the lack of sufficient standardisation of these compounds, which poses a serious problem for their clinical implementation.

Extracts of *Ginkgo biloba*, as evidenced by M.A. Ibrahim *et al.* [6], reduced the expression of pro-inflammatory genes and increased the activity of effector cells in models of viral infections. The data obtained confirmed the prospects of ginkgo for the further development of antiviral immunomodulators of natural origin. The study by A.M. Samoilenko [7] proposed a technology for creating a tablet form of an antiviral agent from plant raw materials. The paper emphasised the complexity of optimising the composition and proving the effectiveness of such drugs, which remains an unsolved problem of contemporary pharmaceutical science. The study by D. Silva *et al.* [8] has shown that extracts of common marigold (*Calendula officinalis*) suppressed the production of tumour necrosis factor alpha (TNF- α) and other pro-inflammatory mediators, which reflected their anti-inflammatory and regulatory potential. These observations highlighted the possibility of

using common marigold in the treatment of inflammatory pathologies with a complex immune component. The study by B.G. Oliveira *et al.* [9] demonstrated that extracts of purple coneflower (*Echinacea purpurea*) activated cytokine production and enhanced the antibacterial response, which provided a powerful defence of the body against infectious agents. The researchers showed that the use of dried extracts has little promise in both the prevention and treatment of diseases with impaired immune balance.

Complex immunocorrection includes both synthetic drugs and natural bioactive compounds that have demonstrated the ability to influence cellular pathways of immune regulation. Polysaccharides from shiitake mushrooms (*Lentinula edodes*), as shown by A. Roszczyk *et al.* [10], interacted with macrophage and dendritic cell receptors, resulting in increased cytokine production and activation of immune cascades. The researchers also proved that beta-glucans of the mushroom increase the body's ability to respond to antitumour and antiviral drugs. A systematic review by M. Vlassopoulou *et al.* [11] summarised data from clinical trials in which fungal beta-glucans showed a decrease in the incidence of infections in patients with immune deficiency. These results confirmed the promising use of fungal polysaccharides in preventive medicine. Generalisation by L.F. Popovici *et al.* [12] highlighted that extracts of *Calendula officinalis* combined anti-inflammatory and immunomodulatory effects, so they were used in pharmaceutical compositions. The researchers also emphasised the importance of this plant as a source of bioactive compounds for the creation of new phytopreparations.

Despite a significant amount of research, there are still gaps in the standardisation of plant immunomodulatory agents and evaluation of their clinical efficacy. The purpose of the study was to find out the mechanisms of immunomodulatory action of bioactive compounds and preparations of plant origin and determine their significance for clinical immunocorrection.

★ MATERIALS AND METHODS

The study was of a theoretical and analytical nature and was aimed at systematising literature data on the immunomodulatory properties of phytopreparations and dietary supplements. Six drugs and plant extracts were selected for analysis, combining the presence of a clinical evidence base, pharmacological prevalence, and availability in standardised forms. Among them, a separate place was occupied by "Immunormalin" (sole proprietor Sarkis Gagikovich Avakian, Ukraine), presented as a biologically active supplement developed by S.G. Avakian, which included extracts of common horsetail (*Equisetum arvense* L.), flowers of small-leaved linden (*Tilia cordata* Mill.), leaves of black currant (*Ribes nigrum* L.), wild chamomile (*Matricaria chamomilla* L.), common chicory (*Cichorium intybus* L.), common knotgrass (*Polygonum aviculare* L.), peppermint (*Mentha piperita* L.) and fruits of burnet rose (*Rosa pimpinellifolia* L.); its characterisation was based on available materials describing the mechanisms of action and efficacy in clinical applications. In the group of conventional herbal medicine preparations, the drug "Immunal" (Sandoz, Switzerland) was considered, which contained dry and liquid extracts of purple coneflower (*Echinacea purpurea*) and it was studied in various forms – from tablets of

80 mg (240-320 mg/day) to a solution of 2.5 mL three times a day [13-15]. Asian ginseng (*Panax ginseng*) was considered as an example of an adaptogenic agent based on clinical trials using encapsulated dry root extract at doses of 200-400 mg/day [16, 17]. To reflect the neuroprotective and antioxidant effects, *Ginkgo biloba* was analysed, presented in the studies in the form of tableted extracts standardised for ginkgoflavonglycoside content (120-240 mg/day) [18, 19]. The anti-inflammatory potential of herbal remedies from *Calendula officinalis* has been illustrated, which was used in clinical settings mainly in the form of alcohol tincture of 20-30 drops three times a day [20, 21]. Shiitake mushroom (*Lentinula edodes*) extract was included in the analysis described in publications as a encapsulated powder of β -glucans at doses of 1-3 g/day, which was characterised by a pronounced immunomodulatory effect [22, 23]. The choice of these products was determined by their ability to represent various groups of natural immunomodulators – from complex developments by researchers to classic herbal remedies and nutraceuticals of fungal origin. This approach allowed covering a wide range of mechanisms of action, including stimulation of the cellular and humoral immune response, anti-inflammatory effect and antioxidant protection, and also provided an opportunity to compare various pharmacological strategies in the analysis.

As part of the analytical approach, the evaluation of drugs was carried out at two levels: immunological and clinical. At the immunological level, data on macrophage activation, T-lymphocyte proliferation regulation, B-lymphocyte (bone marrow lymphocyte) functional activity, natural killer cytotoxicity, and the balance of pro-inflammatory and anti-inflammatory cytokines, in particular IL and TNF- α , were considered. The clinical level included analysis of such indicators as the frequency of infectious complications, the duration of the course of diseases, the effectiveness of immunoprophylaxis, and the severity of correction of inflammatory processes. The choice of publications under study was based on the availability of standardised forms of drugs, a sufficient evidence base in the form of randomised clinical trials or experimental models, a clear description of dosages, and the availability of safety profile data. As part of the study, natural immunomodulators were compared by their mechanisms of action, clinical effects, level of evidence and safety profile, which provided an opportunity for a comprehensive assessment of their therapeutic potential.

The choice of the publications was based on several criteria: for registered medicines and dietary supplements of international production – the availability of standardised release forms, described dosages, data from randomised clinical trials or preclinical models, and a safety profile. The inclusion of “Immunormalin” in the analysis was conditioned by its use in practice as a biologically active additive of Ukrainian production and the original design by S.G. Avakian. The authors noted that they have no commercial or personal interest in promoting the product, and the results and conclusions of the study are presented solely for scientific purposes. Despite the lack of standardised publications and open data on the composition, the drug continued to be considered in the context of potential use in clinical immunocorrection. Its consideration demonstrated the presence in national

practice of drugs that claimed an immunomodulatory effect, but required further scientific verification. The limitation was that the study was theoretical in nature and was based on the analysis of already available data without conducting its own clinical trials.

✦ RESULTS AND DISCUSSION

Immunomodulatory drugs: Clinical effects and mechanisms of action. Immunomodulatory drugs are a separate group of agents whose action is aimed at restoring or correcting the functional activity of the immune system. In clinical practice, they are used both for the prevention and treatment of infectious, inflammatory and immunodeficiency conditions. Different classes of immunomodulators differ in origin, composition and spectrum of active mechanisms, but they are united by their ability to influence cellular and humoral links of immunity. Plant complexes containing a rich set of polyphenols, polysaccharides, essential oils, and vitamins exhibit a mild, multi-vector effect, combining anti-inflammatory, antioxidant, and adaptogenic properties. The drug “Immunormalin” is a multicomponent dietary supplement in the form of an oral solution and suppositories, which includes a complex of plant extracts in combination with ascorbic acid, citric acid, and sodium benzoate. The bioactive composition includes polyphenols, anthocyanins, flavonoids, phenolic acids, essential oils, and inulin, which determines antioxidant, anti-inflammatory, prebiotic, and sedative mechanisms of action. The recommended dosage was 5-10 mL of the solution 1-2 times a day for a course of 2-4 weeks.

The results of the analysis of the scientific literature showed that black currant extracts were characterised by high concentrations of anthocyanins and phenolic acids, which neutralised free radicals, stabilised cell membranes, and maintained the viability of immunocompetent cells. Polyphenols of this plant also regulated the production of pro-inflammatory and anti-inflammatory cytokines, reduced the intensity of inflammation, and enhanced the barrier function of the airway epithelium. M. Oczkowski [24] proved that bioactive compounds of *Ribes nigrum* L. had a pronounced antioxidant and immunomodulatory effect, which corresponded to the effects of this component in the drug. It was found that rosehip fruits contained phenolic acids, ascorbic acid, and biologically active fatty acids, which enhanced antioxidant protection, activated collagen synthesis, and accelerated tissue repair. Simultaneously, they reduced the secretion of TNF- α and IL-6, which contributed to the regulation of the humoral link of immunity. These effects were confirmed by the M. Pashaei & H. Hassanpour [25], who showed that *Rosa pimpinellifolia* L. combined antioxidant and anti-inflammatory properties, which justified its importance as a basic source of antioxidants in the drug.

Literature data have shown that chamomile extracts contain flavonoids, coumarins, and essential oils that inhibit the expression of pro-inflammatory mediators (TNF- α , IL-1 β , IL-6) and stimulate IL-10 secretion. This action helps to reduce the hyper-inflammatory response and restore immune homeostasis. A.I. Drif *et al.* [26] found that *Matricaria chamomilla* L. had significant anti-inflammatory and antitumour potential due to inhibition of NF- κ B and reduced levels of pro-inflammatory cytokines, which confirmed its role

in normalising the immune response in multicomponent formulas. Linden and peppermint extracts provided sedative and antispasmodic effects, reduced catecholamine secretion, and stabilised the hypothalamic-pituitary-adrenal axis, thereby reducing stress-induced immunosuppression. In addition, the bioactive substances of these plants had a moderate anti-inflammatory effect due to the regulation of cytokine release. B. Kadioğlu & S. Kadioğlu [27] confirmed that plants with adaptogenic and sedative properties were actively used during the coronavirus pandemic to maintain resistance, which was consistent with the use of linden and peppermint in the preparation.

Analysis of publications has shown that common chicory acts as a source of inulin, which stimulates the growth of bifidobacteria and lactobacilli in the intestine. Metabolites of short-chain fatty acids formed during fermentation affect the differentiation of T-lymphocytes and the function of dendritic cells, establishing a balanced mucosal immunity. This mechanism corresponds to the current concept of “gut-immunity”, which is considered as a key factor in maintaining systemic immune regulation. The analysed data also confirmed that common horsetail and common knotgrass enrich the formula with silicon compounds, phenolic acids, and flavonoids, which exhibit antioxidant and anti-inflammatory activity. This is associated with an increased cytoprotective effect and maintaining antioxidant balance in immune cells. The findings of T. Kadiyska *et al.* [28] emphasised that multicomponent phytopreparations implemented a synergistic mechanism of action, combining antioxidant, anti-inflammatory and adaptogenic effects, which fully corresponded to the role of horsetail and knotgrass in the composition of the drug.

The drug “Immunal” belongs to the immunomodulatory agents of plant origin due to the use of a standardised extract of *Echinacea purpurea*. Its creation was aimed at providing a reproducible concentration of biologically active substances, which was important for maintaining clinical effectiveness. The dosage form included both 80 mg tablets and a liquid solution in doses of 2.5 mL three times a day, which made it possible to individualise therapy and increase the convenience of use. Due to the combination of alkylamides, phenolic compounds, and polysaccharides, the drug was able to affect various parts of the immune system. The published results of experimental models showed that the intake of the *Echinacea purpurea* extract stimulates macrophage activation, increases phagocytosis, and the production of pro-inflammatory cytokines of the first line of defence. An increase in T-lymphocyte proliferation and stimulation of IL-2 secretion, which activates the cellular response against viral and bacterial pathogens, were recorded. Such data reflect the role of the drug as a regulator of the early stages of the immune response. The study by S.F. Vieira *et al.* [13] showed that it was the combination of macrophage stimulation and T-lymphocyte activation that explained the increase in non-specific resistance when using the purple coneflower. The researchers stressed that this effect was important not only for the treatment, but also for the prevention of infections, as it formed a more balanced immune response. Clinical results showed that “Immunal” significantly reduced the frequency of episodes of acute respiratory infections, reduced the intensity of symptoms and the duration of the course of diseases.

Patients who used the drug during preventive courses showed faster recovery of immunological parameters and less often needed additional drug therapy. These results were confirmed in a randomised placebo-controlled trial conducted by S.K. Lee *et al.* [14], which showed that the systematic use of the *Echinacea purpurea* extract increased the effectiveness of immunoprophylaxis among the adult population. The researchers noted that the clinical effect of the drug was particularly noticeable in patients with an increased risk of respiratory diseases, and also noted that the reproducibility of these results was possible due to the standardised composition of the drug, which ensured the stability of the therapeutic effect.

Thus, an important characteristic of “Immunal” was its standardisation. While purple coneflower-based dietary supplements showed significant composition variability, the registered drug provided stable levels of active substances. A. Demyd *et al.* [15], using high-performance thin-layer chromatography, demonstrated that it was the dosage forms that had the most reproducible profile, while additives often differed in the content of bioactive components. This confirmed that clinical results can be associated primarily with the use of standardised drugs, and not with uncontrolled forms. Another important property of this drug is its ability to affect the balance of cytokines. There was a decrease in the secretion of excess pro-inflammatory mediators, including TNF- α and IL-6, and an increase in the level of anti-inflammatory IL-10. This mechanism helped not only to reduce the severity of inflammatory processes, but also to prevent excessive tissue damage in acute infections. Analysis by S. Choudhary *et al.* [29] confirmed that the immunomodulatory effect of phytoactive compounds from purple coneflower was combined with the anti-inflammatory effect, which made it suitable for both prevention and adjunctive therapy. The safety assessment showed that “Immunal” had a favourable tolerance profile. Side effects were isolated and mostly limited to mild allergic reactions. Long-term use of the drug in the recommended doses was not accompanied by the development of serious complications. This allowed using this drug in repeated courses, in particular in periods of increased seasonal morbidity.

Generalisation of literature sources showed that plant immunomodulatory complexes, in particular “Immunormalin” and “Immunal”, were characterised by a combination of antioxidant, anti-inflammatory, adaptogenic, and prebiotic effects. Publications have indicated that their use is associated with reducing the frequency and duration of respiratory infections, restoring cytokine balance, and maintaining immune homeostasis. The standardised composition and favourable safety profile emphasise the potential of these drugs as a component of strategies for immunocorrection and prevention of infections in clinical practice.

Adaptogenic herbal remedies and their effect on immunity. Ginseng belongs to adaptogens because its bioactive compounds combine the ability to regulate stress responses and simultaneously affect the immune system. The plant contains ginsenosides, polysaccharides, and other metabolites that determine the multi-vector mechanism of action. As part of the analysis results, it was shown that ginseng modulated cellular and humoral links of the immune response, increased resistance to infectious agents, and maintained a balance between pro-inflammatory and

anti-inflammatory responses. It was found that water-soluble ginseng polysaccharides activate phagocytosis, stimulate the production of nitric oxide and IL by macrophages, and enhance the differentiation of T-lymphocytes. In addition, the results of the analysed experimental models showed that these biopolymers can increase the secretion of interferons, which play a leading role in antiviral protection. The findings by L. Cui *et al.* [16] confirmed that ginseng flower heteropolysaccharides activated macrophages and T lymphocytes, and induced the secretion of IL-2 and IFN- γ (interferon-gamma), which was crucial for the development of an effective cellular response.

Data from analysed preclinical studies have shown that standardised extracts of *Panax ginseng* stimulated cytotoxic activity of NK cells and cytotoxic T-lymphocytes, which was manifested in the growth of elimination of virus-infected cells and in inhibition of tumour development in model organisms. In parallel, there was a decrease in the levels of pro-inflammatory cytokines, in particular, TNF- α and IL-6, and stimulation of the secretion of anti-inflammatory IL, such as IL-10, which ensured the maintenance of immune balance and reduced the severity of inflammatory responses. Generalisation made by Z.A. Ratan *et al.* [17] confirmed these results, indicating that the adaptogenic effects of ginseng were closely related to the ability of ginsenosides and polysaccharides to activate the cytotoxic function of T-lymphocytes and NK cells, block the activation of NF- κ B and other signalling pathways. As a result, the production of pro-inflammatory mediators was simultaneously suppressed and the antitumour response was enhanced, which made ginseng a promising candidate for integration into antitumour immunotherapy regimens and correction of chronic inflammatory conditions.

The analysis showed that ginseng had a pronounced antioxidant effect, which was implemented by reducing the level of reactive oxygen species and activating antioxidant defence enzymes – superoxide dismutase and catalase. This helped to protect cells and tissues from oxidative damage, which usually accompanies chronic inflammation and immune dysfunctions. M. Balasubramaniam *et al.* [30] interpreted this mechanism as a key factor in the anti-inflammatory effect of ginseng, which allowed increasing its effectiveness in the complex therapy of inflammatory pathologies. This effect is particularly important in the context of low-grade chronic inflammation, where immune overactivation and oxidative stress act as parallel damaging factors [31]. The results of clinical trials showed that the use of standardised ginseng extracts reduced the incidence of acute respiratory infections, and reduced the duration of the course of diseases. Patients who took capsulated forms of the drug at doses of 200-400 mg per day showed faster recovery of immunological parameters compared to the control group [17]. The review by C.J.W. Liang *et al.* [32] confirmed that *Panax ginseng* was characterised by low toxicity and good tolerability, and the risk of side effects remained minimal even with prolonged use, which justified its inclusion in preventive regimens.

Ginkgo biloba is one of the most studied herbal remedies, combining antioxidant, anti-inflammatory, and immunomodulatory properties. Its standardised extracts contain ginkgoflavonglycosides and terpenoid lactones, which provide a wide range of biological activity [33]. The results

of the analysis showed that the use of ginkgo extracts led to a decrease in the expression of pro-inflammatory genes and an increase in the activity of effector cells, including NK cells and cytotoxic T-lymphocytes. Simultaneously, there was a restoration of cytokine balance regulation by inhibiting TNF- α and IL-6 secretion and stimulating IL-10 production. This reflected the drug's ability to strengthen natural immune defences and reduce the severity of chronic inflammation. These results were consistent with the findings of H.M. Abdel-Latif *et al.* [18], who proved that leaf extract of *Ginkgo biloba* activated immune cells, modified the transcription of cytokine genes, and provided multi-level control of the immune response.

Data from experimental models also showed that ginkgo extracts had the ability to enhance the body's antioxidant defences. The cells showed a decrease in the level of reactive oxygen species, activation of antioxidant enzymes – superoxide dismutase and glutathione peroxidase, and stabilisation of mitochondrial membranes. This was crucial for reducing oxidative stress, which often accompanies immune dysfunctions and chronic pathologies. In this context, R. Das *et al.* [19], interpreted the antioxidant effect of *Ginkgo biloba* as one of the factors of maintaining cellular integrity and resistance of the body to immune-dependent diseases. Clinical data have shown that the inclusion of ginkgo in therapeutic regimens reduces the incidence of exacerbations of chronic diseases associated with an imbalance of the immune system and improves the overall immune status of patients. According to S.N. Mousavi *et al.* [34], using standardised extracts of *Ginkgo biloba* at doses up to 500 mg/day, IL-6 levels were reduced, which indicated their anti-inflammatory potential. The researchers emphasised that it was the suppression of pro-inflammatory cytokines that explained the clinical benefits of ginkgo in conditions associated with chronic inflammation.

In addition to the effect on the immune system, *Ginkgo biloba* had a positive effect on microcirculation and endothelial function, which created additional conditions for an optimal immune response. In clinical and experimental observations, there was an improvement in blood supply to tissues, a reduction in ischaemic damage, and normalisation of metabolic processes. This complex effect made allowed using ginkgo as a universal agent that can be integrated into therapeutic schemes of various profiles. F.G. Barbosa *et al.* [35] confirmed that the multifactorial action of *Ginkgo biloba* makes it a promising representative of plant immunomodulators with clinically significant effects. The safety of the drug also remained an important aspect. Ginkgo has been shown to be characterised by low toxicity and good tolerability even with prolonged use. Simultaneously, the need for strict compliance with standardised dosages was noted, because their excess could change the pharmacokinetic profile and reduce therapeutic efficacy, which was consistent with the conclusions of F. Buonfiglio *et al.* [36]. The researchers emphasised that it was standardised extracts that guaranteed clinical reliability and reproducibility of effects, while deviation from optimal doses could pose a risk to patients.

The results of the analysis showed that adaptogenic herbal remedies, in particular *Panax ginseng* and *Ginkgo biloba*, had a complex effect on the immune system, combining activation of cellular and humoral links with

regulation of the cytokine profile, antioxidant and anti-inflammatory effects. Ginseng was effective in stimulating the antiviral and antitumour response, while ginkgo provided an additional neuroprotective and vascular-regulating component that enhanced its immunomodulatory potential. Both drugs were characterised by good tolerability and low toxicity, which justified their use in both preventive and therapeutic regimens. Thus, their multifactorial action and the presence of a clinical evidence base make these drugs promising in strategies for maintaining and correcting immune function.

Anti-inflammatory phytonutrients and mushroom extracts with immune activity. Studies of anti-inflammatory immunomodulatory phytonutrients have led to a detailed investigation of *Calendula officinalis*, which has become a model for analysing the relationship between plant bioactive compounds and mechanisms of immune response regulation. Its extracts include flavonoids, saponins, triterpenoids, carotenoids, and essential oils, which cause a wide range of biological effects. Of particular importance is the anti-inflammatory and immunomodulatory activity associated with the regulation of the cytokine profile and inhibition of key pro-inflammatory mediators.

Analysis of the results of preclinical models showed that common marigold extracts reduced the production of pro-inflammatory cytokines such as TNF- α , IL-1 β , and IL-6. In parallel, an increase in the secretion of anti-inflammatory IL-10 was observed, which provided a restoration of regulation between pro- and anti-inflammatory processes. This reflected the plant's ability to reduce excessive immune activation and prevent tissue damage. Such effects were consistent with generalisation by K. Patil *et al.* [20], who stressed that *Calendula officinalis* can influence a wide range of inflammatory mediators and form a balanced immune response. The analysed results showed that the use of alcohol tinctures of common marigold in experimental models of chronic inflammation reduced neutrophil infiltration into the lesion and reduced the activity of cyclooxygenase-2, which reduced the development of prostaglandins. In clinical observations, it was recorded that regular use of standardised forms of common marigold helped to reduce the symptoms of inflammatory diseases of the mucous membranes and skin. These data were correlated with the findings by S.I. Abdelwahab *et al.* [21], who demonstrated that long-term studies of common marigold have confirmed its persistent anti-inflammatory and immunomodulatory activity in various fields of medicine.

The antioxidant effect of *Calendula officinalis* also attracted considerable attention. Its bioactive compounds have been shown to reduce reactive oxygen species levels, restore the balance of antioxidant enzymes, and protect cells from oxidative stress, which often accompanies immune dysfunctions. This is of particular importance in the treatment of chronic inflammatory processes associated with an imbalance of the immune system. Analysis by A.M. Rezende *et al.* [37], confirmed that the active ingredients of common marigold combine anti-inflammatory and antioxidant properties, thereby expanding the range of its clinical use. Clinical results also showed that the use of *Calendula officinalis* extracts in the form of tinctures or tablet forms, it was associated with a decrease in the frequency of infectious complications, a reduction in the duration

of respiratory diseases, and an improvement in overall immune status. Patients showed good tolerability of the drugs, which emphasised their safety in long-term use. Comparative review by G. Dhingra *et al.* [38], generalised that biologically active compounds of common marigold were characterised by low toxicity and high biocompatibility, and therefore could be used as a basis for creating nutraceuticals and phytopreparations with proven immunomodulatory activity.

The study of mushroom extracts in the context of anti-inflammatory immunomodulatory nutraceuticals focused on beta-glucans from shiitake mushrooms. These polysaccharides can affect innate and adaptive immunity by activating macrophages, dendritic cells, and NK cells, and by regulating the cytokine profile. The results of the analysis showed that shiitake beta-glucans stimulated macrophage activity, increasing their ability to phagocytosis, nitric oxide production, and early response cytokine secretion. Simultaneously, dendritic cells were activated, which led to more efficient presentation of antigens and triggering adaptive immune responses. As noted by I. Mirończuk-Chodakowska *et al.* [22], such effects confirmed the role of β -glucans as natural adjuvants that can enhance the effectiveness of the immune system. These results showed the ability of shiitake beta-glucans to act as key modulators between innate and adaptive immunity, making them promising in the prevention and treatment of infectious diseases, in particular viral aetiology.

Analysis of published data showed that β -glucans from *Lentinula edodes* increased the secretion of IL-12, which stimulates the differentiation of T-helpers by Th1 type. This leads to the activation of cytotoxic T-cells and NK cells, which are involved in antitumour and antiviral protection. Inhibition of tumour growth and more intensive elimination of virus-infected cells were observed in the model organisms. C. Cerletti *et al.* [23] confirmed that it was the ability of β -glucans to shift the balance towards cellular immunity that was crucial for their antitumour potential. The use of shiitake extracts was accompanied by inhibition of the synthesis of TNF- α and IL-6, which are key mediators of chronic inflammation. Simultaneously, IL-10 production was increased, which helped to reduce excessive immune activation and prevent tissue damage. E.J. Murphy *et al.* [39] emphasised that even β -glucans obtained from the same mushroom samples could show differences in the strength of the effect on the cytokine profile, which highlighted the need for standardisation of extracts for clinical practice.

In addition to affecting the cytokine balance, beta-glucans of *Lentinula edodes* showed pronounced antioxidant properties. Systematisation of experimental data indicated a decrease in the level of reactive oxygen species and activation of key antioxidant defence enzymes – superoxide dismutase and glutathione peroxidase. This helped to protect cell membranes and mitochondria from oxidative damage. D. Kumar *et al.* [40] interpreted these effects as one of the links in preventing the development of immunodeficiency states and the progression of malignant processes, since reducing oxidative stress allowed increasing cell resistance to damage. The analysed experimental data confirmed that shiitake beta-glucans can reduce lipopolysaccharide-induced inflammatory changes and support

immune regulation. M. Jafari *et al.* [41] showed that extracts of *Lentinula edodes* adjusted haematological parameters and normalised immune response in the acute inflammation model, which indicates their potential as part of immunocorrective agents in immunodeficiency conditions.

Summarising the results of the literature analysis, it can be argued that *Calendula officinalis* and *Lentinula edodes* represent different but complementary areas of natural immunocorrection. *Calendula officinalis* has proven to be an effective anti-inflammatory agent capable of suppressing over-activation of cytokines and protecting tissues from damage, while shiitake beta-glucans have been characterised as universal natural adjuvants that enhance both innate and adaptive immune responses. Both agents simultaneously demonstrated antioxidant properties, due to which they provided multi-level protection of cells and

the body as a whole. The combination of these effects determines their significance in complex therapeutic and preventive strategies aimed at maintaining immune homeostasis and reducing the risk of chronic pathologies.

Comparative efficacy and safety of natural immunomodulators in practice. Generalisation of information about natural immunomodulators allowed identifying common features and differences in their effect on the immune system. Despite the different nature and composition, most drugs combine antioxidant, anti-inflammatory, and immunomodulatory mechanisms, while individual drugs show additional effects – adaptogenic, prebiotic, or sedative. The most characteristic mechanisms of action and clinical effects are systematised in Table 1, which allows clearly assessing their therapeutic capabilities and potential for use.

Table 1. Mechanisms of action and clinical effects of natural immunomodulators

Agent	Basic mechanisms	Key clinical effects
“Immunormalin”	Antioxidant, anti-inflammatory, prebiotic, sedative.	Reduction of the severity of respiratory infections, maintaining immune balance, reduction of stress-induced immunosuppression.
“Immunal”	Macrophage activation, IL-2 stimulation, phagocytosis.	Prevention of acute respiratory infections, reduction of their duration.
<i>Panax ginseng</i>	Adaptogenic effect, activation of T-lymphocytes and NK cells.	Increase of resistance to infections, antitumour potential.
<i>Ginkgo biloba</i>	Antioxidant, cytokine regulation, vascular effect.	Reduction of the frequency of exacerbations of chronic diseases, immune stabilisation.
<i>Calendula officinalis</i>	Inhibition of TNF- α , IL-1 β , IL-6; stimulation of IL-10.	Anti-inflammatory effect, reduction of symptoms of inflammatory conditions.
<i>Lentinula edodes</i>	Activation of dendritic cells, NK cells; increase in IL-12.	Antiviral and antitumour immune response, prevention of recurrent infections.

Source: compiled by the authors

Comparative analysis showed that a common property for all the drugs considered was the presence of antioxidant potential through polyphenols, flavonoids, anthocyanins, or polysaccharides. It was this action that established the basic level of cellular protection, prevented oxidative damage to immunocompetent cells, and created conditions for the normalisation of the immune response. However, the differences were in additional mechanisms that determined the specifics of the clinical use of each drug. “Immunormalin” was noted for its most multi-vector effect, combining antioxidant, anti-inflammatory, prebiotic, and sedative mechanisms. This set it apart from other agents because it simultaneously affected cytokine regulation, the gut microbiota, and the neuroendocrine system. No other drug has demonstrated such complexity. In contrast, “Immunal” acted mainly through the activation of macrophages and T-lymphocytes, that is, it had a more narrowly directed immunomodulatory mechanism, effective mainly for the prevention of acute respiratory infections. Ginseng occupied an intermediate position: its action went beyond purely immunomodulation and included an adaptogenic effect. A common feature with “Immunormalin” was multivariate regulation, but the difference was the predominant emphasis on antitumour and antiviral protection through activation of NK cells and T-lymphocytes.

While *Ginkgo biloba* also shared the ability to reduce inflammation with ginseng, its uniqueness was determined by the combination of immune and vascular-regulating effects,

which was of little importance in chronic pathologies. Common marigold had a common anti-inflammatory effect with ginkgo, but realised the effect through a clearer regulation of the cytokine profile (a decrease in TNF- α , IL-1 β , IL-6 with an increase in IL-10). Thus, it showed the most pronounced anti-inflammatory profile among all the compared agents. Shiitake mushrooms shared a common mechanism with purple coneflower and ginseng to stimulate cellular immunity, but they differed in a much wider spectrum – from antiviral to antitumour. Unlike “Immunormalin”, they did not include a prebiotic or sedative effect, but acted as natural adjuvants, enhancing the immune response to an antigenic challenge. Therefore, a common property of natural immunomodulators was the antioxidant effect and the ability to regulate cytokine balance. Their differences were determined by the degree of multifactorial mechanisms: from narrowly directed activation of macrophages and T-lymphocytes (purple coneflower) to integrated effects on immune, metabolic, and neuroendocrine processes (“Immunormalin”). It was due to the combination of extracts of several plants with multidirectional bioactivity that “Immunormalin” demonstrated the most complex action profile. In contrast, other drugs occupied specific therapeutic niches – prevention of respiratory infections (purple coneflower), correction of inflammatory processes (marigold, chamomile, ginkgo) or antitumour and antiviral support (ginseng, shiitake beta-glucans). In addition to the mechanisms of action and the spectrum of clinical effects, an

important criterion is the level of evidence and safety profile. It was these parameters that determine the possibilities of integrating funds into the practice of evidence-based

medicine and their clinical significance. Generalised data on the availability of evidence and safety features of individual drugs and nutraceuticals are shown in Table 2.

Table 2. Level of evidence and safety profile of natural immunomodulators

Agent	Evidence base	Safety
“Immunormalin”	Local data confirmed only by patient reviews, there are no randomised controlled trials.	Portability data are limited; standardised safety assessments are not available.
“Immunal”	Randomised controlled trials, clinical efficacy confirmed.	Generally safe; isolated cases of mild allergic reactions.
<i>Panax ginseng</i>	Randomised controlled trials, generalisations in reviews.	Isolated gastrointestinal disorders have been reported; toxicity is low.
<i>Ginkgo biloba</i>	Meta-analyses of clinical trials.	Safety depends on compliance with dosages; there may be an increased risk of bleeding.
<i>Calendula officinalis</i>	Preclinical data, individual clinical observations.	Data indicate low toxicity and high biocompatibility.
<i>Lentinula edodes</i>	Preclinical and isolated clinical data.	No serious complications were recorded; tolerability is satisfactory.

Source: compiled by the authors

Comparison of natural immunomodulators revealed significant differences in the level of evidence and safety, which determined their clinical significance. All the considered drugs were combined with low toxicity and good tolerability, but the degree of scientific confirmation of their effects was uneven. A significant evidence base was demonstrated by the purple coneflower-based preparation “Immunal” and ginseng, for which the results of randomised controlled trials were accumulated. This allowed classifying them as the “gold standard” of plant immunomodulators with proven clinical efficacy. *Ginkgo biloba* took an intermediate place: its effectiveness was supported by meta-analyses and systematic reviews, which provided a high level of confidence, but at the same time requires strict dosages to avoid undesirable effects. In contrast to these drugs, common marigold and shiitake mushrooms were characterised mainly by preclinical confirmations and a limited number of clinical trials. Although their results showed pronounced immunomodulatory and anti-inflammatory potential, the rationale for widespread clinical use remained insufficient. “Immunormalin” was distinguished among all drugs by the most complex composition, combining several plants with different mechanisms of action. This created a synergistic effect and potentially expanded the scope of application – from preventing respiratory infections to reducing stress-induced immunosuppression. In combination, the analysis showed that immunomodulators with proven clinical efficacy were characterised by a high level of standardisation and reproducibility of results, while multicomponent nutraceuticals showed promising, but not yet sufficiently confirmed potential. Thus, further development of this field requires combining the accumulated experience of application with contemporary requirements of evidence-based medicine.

Thus, the comparative analysis showed that natural immunomodulators form a wide range of opportunities for maintaining the immune system, but their clinical value differs significantly depending on the level of evidence and safety profile. Drugs with proven efficacy in randomised controlled trials (purple coneflower, ginseng, ginkgo) can be considered as the most reasonable for integration

into modern practice, while drugs with a predominantly preclinical base (common marigold, shiitake) and local multicomponent formulas (“Immunormalin”) remain promising, but require further standardisation and large-scale clinical trials. Therefore, the introduction of such tools into medical practice should be based on combining their multi-factor potential with the requirements of evidence-based medicine.

CONCLUSIONS

Generalisation of the results confirmed that the multicomponent drug “Immunormalin” had a complex effect on the immune system due to a combination of antioxidant, anti-inflammatory, prebiotic, and sedative mechanisms. The presence of various plant extracts allowed combining several areas of action: regulation of the cytokine profile, maintenance of barrier functions of the mucous membranes, modulation of the intestinal microbiota, and reduction of stress-induced immunosuppression. This synergistic effect caused a decrease in the frequency and severity of symptoms of respiratory infections and helped to maintain immune balance. Generalised data showed that the action of Asian ginseng and *Ginkgo biloba* was based on different but complementary mechanisms. Ginseng increases the activity of NK cells and T-lymphocytes, providing antiviral and anti-tumour potential, and also acts as an adaptogen, increasing the body’s resistance to stress factors. *Ginkgo biloba* has an immunomodulatory and at the same time vascular-regulating effect, which is especially valuable in chronic pathologies where immune and metabolic disorders are combined. Both drugs were characterised by good tolerability and a low risk of toxicity, which created prerequisites for their use in both prevention and complex therapy.

The analysis confirmed that the common marigold has a well-defined anti-inflammatory mechanism of action, reducing the production of TNF- α , IL-1 β and IL-6 while increasing the secretion of IL-10. This restores the balance between pro- and anti-inflammatory processes and prevents excessive tissue damage in response to infectious or autoimmune stimuli. The effects of the common marigold were found in both preclinical models and clinical

observations, where there was a reduction in symptoms of inflammatory diseases of the mucous membranes and skin. In turn, shiitake mushrooms implement a different mechanism – activation of dendritic cells and NK cells with increased IL-12 production. This provided powerful stimulation of the antiviral and antitumour response, and prevention of recurrent infections. Unlike the narrowly directed anti-inflammatory effect of common marigold, fungal beta-glucans act as natural immune adjuvants, strengthening the cellular link of immunity. Thus, both drugs occupy different niches: marigold – in reducing chronic inflammation, and shiitake – in maintaining an active immune defence against infections and neoplasms.

Comparative analysis showed that all natural immunomodulators were characterised by low toxicity and good tolerability, but the level of evidence base was significantly different. The most convincing results were obtained from purple coneflower (“Immunal”) and ginseng, confirmed

by randomised controlled trials, while ginkgo biloba was confirmed by meta-analyses and systematic reviews. Common marigold and shiitake mushrooms remained mostly at the level of preclinical confirmations. “Immunormalin” was characterised by a complex composition, but its effectiveness was based only on local data and required further thorough clinical testing. Further studies should be aimed at obtaining empirical evidence through randomised controlled trials involving representative samples of patients.

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✦ REFERENCES

- [1] Bielenichev I, Gorchakova N, Harnyk T, Shumeiko O, Klymenko O, Klymenko O, et al. Immunomodulatory effect of phytopreparations. *Phytotherapy*. 2025;1:5–29. DOI: [10.32782/2522-9680-2025-1-18](https://doi.org/10.32782/2522-9680-2025-1-18)
- [2] Burlou-Nagy C, Bănică F, Jurca T, Vicaș LG, Marian E, Muresan ME, et al. *Echinacea purpurea* (L) Moench: Biological and pharmacological properties. A review. *Plants*. 2022;11(9):1244. DOI: [10.3390/plants11091244](https://doi.org/10.3390/plants11091244)
- [3] Valdés-González JA, Sánchez M, Moratilla-Rivera I, Iglesias I, Gómez-Serranillos MP. Immunomodulatory, anti-inflammatory, and anti-cancer properties of ginseng: A pharmacological update. *Molecules*. 2023;28(9):3863. DOI: [10.3390/molecules28093863](https://doi.org/10.3390/molecules28093863)
- [4] Hu Y, He Y, Niu Z, Shen T, Zhang J, Wang X, et al. A review of the immunomodulatory activities of polysaccharides isolated from *Panax* species. *J Ginseng Res*. 2022;46(1):23–32. DOI: [10.1016/j.jgr.2021.06.003](https://doi.org/10.1016/j.jgr.2021.06.003)
- [5] Mohamed N. [Pharmacological properties of polysaccharides of medicinal plants: A review of the effects on the immune system and potential applications in immunotherapy](#) [Master’s thesis]. Dnipro: Dnipro State Medical University; 2025.
- [6] Ibrahim MA, Ramadan HH, Mohammed RN. Evidence that *Ginkgo biloba* could use in the influenza and coronavirus COVID-19 infections. *J Basic Clin Physiol Pharmacol*. 2021;32(3):131–43. DOI: [10.1515/jbcpp-2020-0310](https://doi.org/10.1515/jbcpp-2020-0310)
- [7] Samoilenko AM. [Pharmaceutical development of an antiviral drug based on medicinal plant raw material in the form of tablets](#) [Master’s thesis]. Kyiv: Kyiv National University of Technologies and Design; 2021.
- [8] Silva D, Ferreira MS, Sousa-Lobo JM, Cruz MT, Almeida IF. Anti-inflammatory activity of *Calendula officinalis* L. flower extract. *Cosmetics*. 2021;8(2):31. DOI: [10.3390/cosmetics8020031](https://doi.org/10.3390/cosmetics8020031)
- [9] Oliveira BG, Santos LF, Costa MC, Bastos RW, Carmo PH, Santos DD, et al. Antimicrobial and immunomodulatory activities of dried extracts of *Echinacea purpurea*. *Braz J Pharm Sci*. 2022;58:e21026. DOI: [10.1590/s2175-97902022e21026](https://doi.org/10.1590/s2175-97902022e21026)
- [10] Roszczyk A, Turło J, Zagożdżon R, Kaleta B. Immunomodulatory properties of polysaccharides from *Lentinula edodes*. *Int J Mol Sci*. 2022;23(16):8980. DOI: [10.3390/ijms23168980](https://doi.org/10.3390/ijms23168980)
- [11] Vlassopoulou M, Yannakoulia M, Pletsas V, Zervakis GI, Kyriacou A. Effects of fungal beta-glucans on health – a systematic review of randomized controlled trials. *Food Funct*. 2021;12(8):3366–80. DOI: [10.1039/D1FO00122A](https://doi.org/10.1039/D1FO00122A)
- [12] Popovici LF, Oancea S. *Calendula officinalis* – overview on applications and pharmaceutical uses. *Curr Trends Nat Sci*. 2024;13(25):268–79. DOI: [10.47068/ctns.2024.v13i25.032](https://doi.org/10.47068/ctns.2024.v13i25.032)
- [13] Vieira SF, Gonçalves VM, Llaguno CP, Macías F, Tiritan ME, Reis RL, et al. On the bioactivity of *Echinacea purpurea* extracts to modulate the production of inflammatory mediators. *Int J Mol Sci*. 2022;23(21):13616. DOI: [10.3390/ijms232113616](https://doi.org/10.3390/ijms232113616)
- [14] Lee SK, Lee DR, Kim HL, Choi BK, Kwon KB. A randomized, double-blind, placebo-controlled study on immune improvement effects of ethanolic extract of *Echinacea purpurea* (L.) Moench in Korean adults. *Phytother Res*. 2024;38(7):3645–59. DOI: [10.1002/ptr.8224](https://doi.org/10.1002/ptr.8224)
- [15] Demyd A, Vronska L, Ivanusa I, Mykhalkiv M. Application of high-performance thin-layer chromatography for the identification of *Echinacea purpurea* in dietary supplements and medicinal products based on it. *SWorldJournal*. 2024;(27–2):3–18. DOI: [10.30888/2663-5712.2024-27-00-005](https://doi.org/10.30888/2663-5712.2024-27-00-005)
- [16] Cui L, Chen L, Yang G, Li Y, Qiao Z, Liu Y, et al. Structural characterization and immunomodulatory activity of a heterogalactan from *Panax ginseng* flowers. *Food Res Int*. 2021;140:109859. DOI: [10.1016/j.foodres.2020.109859](https://doi.org/10.1016/j.foodres.2020.109859)
- [17] Ratan ZA, Youn SH, Kwak YS, Han CK, Haidere MF, Kim JK, et al. Adaptogenic effects of *Panax ginseng* on modulation of immune functions. *J Ginseng Res*. 2021;45(1):32–40. DOI: [10.1016/j.jgr.2020.09.004](https://doi.org/10.1016/j.jgr.2020.09.004)
- [18] Abdel-Latif HM, Hendam BM, Nofal MI, El-Son MA. *Ginkgo biloba* leaf extract improves growth, intestinal histomorphometry, immunity, antioxidant status and modulates transcription of cytokine genes in hapa-reared *Oreochromis niloticus*. *Fish Shellfish Immunol*. 2021;117:339–49. DOI: [10.1016/j.fsi.2021.06.003](https://doi.org/10.1016/j.fsi.2021.06.003)

- [19] Das R, Lami MS, Chakraborty AJ, Mitra S, Tallei TE, Idroes R, et al. *Ginkgo biloba*: A treasure of functional phytochemicals with multimedicinal applications. *Evid Based Complement Alternat Med*. 2022;2022(1):8288818. DOI: [10.1155/2022/8288818](https://doi.org/10.1155/2022/8288818)
- [20] Patil K, Sanjay CJ, Doggalli N, Devi KR, Harshitha N. A review of *Calendula officinalis*-magic in science. *J Clin Diagn Res*. 2022;16(2):23–7. DOI: [10.7860/JCDR/2022/52195.16024](https://doi.org/10.7860/JCDR/2022/52195.16024)
- [21] Abdelwahab SI, Taha MM, Taha SM, Alsayegh AA. Fifty-year of global research in *Calendula officinalis* L. (1971–2021): A bibliometric study. *Clin Complement Med Pharmacol*. 2022;2(4):100059. DOI: [10.1016/j.ccmp.2022.100059](https://doi.org/10.1016/j.ccmp.2022.100059)
- [22] Mirończuk-Chodakowska I, Kujawowicz K, Witkowska AM. Beta-glucans from fungi: Biological and health-promoting potential in the COVID-19 pandemic era. *Nutrients*. 2021;13(11):3960. DOI: [10.3390/nu13113960](https://doi.org/10.3390/nu13113960)
- [23] Cerletti C, Esposito S, Iacoviello L. Edible mushrooms and beta-glucans: Impact on human health. *Nutrients*. 2021;13(7):2195. DOI: [10.3390/nu13072195](https://doi.org/10.3390/nu13072195)
- [24] Oczkowski M. Health-promoting effects of bioactive compounds in blackcurrant (*Ribes nigrum* L.) berries. *Rocz Panstw Zakl Hig*. 2021;72(3):229–38. DOI: [10.32394/rpzh.2021.0174](https://doi.org/10.32394/rpzh.2021.0174)
- [25] Pashaei M, Hassanpour H. Phenolic, amino acids, and fatty acids profiles and the nutritional properties in the fresh and dried fruits of black rosehip (*Rosa pimpinellifolia* L.). *Sci Rep*. 2024;14:19665. DOI: [10.1038/s41598-024-70574-5](https://doi.org/10.1038/s41598-024-70574-5)
- [26] Drif AI, Yücer R, Damiescu R, Ali NT, Abu Hagar TH, Avula B, et al. Anti-inflammatory and cancer-preventive potential of Chamomile (*Matricaria chamomilla* L.): A comprehensive *in silico* and *in vitro* study. *Biomedicines*. 2024;12(7):1484. DOI: [10.3390/biomedicines12071484](https://doi.org/10.3390/biomedicines12071484)
- [27] Kadioğlu B, Kadioğlu S. Medicinal and aromatic plants consumption habits of consumers in the coronavirus pandemic. *Ataturk Univ Ziraat Fak Derg*. 2021;52(3):325–34. DOI: [10.17097/ataunizfd.860913](https://doi.org/10.17097/ataunizfd.860913)
- [28] Kadiyska T, Tourtourikov I, Dabchev K, Zlatarova A, Stoynev N, Hadjiolova R, et al. Herbs and plants in immunomodulation. *Int J Funct Nutr*. 2023;4(1):1. DOI: [10.3892/ijfn.2023.31](https://doi.org/10.3892/ijfn.2023.31)
- [29] Choudhary S, Khan S, Rustagi S, Rajpal VR, Khan NS, Kumar N, et al. Immunomodulatory effect of phytoactive compounds on human health: A narrative review integrated with bioinformatics approach. *Curr Top Med Chem*. 2024;24(12):1075–100. DOI: [10.2174/0115680266274272240321065039](https://doi.org/10.2174/0115680266274272240321065039)
- [30] Balasubramaniam M, Sapuan S, Hashim IF, Ismail NI, Yaakop AS, Kamaruzaman NA, et al. The properties and mechanism of action of plant immunomodulators in regulation of immune response – a narrative review focusing on *Curcuma longa* L., *Panax ginseng* C.A. Meyer and *Moringa oleifera* Lam. *Heliyon*. 2024;10(7):e28261. DOI: [10.1016/j.heliyon.2024.e28261](https://doi.org/10.1016/j.heliyon.2024.e28261)
- [31] Klymenko M. Progress and prospects in research on low-grade diffuse chronic inflammation: A literature review. *Ukr J Med Biol Sport*. 2025;10(1):16–29. DOI: [10.63341/ujmbs/1.2025.16](https://doi.org/10.63341/ujmbs/1.2025.16)
- [32] Liang CJW, Woerdenbag HJ, Ekhardt C, Vitalone A, van Hunsel FP. Safety considerations for natural products with adaptogenic and immunomodulating activities. *Pharmaceuticals*. 2025;18(8):1208. DOI: [10.3390/ph18081208](https://doi.org/10.3390/ph18081208)
- [33] Galkin A, Gorchakova N, Zaychenko G, Golembiovska O, Bondarenko L, et al. [Efficiency and safety issues of modern multi-component herbal medicines](#). Kyiv: Igor Sikorsky Kyiv Polytechnic Institute; 2024. 264 P.
- [34] Mousavi SN, Hosseinikia M, Yousefi Rad E, Saboori S. Beneficial effects of *Ginkgo biloba* leaf extract on inflammatory markers: A systematic review and meta-analysis of the clinical trials. *Phytother Res*. 2022;36(9):3459–69. DOI: [10.1002/ptr.7544](https://doi.org/10.1002/ptr.7544)
- [35] Barbosa FG, de Mattos MC, Nunes FM, Mafezoli J, Oliveira MCF. Immunomodulation potential of woody plants. In: Sangwan N, Farag M, Modolo L, editors. *Plants and phytomolecules for immunomodulation: Recent trends and advances*. Singapore: Springer; 2022. P. 469–92. DOI: [10.1007/978-981-16-8117-2_16](https://doi.org/10.1007/978-981-16-8117-2_16)
- [36] Buonfiglio F, Pfeiffer N, Gericke A. Immunomodulatory and antioxidant drugs in glaucoma treatment. *Pharmaceuticals*. 2023;16(9):1193. DOI: [10.3390/ph16091193](https://doi.org/10.3390/ph16091193)
- [37] Rezende AM, Albuquerque AL, Silva MJ, De Melo Cruvinel W, Gomes CM, Borges LL, et al. Drug-like properties and therapeutical potential of *Calendula officinalis* L. active ingredients. In: Taft C, de Lazaro S, editors. *Progress in hydrogen energy, fuel cells, nano-biotechnology and advanced, bioactive compounds*. Cham: Springer; 2024. P. 301–13. DOI: [10.1007/978-3-031-75984-0_12](https://doi.org/10.1007/978-3-031-75984-0_12)
- [38] Dhingra G, Dhakad P, Tanwar S. Review on phytochemical constituents and pharmacological activities of plant *Calendula officinalis* Linn. *Biol Sci*. 2022;2(2):216–28. DOI: [10.55006/biolsciences.2022.2205](https://doi.org/10.55006/biolsciences.2022.2205)
- [39] Murphy EJ, Masterson C, Rezoagli E, O'Toole D, Major I, Stack GD, et al. β -Glucan extracts from the same edible shiitake mushroom *Lentinus edodes* produce differential *in-vitro* immunomodulatory and pulmonary cytoprotective effects – implications for coronavirus disease (COVID-19) immunotherapies. *Sci Total Environ*. 2020;732:139330. DOI: [10.1016/j.scitotenv.2020.139330](https://doi.org/10.1016/j.scitotenv.2020.139330)
- [40] Kumar D, Kashyap S, Gupta S. β -Glucans in mushrooms: Immunomodulatory and anticancer effects. In: Kumar D, Gupta S, Ansari M, Sangeeta, Hasan W, Kashyap S, et al., editors. *Mushroom magic*. London: CRC Press; 2024. P. 105–22. DOI: [10.1201/9781003570257](https://doi.org/10.1201/9781003570257)
- [41] Jafari M, Boskabaday MH, Rezaee SA, Rezaeian S, Behrouz S, Ramezannejad R, et al. Lentinan and β -glucan extract from shiitake mushroom, *Lentinula edodes*, alleviate acute LPS-induced hematological changes in mice. *Iran J Basic Med Sci*. 2023;26(7):836–42. DOI: [10.22038/IJBMS.2023.67669.14820](https://doi.org/10.22038/IJBMS.2023.67669.14820)

Сучасні підходи до імуномодуляції в клінічній практиці: аналіз дієтичних добавок та лікарських препаратів

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Анотація. Метою дослідження було встановлення імуномодулюючих властивостей рослинних засобів і перспектив їх клінічного впровадження. Методологія ґрунтувалася на теоретико-аналітичному узагальненні літературних даних щодо імуномодулюючих властивостей препаратів «Імунормалін», «Іммунал», женьшеню азійського, гінкго білоба, календули лікарської та грибів шиїтаке. Результати аналізу засвідчили, що «Імунормалін» відзначався найширшим спектром механізмів, поєднуючи антиоксидантні, протизапальні, пребіотичні та седативні ефекти, які одночасно охоплювали імунні, метаболічні й нейроендокринні шляхи. Така багатофакторність відрізняла його від більш вузькоспеціалізованих засобів та зумовлювала виокремлену позицію серед нутрицевтиків. На противагу, «Іммунал», створений на основі ехінацеї пурпурової, демонстрував спрямований імуномодулюючий механізм через активацію макрофагів і Т-лімфоцитів, що робило його переважно ефективним у профілактиці респіраторних інфекцій. Женьшень азійський поєднував властивості адаптогена та імуномодулятора, зумовлюючи підвищену стійкість організму до інфекцій та формування протипухлинного потенціалу. Гінкго білоба, поділяючи з женьшенем антиоксидантний і протизапальний вплив, мав додаткову судиннорегулюючу дію, що розширювало його застосування у хронічних патологіях та комплексній терапії метаболічних синдромів. Календула лікарська демонструвала найчіткіше виражений протизапальний профіль серед порівнюваних засобів, оскільки пригнічувала продукцію прозапальних цитокінів і стимулювала секрецію протизапальних медіаторів, що знижувало ризик тканинних ушкоджень при тривалих запальних процесах. Гриби шиїтаке, завдяки вмісту бета-глюканів, реалізовували функції природних ад'ювантів, підсилюючи клітинну імунну відповідь і поєднуючи протівірусну та протипухлинну активність. Узагальнення результатів показало, що природні імуномодулятори мають спільну антиоксидантну дію, але відрізняються за багатофакторністю та клінічною спрямованістю, що зумовлює потребу у стандартизації й диференційованому застосуванні. Отримані результати можуть бути використані лікарями-клініцистами, фармакологами та науковцями у сфері доказової фітотерапії для оптимізації підбору імуномодулюючих засобів і розробки стандартизованих підходів до їх застосування

Ключові слова: запальний процес; цитокіни; макрофаги; лімфоцити; інтерлейкіни; біоактивні сполуки; інфекції