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Review Article

Herbal Immunomodulators: A Natural Strategy for Immune System Regulation

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Abstract

Ayurveda, the ancient Indian medical science, aims to prevent illness through a holistic approach that emphasizes daily health practices aligned with individual and seasonal biorhythms. This contrasts with modern medicine, which focuses on activating the body's defense mechanisms using microbial preparations for immunization. Recent interest has emerged in natural compounds that can modulate immune responses, known as immunomodulators, which can either stimulate or suppress immune functions. The immune system comprises two primary responses: the innate response, which is rapid and non-specific, and the adaptive response, which is slower but highly specific. Immunomodulators play a crucial role in managing various diseases by either enhancing or inhibiting immune responses, making them essential in clinical applications such as autoimmune disorders, cancer immunotherapy, and organ transplantation. Natural immunomodulators, derived from plants, are gaining attention for their potential benefits and lower side effects compared to synthetic counterparts. This abstract explores the categories of immunomodulators, their clinical applications, and the role in immune regulation, highlighting the significance of traditional medicinal plants in contemporary health practices.

Keywords: Herbal Drugs; Ayurveda; Immunomodulatory; Diseases

Introduction

The primary goal of the ancient Indian medical science known as Ayurveda is to delay the onset of illness. It promotes a variety of everyday health care practices in order to accomplish this. These practices include a particular way of living with a well-defined daily schedule that aligns with personal biorhythms and a seasonal biorhythm that maintains the body's physiological rhythm throughout the day or year. Comprehensive harmonization is achieved through this method on a cellular and systemic level [1]. Modern medicine, in contrast to Ayurveda, emphasizes activating the body's non-specific defense mechanisms. Microbial preparations are used in active immunization techniques, which boost the host's resistance to infections. A new class of compounds that come from natural sources and have the ability to alter the immune response and the course of disease have recently piqued interest. Any drug that modifies the innate and adaptive immune responses, as well as other immune system components or functions, either specifically or broadly, is referred to as an immunomodulator [2]. The innate system response and the adaptive system response are the two primary types of immune system reactions. All vertebrates share a surveillance mechanism called the adaptive immune response, which is very specific but slow to respond to the antigen. Known as the first line of defense, the innate immune response is non-specific and incredibly fast to a foreign body (antigen); it operates in the early phase.

This could be accomplished by (i) suppressing the synthesis of effector cells or (ii) removing the immunity inhibitory mechanisms, which would promote the synthesis of immunostimulants. Immunosuppression is produced by humoral and dietary factors,

as well as by effector or inhibitor cells. Immunostimulation is necessary while receiving chemotherapy for cancer [3]. The immune system's mission is to protect the body from pathogenic microbes and make sure that the illness is cured. The prior goal of donor organ transplantation was to compromise immune function. Antigen processing by phagocytosis-capable cells, such as macrophages, monocytes, and related cells, is widely believed to be the process by which an antigen recognized as "self" (autoantigen) or as foreign ("nonself") activates the immune system. Although bacteria, viruses, and archaea are among the most complex organic substances in the human body and can cause diseases when they enter the body and challenge the body's defenses, the human immune system is fully capable of defending against a variety of infections [4]. The body's system is the single location where all human antibodies are made. When a person's immune system is less active than usual, they have human immunodeficiency, which can lead to recurring infections that are potentially fatal. Immunodeficiency in humans can arise from immunosuppressive medication use, acquired diseases like HIV/AIDS, or genetic diseases like severe combined immunodeficiency. Conversely, autoimmunity results from an overly active immune system that targets healthy bodily tissues as though they were alien invaders. A few of the most common examples of autoimmune disorders are Hashimoto's thyrotrophic hypothyroidism, rheumatoid arthritis, diabetes mellitus type 1, and systemic lumps erythematosus. A topic of immunology is the study of all aspects of the immune system [5]. The goal of immunomodulation as a therapeutic approach is to disrupt the defense system's self-regulating processes. Extrinsic or intrinsic substances that regulate or alter the immune response's scope, type, duration, or competency are known as immunomodulators. Immunomodulators help the immune system return to balance. Because immunomodulators change the immune system's behavior, the inflammatory response is subsequently reduced. This indicates that immunomodulators regulate the immune response by either stimulating or suppressing it while maintaining a disease-free state. These can also be used as an adjuvant therapy in addition to chemotherapy. Both synthetic and natural immunomodulators contribute to the immune system's normalization or regulation. Compared to prescription immunomodulators, natural immunomodulators appear to be less effective and cause fewer side effects. Because they reduce that immune response, synthetic immunomodulator medications have an anti-inflammatory effect on the gastrointestinal tract in ulcerative colitis and Crohn's disease [6].

Immunomodulator categories

Three categories are used to group them.

A Stimulant for immune

These agents work by leveraging the body's innate immunity to help humans combat a variety of microbes, including viruses, bacteria, and fungi. They can also include immune system strengthening at the same time [7].

IMMUNOEVIL: Immunosuppressive drugs, also known as immune system suppressants, are a structurally and functionally diverse class of pharmaceuticals that are typically used to treat a variety of surgical reactions following keratoplasty [8].

Adjuvants for immunity

What gives these vaccine enhancers their effectiveness are these adjuvants, as the term puts it. They also function as immunostimulatory agents by binding to particular antigens. Since the cellular and hormonal worker cells (T1 and T2) of the immune system are thus characterized among different immunity types, they really are the ones who choose which immune cells to be escorted to and from the specific body areas, namely the immune-protective, immune-destructive, and immune-inhibitory (IG) [9]. Immunomodulatory medications have the ability to both stimulate and inhibit (immunosuppressive and immunostimulatory) immune responses through the production of serum antibodies. Soluble mediators in the immune system, e.g. cytokines, agents for communication between cells, are also important. Higher cells are also affected by these regulators of the immune system, and are mainly CTL, neutrophils, natural killer (NK) cells, lymphocytes, and macrophages [10].

The aim of the latter type of drugs is to either directly inhibit the cell populations and subpopulations that lead to the safe immune response or to enhance the function of the immune response principal types and T cell mediated immune response pathways, besides SIRS disease [11].

Clinical applications of immunomodulators

By boosting or inhibiting the immune system, immunomodulators help control a number of diseases and are essential in a variety of clinical settings.

- Corticosteroids, a class of immunosuppressants, are frequently prescribed for autoimmune conditions such as multiple sclerosis, lupus, and rheumatoid arthritis. They suppress immune cell function and the production of inflammatory cytokines [12].
- An immunostimulant called granulocyte colony-stimulating factor (G-CSF) encourages the production of white blood cells, which are essential for fighting infection. It is frequently administered to cancer patients whose chemotherapy has increased their risk of infection [13].
- Immunotherapy for cancer employs the body's immune system to target and eliminate cancer cells, with the aid of immunomodulators to boost effectiveness. Notable examples include checkpoint inhibitors, which block checkpoint proteins that otherwise suppress immune activity. Drugs like nivolumab, pembrolizumab, and atezolizumab have been found to be effective against various cancers, including kidney, lung, and melanoma [14].
- By inhibiting the calcineurin pathway, which is necessary for T cell activation, calcineurin inhibitors, like tacrolimus and cyclosporine, stop organ rejection. Similarly, by inhibiting the mTOR pathway, which is necessary for T cell growth and proliferation, mTOR inhibitors such as sirolimus and everolimus stop rejection. By regulating immune responses to transplanted organs, these immunomodulators are essential to obtaining positive transplant outcomes. [15,16].Immunomodulators aid in modifying the responses of the immune system. They accomplish this through intricate interactions with molecules and cells. These compounds interact with to control the immune system's activities using various molecules and signaling pathways. Cytokines, which function as messengers in the immune system, are a prime target for immunomodulators. The production and function of cytokines such as interleukins (ILs) and interferons (IFNs) can be altered by immunomodulators, which can affect the immune system's reaction. For instance, certain immunomodulators promote the release of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) to improve disease protection. Other immunomodulators may inhibit the flow of these cytokines in conditions such as rheumatoid arthritis in order to reduce inflammation and prevent tissue damage [17].

Immunomodulators also affect cellular signaling pathways. For example, the regulation of gene expression during immune responses depends on the NF-κB pathway. Immunomodulators have the ability to alter this pathway by either starting the expression of pro-inflammatory genes or by activating it. or preventing it in order to lessen inflammation. Additionally, they can have different effects on the JAK-STAT signaling pathway. This pathway affects immune functions by transmitting signals from cytokine receptors to the cell nucleus [18].

The body's unique cells known as mesenchymal stem cells (MSCs) have the capacity to differentiate into various cell types. They can be found in a number of locations, including fatty tissue, bone marrow, and umbilical cord blood [19]. MSCs are essential for immune system relaxation. They have the ability to prevent immune cells from becoming overactive, such as T cells, B cells, and dendritic cells [20]. By interacting directly with these immune cells and releasing unique molecules that aid in lowering immune activity, MSCs are able to accomplish this. This capacity is essential for controlling the immune system and reducing inflammation [21]. MSCs also aid in the regulation of inflammation by lowering pro-inflammatory cytokines, which are the chemicals that cause inflammation to flare up. They also increase the synthesis of cytokines that are anti-inflammatory, which aid in the reduction of inflammation. This delicate balance is especially helpful in the treatment of conditions like autoimmune diseases and graft-versus-host disease (GVHD), which are marked by high levels of inflammation [22]. Owing to these characteristics, MSCs are thought to be a promising treatment for illnesses linked to the immune system, assistance with organ transplants, and support for tissue regeneration. To completely grasp their function and advantages, researchers are still investigating their potential in medicine [23].

Name	Common name	Scientific name	Family	Chemical constituents.
Garlic	Lasan, Allium	Allium sativam	Liliaceae	Allin, fatty oils, volatile oil, mucilage and albumin.[24]
Turmeric	Saffron indian, Haldi, Curcuma, Rhizoma curcumae	Curcuma longa	Zingiberaceae	Turmeric powder is made up of 60 to 70% carbohydrates, 6 to 13% water, 6 to 8% protein, and 5 to 10% fat. It also has 2 to 7% dietary oils, 3 to 7% dietary minerals, 1 to 6% curcuminoids, and lots of fiber. The volatile oil in turmeric includes zingiberene, phellandrene, sabinene, turmerone, arturmerone, borneol, and cineole. The special property that acts on the liver, known as choleretic, comes from tolylmethyl carbinol [24].
Ginger	Adarak, Rhizoma zingiberis, Zingibere	Zingiber officinale	Zingiberaceae	Ginger has 1 to 2% volatile oil, 5 to 8% spicy resin, and starch. The spicy taste of ginger is due to gingerol, which is a yellowish oil without a smell. In the volatile oil, there are sesquiterpene hydrocarbons like zingiberol, bisabolene, farnesene, and sesquiphellandrene. Other less acidic substances like shogaol and gingerone are present too. Shogaol comes from the drying of gingerol and isn't found in fresh ginger [24].
Amla	Indian Gooseberry	Emblica officanalis	Euphorbiaceae	Amla includes special components like emblicanin A (37%) and emblicanin B (33%). It also has 14% Pedunculagin and 12% punigluconin. This fruit is rich in punicafolin and phyllanemblin A, and it contains various beneficial elements like flavonoids, gallic acid, ellagic acid, and kaempferol. Amla is known for its diverse nutrients, offering minerals, vitamins, amino acids, fixed oils, and a flavonoid called rutin [25].
Aloe vera	Aloe or Ghrikumari	Aloe perryi Baker, Aloe vera, and Aloe ferox	Liliaceae	Aloe vera contains sugars, lignin, saponins, enzymes, minerals, and vitamins. It also includes salicylic acid and amino acids. It is particularly rich in vitamins C and E, beta-carotene, choline, folic acid, and vitamin B12 [26].
Tulsi	Sacred Basil	Ocimum sanctum	Lamiaceae	These leaves have a bright yellow, aromatic oil that varies from 0.1% to 0.9%. The amount of oil depends on its type, growing area, and harvest time. The oil, extracted through steam distillation from leaves and flowers, mainly consists of eugenol (70%), carvacrol (3%), and eugenol-methyl-ether (20%). [27]
Neem	Nimtree or Indian lilac	Azadirachta indica	Meliaceae	Neem includes compounds like Azadirachtin, meliacin, and quercetin. It also has things like Nembosterol, vitamin C, carotenoids, and amino acids. The oil from neem seeds is called Azadirachtin, and the oil from neem kernels is margosa oil [28]
Black pepper	Madagascar pepper	Piper nigrum	Piperaceae	Its main components are Pinpene and Terpinene.[29].
Onions	bulb or common onions	Allium ascalonicum	Amaryllidaceae	They include healthy molecules like polyphenolic compounds, phenolic acids, flavonoids such as fisetin and quercetin, vitamin C, and sulfur compounds.[30]
Clove	Loung	Eugenia caryophyllus	Myrtaceae	Clove has 14 to 21% oil that evaporates easily. It also contains eugenol, acetyl eugenol, gallotannic acid, crystalline components, caryophyllenes, methyl furfural, gum, resin, and fiber. Caryophyllin is like a phytosterol but has no smell, unlike eugenol, which is a colorless liquid.[31].
Gulvel	Amrita, Giloy, or Guduch,	Tinospora cordifolia Miers	Menispermaceae	It contains various chemical compounds, including N-methyl-2-(11-hydroxymustakone), Cordifolioside A, pyrrolidone, N-formyl annonain, Magnoflorine, syringin, and Tino cordiside, which have been studied for their health benefits.[32].

Coriander	Dhania	Coriandrum sativum	Umbellifera	This herb is rich in a variety of compounds such as alcohols, hydrocarbons, ketones, and esters. Linalool is the key component of its essential oil, which gives coriander its distinct aroma and potential health properties[33]
Mango	Aam	Mangifera indica	Anacardiaceae	Mangoes are known for being rich in essential amino acids like lysine, leucine, cysteine, valine, arginine, phenylalanine, and methionine. These nutrients play significant roles in the body, supporting growth and repair.[34]
Fenugreek	Methi or Greek hay	Trigonella foenum-graecum	Legumeceae	Polyphenol chemicals, such as rhaponticin and isovitexin[35]
Cardamom	Ela or Elaichi	Elettaria cardamomum	Zingiberaceae	It is loaded with several chemical compounds, including 1,8-cineole, α-terpinyl acetate, and borneol. These compounds contribute to cardamom's unique flavor and potential health benefits.[36]
Cumin	often called Jeera,	Cuminum cyminum	Apiaceae	This spice contains numerous compounds like alkaloids, anthraquinones, coumarins, flavonoids, glycosides, proteins, resins, saponins, tannins, and steroids. Such a diverse chemical composition makes cumin a staple in culinary and traditional medicine.[37]
Lemons	Lemon	Citrus limon	Rutaceae	They are composed of several chemical constituents, including acids, minerals, flavonoids, and essential oils. These components give lemons their characteristic sour taste and make them beneficial for various culinary and health applications.[38]
Papaya	pawpaw or melon tree	Carica papaya	Caricaceae	This fruit is packed with good stuff like vitamins, minerals, enzymes, and phytochemicals that are beneficial for health.[39]
Pomegranate	Greeny apple	Punica granatu	Punicaceae	This fruit has many important components, including sugars, acids, and minerals. It also contains bioactive compounds that interact with our body. [40]

Table 1: Some plants used as Immnomodulatos.

Conclusion

Immunomodulators are vital in therapeutic applications such organ transplantation, cancer immunotherapy, and autoimmune illnesses because they can either boost or suppress immune responses, which helps manage a variety of diseases. Plant-based natural immunomodulators are attracting interest due to their possible advantages and less adverse effects when compared to their synthetic counterparts. This abstract highlights the importance of traditional medicinal herbs in modern health practices by examining the types of immunomodulators, their clinical uses, and their function in immune regulation.

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