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Review article

Ayurvedic concept of immunity with special reference to immunomodulatory herbs

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ABSTRACT

A systematic literature review on immunomodulatory herbs of Ayurveda was conducted to explore their clinical potential. A variety of plant-based principles with potential immunomodulatory action have been identified, which may explain and justify their usage in traditional medicine in the past and can also serve as a foundation for future studies. This review aims to highlight the findings of research on plant-derived immunomodulators. Focusing the ethnopharmacological usage, the most relevant articles were chosen from the authentic databases of biomedical sciences. Different scientific online databases including Academic Search Premier, Embase, PubMed, Biological Abstracts, PLOS, Natural Standard, and Web of Science were used to conduct the present systematic literature search. Many plants, as well as certain phytoconstituents, have been implicated in the present study. The study also focuses on the mechanism of action of different plant medicines. The present review would be helpful in designing new research studies on medicinal plants with immunomodulatory properties.

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INTRODUCTION

According to the World Health Organization (WHO), traditional medicines (mostly herbs) are used by approximately three-quarters of the world's population for medical care. Herbs and/or plants are, in reality, mankind earliest allies. They do not only function as a source of food and shelter, but also as a treatment for a variety of illnesses. Herbal medicine, often known as traditional or natural medicine, has long existed in many cultures and civilizations, including Ayurvedic (India), Egyptian, Western, Chinese, Kampo (Japan), and Greco-Arab or Unani-Tibb (South Asia). Traditional medicine is now being revalued all over the globe as a result of significant studies on different plant species and their medicinal qualities.

Plant-based medications and therapies have emphasized Ayurveda. The Ayurvedic School of medicine in India has discovered a variety of plants with a wide range of pharmacological characteristics. Tonic, immunostimulation, neurostimulation, antibacterial, anti-ageing, antiviral, antirheumatic, anticancer, adaptogenic, and other ethnopharmacological actions are included in the Ayurvedic system of medicine, which is one of the oldest systems of medicine. The Ayurvedic Materia Medica devotes an entire section to 'Rasayana' or medicines that are said to improve body resistance. Rasayana is a class of plants that are said to improve physical and mental health, strengthen the body defensive systems, and lengthen life expectancy. These characteristics are comparable to the contemporary notion of adaptogenic agents, which have been shown to protect the human physiological system against a variety of stresses. Many medicinal herbs, such as *Withania somnifera*, *Tinospora cordifolia*, and *Mangifera indica*, have been reported to have immunomodulatory action as Rasayanas. They may suppress or enhance the host ability to fight infection and malignancies in a non-specific way, or they can respond to a foreign material specifically. Immunomodulators have yet to be completely understood how they interact with the immune system's vast network of processes.

CONCEPT OF IMMUNOMODULATORY HERBS USED IN AYURVEDA

Modulation of immunological processes is applying medicinal plants and their compounds as a potential therapeutic strategy has become commonplace. Plants and minerals have been applied to cure a variety of illnesses and diseases since ancient times. Immunomodulation of immune response is now being identified as a viable alternative to traditional chemotherapy for a variety of diseases, particularly when the host defence mechanism activates conditions of impaired immune responsiveness or when a selective immunosuppressant induces situations like autoimmune disorders and organ transplantation.

Immunity is a finely balanced complex, multicellular, and physiologic process that allows a person to differentiate foreign material from 'self' and neutralise and/or remove the foreign matter (Kaminski et al., 2008).

Immunomodulatory comes from immunity words which can be defined as follows.

Immunity

This is described as the body's capacity to identify and fight a wide variety of contagious and potentially dangerous bacteria, allowing it to avoid illness and prevent organ and tissue damage. The immune system is distributed throughout the body. Immune stem cells are generated in the bone marrow and may either stay there until they mature or move to other parts of the body to mature. As a result, the majority of immune cells circulate throughout the body, each having a distinct impact. The antibody-mediated defence system (humoral immunity) and the cell-mediated defence system are two separate but overlapping processes used by the immune system to combat invading pathogens (cellular immunity).

Immune systems

The immune system fundamental design is multilayered, with protections on many levels. The skin is the most visible and important barrier against infection. Another is physiological, in which the body's temperature and pH create unsuitable dwelling circumstances for alien organisms. The innate and/or acquired or adaptive immune systems respond to infections that have effectively entered the body. Both systems are made up of a complicated network of cells and chemicals that work together to identify and destroy infections. Chemical bonding is required for detection and elimination: immune system cells have a variety of receptors on their surfaces, some of which chemically attach to pathogens and others to other immune system cells or substances to allow the complicated signalling system that controls the immune response.

Immunomodulation

Many infectious illnesses and disorders are thought to be caused by stressful environmental circumstances that suppress the immune system, according to recent advances in clinical and experimental immunology. It is clear that some kinds of stress may affect physiological changes that affect infection and cancer susceptibility. The capacity to manipulate the immune response in animals and people arose from a desire to provide better protection against infectious agents by gaining a better knowledge of how the immune system works and how nonspecific and specific immune mechanisms emerged. Additional options for regulating immune responses included naturally synthesized or occurring substances capable of changing those processes (Quinn, 1990).

History of Immunology

Immunology is a branch of science that studies the immune system's structure and function. It comes from medicine and early research into the sources of disease immunity. The first time immunity was mentioned was during the plague of Athens in 430 BC. People who had recovered from a prior attack of the sickness could nurse the sick without catching the ailment again, according to Thucydides (Retief and Cilliers, 1998). Pierre-Louis Moreau de Maupertuis conducted research with scorpion venom in the 18th century and discovered that some dogs and mice were resistant to it (Ostoya, 1954). Louis Pasteur used this and other findings of acquired immunity in the creation of vaccination and his hypothesised germ theory of illness (Plotkin, 2005). Pasteur's hypothesis was diametrically opposed to current illness beliefs like the miasma theory. Microorganisms were not established as the cause of infectious illness until Robert Koch's 1891 proofs, for which he was given the Nobel Prize in 1905. With the identification of the yellow fever virus by Walter Reed in 1901, viruses were verified as human diseases.

Immunomodulators

These are biological or synthetic compounds that have the ability to activate, inhibit, or regulate any component of the immune system, including both the adaptive and innate arms.

CLASSIFICATION OF IMMUNOMODULATORS

Immunomodulators are divided into the following three groups in clinical practice.

Immunoadjuvants

Immunoadjuvants are used to boost the effectiveness of vaccinations and therefore may be classified as particular immune stimulants. Immunoadjuvants have the potential to be genuine immune response modulators. They've been suggested as selectors between cellular and humoral helper T1 (Th1) and helper T2 (Th2) cells, immunoprotective, immunodestructive, and reagenic [immunoglobulin E (IgE)] vs IgG type immune responses, presenting a major challenge to vaccine makers.

Immunostimulants

Immunostimulants are by definition non-specific since they are intended to improve the body's response against infection. They have the ability to operate via both innate and adaptive immune responses. Immunostimulants are anticipated to function as preventive and promoter agents, or immunopotentiators, in healthy people by increasing the fundamental level of the immune response. They are anticipated to function as immunotherapeutic drugs in those who have impaired immune responses.

Immunosuppressants

Immunosuppressants are a structurally and functionally diverse category of medicines that are often used together in combination regimens to treat organ transplant rejection and autoimmune disorders.

Immunomodulators in Ayurveda

Ayurveda is a very old and yet very important tradition that is extensively practised in India, Sri Lanka, and other nations. It is philosophically and experimentally sound. The three famous reference collections that provide a comprehensive account of over 700 plants are the

Atharvaveda (about 1200 BC), Charak Samhita (1000–500 BC), and Sushrut Samhita (1000–500 BC).

Several therapeutic plants employed in the Indian traditional system known as Rasayana (dedicated to improving body resistance) have piqued scientists' interest across the globe. Several medicinal plants, as described below, have a broad variety of antioxidant, antiasthmatic, antiarrhythmic, inflammatory, antifungal, anti-hepatoprotective, hypocholesterolemic, cardiotonic, diuretic, and other therapeutic properties in addition to immunomodulatory activity.

Immunological factors testing methods

The standard screening procedure is to extract a single component or distilled fraction from herbal medicines and evaluate its bioactivity using traditional pharmacological methods. The whole animal model is the most common pharmacological screening model, and it is important in medication assessment since it seems to react to the effectiveness, side effects, and toxicity of medicines in their whole. Several techniques of pharmacological screening of medicinal plants with immunomodulatory action have been described *in vitro* and *in vivo* (Vogel, 2002).

MECHANISM OF IMMUNOSTIMULATION

Immunological defence is a complex combination of nonspecific and specific immunological responses, cellular and humoral immune responses, immunocompetent cell activation and repression, and the impact of endocrine and other processes on the immune system. T or B lymphocytes or the complement system are the primary targets of the immunostimulant, and an increase in macrophage and granulocyte phagocytosis plays a key role in immunostimulation (Kuby, 1994). Macrophage activation is likely required for the stimulating chemicals to stay in touch with the reacting cell. The activation of T cells, which may be done directly or indirectly through macrophages, is the second most significant function (Wagner et al., 1985).

MODERN DRUGS AND IMMUNOMODULATION

Immunosuppressant

Immunosuppression refers to a reduction in resistance to infections and stress, and it may be caused by environmental or pharmacological causes (Makare et al., 2001). These drugs may be used to treat autoimmune disorders, graft rejection, graft versus host disease, hypersensitive immunological reactions (both immediate and delayed), and immune pathology linked with infections. The most common use of these drugs has been in the prevention of graft rejection and the treatment of autoimmune disorders.

Immunostimulant

The word immunostimulation refers to a preventive or therapeutic strategy for stimulating our nonspecific immune system. This mainly entails non-antigen-dependent stimulation of granulocytes, macrophages, complement, and natural killer (NK) cells activity and efficiency (Makare et al., 2001).

Side effects of immunomodulator drug

Pulmonary toxicity, myelosuppression, alopecia, increased infection risk, hepatic fibrosis, Epstein-Barr virus associated-lymphoma, nephrotoxicity, neurotoxicity (tremor, headache, motor disturbances, and seizures), GI complaints, hypertension, hyperkalemia, hyperglycemia, and diabetes are all side effects of these drugs. Renal dysfunction, tremor, hirsutism, hypertension, hyperlipidemia, gum hyperplasia, hyperuricemia, hypercholesterolemia, nephrotoxicity, hypertension, diabetogenic, nephrotoxicity, and hypertension LDL cholesterol levels that be too high, for example (Kremer et al., 1994).

MEDICINAL PLANTS AS IMMUNOMODULATOR

The chemoprotective and immunomodulatory properties of plant extracts used in the conventional treatment are being investigated. Immunomodulators are biological response modifiers that work against tumours by boosting the host defensive systems. They have a direct anti-proliferative impact on tumour cells, as well as improving the host capacity to withstand harm from toxic chemicals used to treat cancer.

Immunomodulatory therapy may be a viable alternative to traditional chemotherapy for a variety of diseases, particularly when the host defence mechanisms must be activated in the face of impaired immune responsiveness or when selective immunosuppression is required in situations such as inflammatory diseases, auto-immune disorders, or organ/bone marrow transplantation (Upadhyay, 1997). Immunomodulatory action has been reported for a variety of Indian medicinal herbs and different 'Rasayana.' *Withania somnifera*, *Tinospora cordifolia* and *Mangifera indica* are some of these plants (Dahanukar and Thatte, 1997; Davis and Kuttan, 2000). There are many more that have yet to be discovered and investigated. Selected most explored plants known for their immunomodulatory activities are given below.

Withania somnifera

The administration of a powdered root extract from the herb *Withania somnifera* stimulated immunological activity in Babl/c mice. On the tenth day, treatment with five doses of Withania root extract (20 mg/dose/animal; i.p.) increased the overall WBC count (17125 cells/mm^3). After receiving Withania extract, bone marrow cellularity (27x10^6 cells/femur) and alpha-esterase positive cell number (1800/4000 cells) both rose substantially (P = 0.001). The circulating antibody titre and the number of plaque-forming cells (PFC) in the spleen increased after treatment with Withania extract and the antigen (SRBC). On the fourth day, the highest quantity of PFC (985 PFC/10^6 spleen cells) was recorded. In mice, Withania extract suppressed the delayed-type hypersensitivity response (Mantoux test). In mice, the administration of Withania extract increased the phagocytic activity of peritoneal macrophages (76.5 pigmented cells/200) as compared to the control (31.5/200 cells). These findings support the immunomodulatory properties of *W. somnifera* extract, a well-known immunomodulator in traditional medicine (Davis and Kuttan, 2000).

Tinospora cordifolia

An immunomodulatory protein (ImP) in guduchi was isolated using anion-exchange chromatography on Q-Sepharose from a dry stem powder extract. SDS-PAGE, periodic acid-Schiff staining, HPLC, and immunochemical investigations were used to characterise guduchi ImP. Lymphocytic proliferation and macrophage activation tests were used to measure immunostimulatory activity. The presence of guduchi ImP was also tested in fresh guduchi stem/leaf, guduchi satwa, and guduchi capsules. The discovery of an immunomodulatory protein in guduchi stem with lymphoproliferative and macrophage-activating characteristics supports the use of guduchi preparations for immunomodulation in various Ayurvedic medications. This is the first time that we have been aware of the immunomodulatory protein identified from guduchi (Dahanukar and Thatte, 1997; Aranha et al., 2012).

Morus alba

Morus alba Linn. (Mulberry) methanolic extract was given orally at low and high doses of 100 mg/kg and 1 g/kg, respectively, with *Ocimum sanctum* (100 mg/kg, po) as the reference drug. In the carbon clearance assay, it exhibited a substantial rise in the phagocytic index, significant protection against cyclophosphamide-induced neutropenia, and enhanced neutrophil adhesion in the neutrophil adhesion test. As a result, it was determined that *M. alba* boosts both humoral and cell-mediated immunity (Bharani et al., 2010).

Acacia catechu

The impact of *Acacia catechu* extract on cell-mediated immunity was shown by a rise in neutrophil adherence to nylon fibres, a substantial increase in the phagocytic index, and considerable protection against cyclophosphamide-induced neutropenia. *A. catechu* extract, on the other hand, caused a substantial rise in serum immunoglobulin levels, increased haemagglutination titre values, and reduced the mortality ratio in mice, indicating that it has an impact on the humoral arm of the immune system. The aqueous extract of *A. catechu* has a substantial impact on both cell-mediated and humoral immunity, according to the findings (Ismail and Asad, 2009).

Jatropha curcas

The impact of an 80% aqueous methanol extract of *Jatropha curcas* L. and its compounds (0.25 mg/kg body wt) on one-day-old specified pathogen-free chicks was investigated. The humoral and cell-mediated responses were stimulated. In blood, there were notable effective increases in antibody titers, lymphocytes, and macrophage cells (Abd-Alla et al., 2009).

Achillea wilhelmsii

In female Swiss albino mice, the immunomodulatory effect of an aqueous extract of *Achillea wilhelmsii* (25, 50, and 100 mg/kg body weight for 5 days) was assessed using body weight, relative organ weight, delayed type of hypersensitivity (DTH), and haemagglutination titre (HT). There were no significant variations in body weight increase between the different groups of animals. At 100 mg/kg, the relative organ weight of the spleen increased significantly. In the studied dosages of the plant, there was no increase in the levels of liver function test enzymes or kidney relative weight. At a dosage of 100 mg/kg, the extract of *A. wilhelmsii* significantly increased the DTH response. Plant extract had a stimulatory impact in the HT test at all dosages, although these changes were substantial at 50 mg/kg. In the dosages that were tested, no one died. In mice, *A. wilhelmsii* had an overall stimulatory impact on both humoral and cellular immunological activities (Sharififar et al., 2009).

Picrorhiza scrophulariiflora

By structure, one glycoside (scrocaffeside A) from methanolic extract of *Picrorhiza scrophulariiflora* has immunomodulatory activities. Scrocaffeside A increased splenocyte proliferation and responsiveness to the polyclonal T-cell mitogen concanavalin A (Con A) and lipopolysaccharide (LPS). When peritoneal macrophages and natural killer cells were given dosages of scrocaffeside, ranging from 5 µg/mL to 125 µg/mL, their activity increased significantly. The numbers of mature T cell subsets also showed a dose-dependent rise. The CD4/CD8 population of splenocytes was also increased, as cytokine production. When cultivated splenocytes were exposed to scrocaffeside A, the levels of interleukin (IL)-2, IL-4, IL-12, and (IFN)-gamma were substantially elevated. These findings suggest that scrocaffeside A may boost the immune system performance. It may become a novel immunostimulating agent in the future, in addition to its conventional usage in certain illnesses (An et al., 2009).

Plantago asiatica

Plantago asiatica L. seeds were often utilised as a traditional Chinese medicine for certain immunologically compromised individuals with chronic diseases. These applications may be linked to the plant's immunomodulatory characteristics. The effects of an extract from the seeds of *Plantago asiatica* L. on the maturation of dendritic cells (DCs), which play an important role in the primary immune system, were studied in this research (Huang et al., 2009).

Caesalpinia bonducella

The immunomodulatory potential of *Caesalpinia bonducella* ethanolic seed extract (200-500 mg/kg) was assessed by oral administration, which resulted in a significant increase in percent neutrophil adhesion to nylon fibres, as well as a dose-dependent increase in antibody titre values, and potentiated the delayed-type hypersensitivity reaction induced by sheep red blood cells. In addition, it reduced myelosuppression in cyclophosphamide-treated rats and showed excellent phagocytosis response in a carbon clearance test (Shukla et al., 2009).

Allium sativum

Garlic (*Allium sativum*), a popular medicinal herb, has a wide range of biological actions, including immunomodulation. Although certain garlic immuno-modulatory proteins have been identified, their exact identities remain unclear. The goal of this research was to extract immunomodulatory proteins from raw garlic and investigate their effects on immune system cells (lymphocytes, mast cells, and basophils) in terms of mitogenicity and hypersensitivity. Q-Sepharose chromatography of a 30 kD ultrafiltrate of raw garlic extract separated three protein components of about 13 kD (QR-1, QR-2, and QR-3 in the ratio 7:28:1). Human peripheral blood lymphocytes, mouse splenocytes, and thymocytes were all shown to have mitogenic activity (Clement et al., 2010).

Cynodon dactylon

Fresh grass juice was made according to traditional medical guidelines and standardised for solid content. The Folin-Ciocalteau technique was used to calculate its total phenol content. In vitro, the impact of freshly produced juice on doxorubicin-induced DNA damage was studied. The humoral antibody response, which was assessed by haemagglutination antibody titer and spleen cell assay in balb/c mice, was used to test its immunomodulatory function (Mangathayaru et al., 2009).

Terminalia arjuna

At 24 hours, *Terminalia arjuna* bark powder (400 mg/kg, po) decreased formalin-induced paw oedema but not carrageenan-induced paw oedema. In the second phase of the immunological response, it substantially enhanced anti-SRBC antibody titre. At a larger dosage (800 mg/kg, po), the same dose substantially decreased the length of licks and bites in both stages of the formalin-induced pain response and exhibited a significant increase in tail-flick latency. Pretreatment with naloxone (1 mg/kg, ip) counteracted the effects of *T. arjuna*. These results support the notion that it possesses anti-inflammatory properties against certain phlogistic compounds, as well as immuno-modulatory and antinociceptive properties which are likely mediated by central opioid receptors (Halder et al., 2009).

Pteridium aquilinum

One of the most frequent plants is *Pteridium aquilinum* (bracken fern). The main goal of this research was to determine the immunomodulatory effects of bracken fern extract after daily consumption by a mouse host for 14 (or up to 30) days. Histological studies showed a substantial decrease in splenic white pulp area in C57BL/6 mice given the extract (via gavage). Both delayed-type hypersensitivity analysis and assessment of IFNgamma production by NK cells after T(H)1 priming were decreased among a range of immune response parameters/functions evaluated in these hosts and isolated cells. Finally, the innate response in these hosts was reduced, as measured by NK cell cytotoxic capability. The findings demonstrated that *P. aquilinum* has immuno-suppressive properties and that several of the activities that were altered may lead to an elevated risk of cancer development in exposed hosts (Latorre et al., 2009).

Actinidia eriantha

In Chinese traditional medicine, the roots of *Actinidia eriantha* Benth (Actinidiaceae) have been used to treat cancer. The goal of this research was to assess the anticancer potential of polysaccharides extracted from the roots of *Actinidia eriantha* and to better understand their immunological processes by observing the effects on tumour development in mice and the immune response in tumour-bearing animals. The anticancer activity of AEP and four pure polysaccharides may be accomplished through enhancing immune response, and the composition of the monosaccharides, uronic acid concentration and molecular weight of the polysaccharides may influence their antitumor and immunomodulatory action (Xu et al., 2009).

Boerhaavia diffusa

Balb/c mice were used to study the impact of Punarnavine on the immune system. Punarnavine (40 mg/kg body weight) was given intraperitoneally and was shown to increase the total WBC count on the 6th day. Punarnavine treatment enhanced bone marrow cellularity and the number of alpha-esterase positive cells. Punarnavine treatment combined with the antigen, sheep red blood cells (SRBC), resulted in an increase in circulating antibody titer and plaque-forming cells (PFC) in the spleen. On the 6th day, the highest number of PFC was achieved. Punarnavine also increased the proliferation of splenocytes, thymocytes, and bone marrow cells in vitro and in vivo in the presence and absence of certain mitogens. Furthermore, punarnavine treatment substantially decreased LPS-induced increased levels of proinflammatory cytokines including TNF-alpha, IL-1beta, and IL-6 in mice. These findings point to Punarnavine's immunomodulatory properties (Manu and Kuttan, 2009).

Dioscorea japonica

The goal of this research was to see how the main storage protein dioscorin, which was isolated from two distinct yam species, Tainong No. 1 (TN1-dioscorins) and Japanese yam (Dj-dioscorins), affected the immunological functions of mice. Dj-dioscorins, like TN1-dioscorins, may trigger pro-inflammatory cytokines and promote RAW 264.7 phagocytosis. Intraperitoneal injection of TN1-dioscorins into mice induced phagocytosis of bone marrow, spleen, and thymic cells. T and B cells extracted from bone marrow, spleen, and thymus of mice injected with Dj-dioscorins, on the other hand, showed greater proliferative responses to mitogens. Dj-dioscorins also increased CD4(+), CD8(+), and Tim3(+) (Th1) cell proliferation in the spleen, as well as CD19(+) cell proliferation in the spleen and thymus. The addition of Dj-dioscorins to lymphoid cells derived from Dj-dioscorins primed mice caused spleen and thymic cell growth (Lin et al., 2009).

Andographis paniculate

The immunomodulatory activity of HN-02, a pure powder extract containing a mixture of andrographolides (i.e., andrographolide [88%] plus 14-deoxyandrographolide and 14-deoxy-11,12-didehydro-andrographolide together [12%]) was tested on different in vivo and in vitro experimental models at 1.0, 1.5, and 2.5 mg/kg. Potentiation of the delayed-type hypersensitivity (DTH) response was found in the delayed-type hypersensitivity (DTH) mice model following treatment with cyclophosphamide (CYP) and HN-02. HN-02 pretreatment, on the other hand, reversed CYP potentiation of the DTH response. Furthermore, HN-02 treatment increased the number of plaque-forming cells (PFCs) and raised the reduced hemagglutination antibody (HA) titer in the spleen cells of mice treated with CYP and challenged with sheep red blood cells (SRBC). In addition, it was discovered that HN-02 therapy induced phagocytosis in mice. During 30 days of treatment with HN-02, mice had a substantial rise in total WBC count and relative weight of spleen and thymus (Naik and Hule, 2009).

Curcuma longa

Curcumin is a polyphenol found in turmeric, a nutritional spice. Numerous transcription factors, cytokines, adhesion molecules, and enzymes related to inflammation have been shown to be regulated by it. Curcumin has been found to have nematocidal action in addition to reducing the development of a number of infections. Curcumin's schistosomicidal efficacy in vivo, as well as immunomodulation of granulomatous inflammation and liver pathology in acute schistosomiasis mansoni, was investigated in this research. Curcumin therapy modifies infected mice's cellular and humoral immune responses, resulting in a substantial decrease in parasite load and liver damage in acute murine schistosomiasis mansoni (Allam, 2009).

IMMUNOMODULATORS AS PROPHYLAXIS

Modulation of immunological responses through a phyto-stimulatory extract's or suppressive action may aid in the maintenance of a disease-free state in healthy or sick individuals. In the face of a weakened immune response, agents that stimulate host defence systems may be used as a supplement to traditional chemotherapy. Because of its rapid rate of cell growth, bone marrow is a particularly vulnerable target for cytotoxic medicines. In reality, the most impacted organ during immunosuppressive treatment with this family of medications is the bone marrow. Thrombocytopenia and leucopenia are caused by the loss of stem cells and the inability of the bone marrow to produce new blood cells. Saponins are triterpenoid or steroidal glycosides that have been shown to be important phytoconstituents with antiallergic, antiphlogistic, cytotoxic, antitumor, antiviral, immunomodulating, antihepatotoxic, molluscicidal and antifungal properties. The immunostimulant activities of three diosgenyl saponins derived from Paris polyphylla have recently been described. To investigate the involvement of saponins in the immunomodulating action of *Astragalus melanophrurius*, lymphocyte stimulation assays were conducted on eight cycloartane-type saponins isolated from the plant. Inhibitory effects have been seen at higher doses of the tested substances. Interleukin-2 activity was clearly increased by cycloartane and oleanane-type triterpenes from these plants. Terpenoid substances including glycyrrhizinic acid, ursolic acid, oleanolic acid, and nomilin have been shown to have immunomodulatory properties. AECHL-1, a new triterpenoid isolated from the root bark of *Ailanthus excelsa* Roxb. (Tree of Heaven), may have anticancer potential.

COVID-19 treatment should have (a) antiviral capabilities against SARS-COV-2, (b) be safe for concurrently given medicines such as antihypertensive, anti-diabetic, anti-asthmatics, and drugs for respiratory tract infections (c) should have the capacity to rejuvenate the immune system (mainly for cardio-respiratory and nervous system) and (d) therapeutic adjuvant activity with medicines used in WHO. Solidarity studies are required to investigate if the botanicals *Withania somnifera*, *Tinospora cordifolia* and *Asparagus racemosus* can replace the need (Borse et al., 2021). To understand the immunomodulatory function of phytochemicals, a network pharmacology model was developed to identify and illustrate the interactions of phytochemicals with molecular targets in the immune system. The phytoconstituents were also docked to three SARS-CoV-2 molecular targets to see whether they have antiviral action. Predictive techniques were also applied to evaluate the possibility for interactions between phytoconstituents and frequently prescribed medications. Following extensive testing, the findings show that Ayurvedic Rasayana botanicals have the potential for immunomodulatory and antiviral action, and may be applied as a therapeutic adjuvant for COVID-19 treatment.

The use of various plant extracts and herbal fed additives in specific doses during the scheduled vaccination regimen may aid in the production and development of more effective cell mediate immune responses for protection against various bacterial, viral, and other diseases, as well as obtaining higher protective antibodies against different infections. As a result, herbal formulations may be suggested for usage as a positive immunomodulator. Because of their great effectiveness, cheap cost, and minimal toxicity, many botanical compounds have potential medicinal uses.

CONCLUSION

The purpose of this review is to look at Ayurvedic Immunomodulatory herbs. Numerous investigations have shown the discovery of immunomodulatory substances with pharmacological efficacy and low toxicity. In this setting, ethnopharmacology is the most effective method for discovering novel and therapeutically useful compounds. The phytochemical study of Rasayana plants showed a significant variety of chemicals with immunomodulatory effects, including tannic acid, flavonoids, tocopherol, curcumin, ascorbate, carotenoids, polyphenols, and others. Because they include plants with immunomodulatory characteristics that work synergistically, herbal combination preparations used in Indian traditional medicine may promote immunomodulation. This theory, coupled with the absence of toxicity, may be crucial to comprehend their usage in the past and now. From the preceding discussion, it should be clear that many medicinal herbs have immunomodulatory action in experimental animals at a certain dosage. To assess their pharmacological efficacy, researchers used a variety of in vivo and in vitro screening techniques. Some medicinal herbs, such as *Ocimum sanctum*, *Tinospora cordifolia*, and *Terminalia arjuna*, may boost the immune system while others can inhibit it (*Alternanthera tenella*). In addition, a variety of secondary metabolites (such as alkaloids, glycosides, saponins, flavonoids, coumarins, and sterols) have immunomodulatory properties. As a result, the aforementioned review resulted in a positive evaluation.

CONFLICTS OF INTEREST

The author declares no conflicts of interest.

DECLARATION

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