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Immunostimulators through natural sources: an enormous global demand for new effective therapies

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Abstract

The immunomodulatory medicinal plants in pharmacognosy are relatively recent. In a number of disease situations, the immune response is impaired. Thus, either activating or inhibiting the immune response can be a valuable treatment for maintaining a disease-free state. Immunomodulators can be used for the treatment of chemotherapy. Even while the immune system iscapable of maintaining immunity and combating infections, germs and viruses can impair it.If our immune system is operating properly, we are protected against viruses and illnesses caused by a lack of immunity. Immune modulators can assist us in interfering with this process while also strengthening our immune system. Immunomodulators serve a wide range of purposes. They increase the number of white blood cells in your body and change them to fight against germs and viruses that cause sickness. Tinospora cordifolia, Asparagus racemosus, Reishi, haritaki, and other plants have been extensively studied for immunostimulant activity. They are also preventing diabetics, improves cognitive functions, heals wounds and infections.

Keywords: Immunomodulators, immune deficiency disease, T-cells and B-cells,Cancer cells, Adaptogens.

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Introduction

Traditional remedies are usually harmless and therefore has no side effects. Various elements of herbal plants are well-known for their antiviral and immune-boosting properties. When combating a dangerous coronavirus like COVID19, it's necessary to take extra care to avoid becoming infected. As a result, we require a healthy and robust immune system. The best strategy to boost our immunity is to use medicinal plants and herbs to do it naturally [3]. Many infectious diseases, like covid-19 and others like Epstein Barr, candida infection, and other chronic infections, are increasingly seen as immune-related disorders. You may become sick more frequently and be more prone to infections if their immune system is compromised. A strong immune system assists in the fight against foreign particles that enter our bodies; to maintain a strong immune system, we must eat healthily, drink enough of water, exercise regularly, and get enough sleep. Using immunomodulators [2] produced from herbs and herbal products to boost our immunity and body's resistance to the infection.

Brief introduction for ayurvedic system

Ayurvedic system of medicine describes the concept called Ras Ayana under which rejuvenating drugs have been described. These rejuvenating drugs have been indicated for various uses like delaying the ageing process, maintenance of youth, improvement of mental health and also removal of diseased conditions caused due to infectious organism and also mental or physical stress. Ras Ayana promote the quality of all body tissues. The precise meaning of Ras Ayana is the therapeutics which promotes dhatus- tissues of body

and increase strength and immunity against diseases. It is one of Ayurveda's eight clinical specialties. The therapeutic plants described in Ras Ayana [4] help to improve the condition of bodily tissues in three different ways:

- Poshaka rasa
- Agni
- Srotasas shatavari

Milk and ghee improve the nutritional content of nutrient plasma, resulting in poshaka rasa. Plants like Bhalla taka and pippali help to improve nutrition by boosting digestion and metabolic activity (Agni). Srotasas causes micro-circulatory channels to become more efficient. They result in increased nutritional availability in the tissues. Gugguls are an excellent example of srotasa [11].

Natural immunomodulators

Natural immunomodulators are more beneficial for developing a strong immune capacity to battle numerous ailments such as malignancies, Epstein-Barr, candidiasis, and other infections such as corona and novel variations such as omicron, Delta, and Alpha, among others. Some herbs have antioxidant components that help slow down the cellular ageing process and strengthen the immune system, while others contain immune boosters that improve the neurological and hormonal systems [9]. Neem, Gilroy, garlic, almond, liquorice, wild carrot, basil, Arnica Montana (arnica), calendula officinalis (calendula) are some of the natural immunomodulators**.** echinacea (echinacea angustifolia), astragalus (astragalus membranous), reishi, Shitake, touch me not, burdock, chaparral, nettles, Wilford, haritaki, khus.

The danger of a weakened immune system

Immune system imbalances or severe disruptions can lead to a wide range of diseases. Recurrent viral infections, as well as fungal infections like candidiasis, are linked to T-cell abnormalities. When the immune system is compromised, not only do infections become more common, but there is also a risk of serious health concerns such as acquired immune deficiency syndrome (AIDS). The T and B-cell systems are the ones that aren't working properly in people with AIDS.

Multiple sclerosis, Epstein-Barr, Graves' disease, cystic fibrosis, and some forms of renal illnesses, as well as asthma, anaemia, and allergies, are all examples of severe immune deficiency disease [8].

Immunomodulation by Allopathic Drugs

Immunosuppressants: Immunosuppression generally refers to a reduction in resistance to stress and infections, although it can also result from environmental or chemotherapeutic factors. These are some clinical uses for immunosuppressants given below [15].

• To prevent transplanted organs and tissues from being rejected (kidney, bone marrow, heart, liver, etc.)

• To prevent graft-versus-host disease, which is the immune system's reaction to the body's own antigens in bone marrow transplants.

• To treat a range of illnesses, such as myasthenia gravis, systemic lupus erythematosus, rheumatoid arthritis, psoriasis, and ulcerative colitis, which though not fully understood, are thought to have an essential autoimmune component in their pathophysiology.[8]

• Selected immunosuppression to protect new-borns against Rh haemolytic illness.

Side Effects of Immunomodulator Drugs in allopathy

These medications have a number of adverse effects, including pulmonary toxicity, myelosuppression, alopecia, and increased infection risk. Diabetes, GI problems, hypertension, hyperkalemia, hyperglycemia, nephrotoxicity, hepatic fibrosis, lymphoma (related with the Epstein-Barr virus), and neurotoxicity (tremor, headache, motor difficulties, and seizures), Nephrotoxicity, hypertension, diabetogenic, elevated LDL cholesterol, tremor, hirsutism, hyperlipidemia, gum hyperplasia, hyperuricemia, hyper cholesterolemia, etc [7].

Immunomodulation by Medicinal Plants

Plant extracts used in conventional therapy are being examined for their immunomodulatory and chemoprotective properties. The biological response modifiers known as immunomodulators work to inhibit tumour growth by strengthening the body's natural defenses. They directly inhibit the proliferation of tumor cells while also improving the host's tolerance to the harm caused by potentially toxic medicines used to treat cancer [5]. When the host's defenses need to be activated due to impaired immune responsiveness or when a selective immunosuppression needs to be induced in a situation like inflammatory diseases, auto-immune disorders, or organ/bone marrow transplantation, immunomodulatory therapy may offer an alternative to conventional chemotherapy [11].

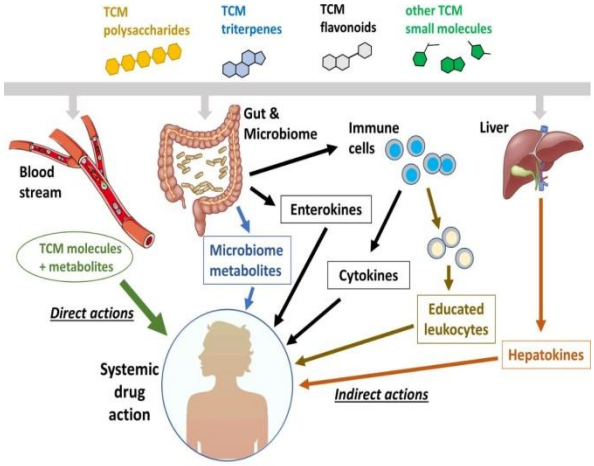
A number of Indian medicinal plants and various “Rasayana” have been claimed to possess immunomodulatory activity [4].

Natural herbs enhancing the immune system

Some of the most effective immune system boosters are found in certain therapeutic herbs that strengthen and

stabilise the neurological and hormonal systems, allowing us to adapt to the many different stressors of contemporary life. Some also include antioxidants, which can help to slow down the ageing of cells while also boosting the immune system. Others include immune-stimulating polysaccharides, which have a wide range of medicinal applications [9]. They can help the immune system fight off invading antigens (bacteria and viruses), and they may even be able to combat cancer. They can also protect against the negative effects of some cancer therapies and aid in the prevention of Cancer metastasis surgery [1]. A variety of other herbs are potent tonics that boost the immune system from the inside out. They've been shown to help regenerate bone marrow reserves, boost T-cell activity, and activate macrophages [10].

Mechanism of action of herbal immunomodulator: HerbalImmunomodulators act at different sites in the body especially on immune system. They strengthen and normalize the nervous and hormonal system thus helping an individual to various stress including physical and psychological stress. Sometimes they also increase the weight of different organ such as spleen, kidney, and liver etc. They can be used as a prophylaxis or in combination with other therapeutic modalities because they can boost or defeat the host response [1].



Role of T Cells and B Cells in Immunity

The most important elements of the adaptive immune system are T cells and B cells. These cells are crucial for the body's defence against disease and are crucial in controlling hypersensitivity to benign or "self" antigens.

T cells and B cells have many characteristics, yet they operate in the immune system in very different ways.

B cells are primarily in charge of humoral immunity, whereas T cells are involved in cell-mediated immunity (related to antibody production). Additionally, the monitoring systemsThese two cell types differ greatly from one another. While B cells can directly recognise the surface antigens of bacteria and viruses, T cells can only detect viral antigens outside of infected cells [9].

It's crucial to first discuss the fundamental roles of each cell type in order to comprehend how these cells cooperate to coordinate an efficient immune response.

B Cells and Humoral Immunity

Before developing into plasma cells that release antibodies to fight infection, B lymphocyte' key role is to recognize antigens.

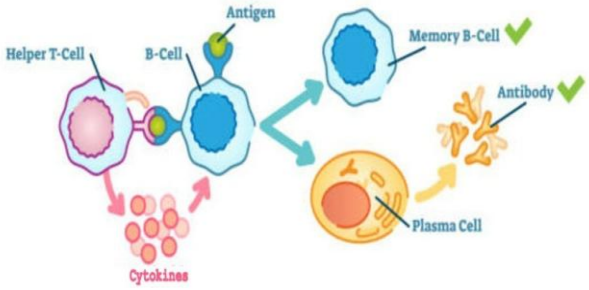
B cells, also known as CD19+ B Cells, use their surface receptors to identify foreign invaders such as bacteria. A B cell will engulf an antigen by a mechanism known as receptor-mediated endocytosis when a B cell receptor interacts to the antigen.

The antigen is then changed into peptides by the B cell, which are then visible on the B cell's surface. These peptides belong to the separate class of MHC class II molecules, which are molecules with high histocompatibility.

Helper T cells, also known as CD4+ T cells, are able to recognise and attach to the MHC class II by this procedure. In turn, the helper T cells' binding causes the release of cytokines.

Important signalling proteins known as cytokines encourage the proliferation anddifferentiation of other B cells into plasma cells.

Antibodies that are exclusive to the antigen that was initially attached to the B cell are released by these plasma cells [21].



B cell Activation Process

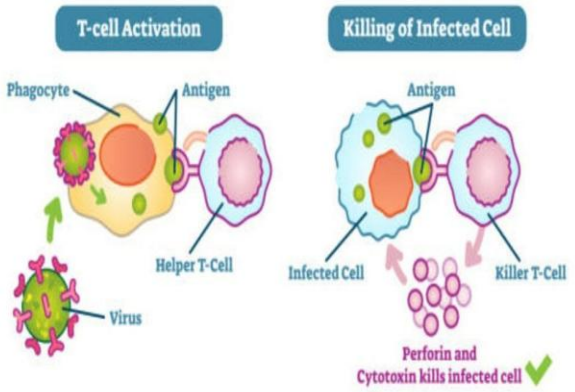
T Cells and Cellular-mediated Immunity

The immune response is guided by the cytokines released by T cells. Cytotoxic T cells, on the other hand, create lethal granules that kill pathogen-infected cells.

A cell that has been infected by a virus is the first step in the activation of cytotoxic T cells, also known as CD8+ T cells. This infected cell produces viral proteins and peptides and harbours viral mRNA and DNA. The MHC class I on the surface of the infected cell displays these viral peptides [6].

By displaying the infectious proteins on its membrane, the infected cell is sending a warning signal to CD8+ T cells. Through their T cell receptors (TCRs), CD8+ T cells identify viral peptides and release cytotoxins like perforin or granulysin that cause programmed cell death.

As an alternative, the Fas ligand pathway can be used by cytotoxic T cells to kill infected cells. The Fas ligand, which is expressed by cytotoxic T cells, binds to transmembrane receptor proteins on the target cell. By altering the Fas proteins through a complicated signalling pathway, this interaction causes cell death [12].



Herbal Plants as Immunostimulators

Reishi

This therapeutic mushroom grows wild, primarily on ancient broad-leaved trees. It has a purplish-brown or reddish-brown stem that is normally 2 to 5 inches in length. It is well-known in China under the name lingchi and in Japan under the name reishi. Reishi was originally regarded to be an excellent medicine for avoiding illness, maintaining health, and extending life expectancy. It's been used as a chi tonic for centuries [1].

Here is a brief summary of the beneficial action of reishi: Reishi provides protection against certain types of cancer, improves vitality, and strengthens internal organs, relieves neurasthenia and stress, improves viral hepatitis conditions, protects the liver from chemical damage, improves body functions, relieves insomnia by improving muscle relaxation, improves blood flow to the coronary arteries, and thus improves circulation [15].

Shitake (Lentinus edodes)

The shitake mushroom, which is linked to the reishi fungus, was discovered growing wild on a Japanese evergreen oak tree. It may also be found on other oak species and is being grown in Japan. It's used to treat liver issues, tiredness, and weakness. It was also utilised to improve overall health and delay the onset of old age. Shitake mushroom is a powerful immune tonic and adaptogen. It contains lentinan, a polysaccharide that has been studied for its immune-stimulating and anticancer properties. It causes T-helper cells to become activated, it activates Interferon is produced by macrophages when they are stimulated. One guy in Japan is believed to have recovered from AIDS after consuming massive amounts of Shitake mushroom [1].

TOUCH- ME-NOT

This tall shrub, which belongs to the same plant family as Panax ginseng, is native to numerous parts of China as well as the southern regions of the Soviet Far East. The shrub has clusters of purple berry-lime fruits that mature in September and blooms with violet or yellowish flowers in July.The adaptogen effects of eleuthero have been studied in over 1,000 research investigations [1]. The herb's ability to increase the human body's adaptive capacity to a variety of abnormal physical, biological, chemical, and psychological factors, as well as its near-total non-toxicity, was discovered. It has antibacterial, antivenom, antifertility, anticonvulsant, antidepressant, aphrodisiac, and other properties that help cure a variety of medical ailments [16].

Mistletoe (Viscum Album)

Therapists utilise mistletoe leaves and twigs, as well as formulations developed in Germany, to try to cure circulatory and pulmonary issues. Although studies have revealed that the extract from these leaves may alter the immune system and have the ability to destroy some types of cancer cells. They are also used to treat exhaustion, anxiousness, and sleeplessness, as well as to improve cardiovascular health, relieve stress and anxiety, and stimulate the immune system to combat colds and respiratory issues [17].

Tripterygium Wilfordii

It's also known as the thunder god vine, and it's employed in Chinese medicine. It has been enhanced for use in rheumatoid arthritis and psoriasis; a chemical isolated from the herb, triptolide, was discovered in Nature Communications. In East Asia, Tripterygium Wilford is commonly used to treat immune-inflammatory illnesses such SLE, RA, psoriasis, and asthma. In traditional Chinese medicine, rheumatoid arthritis, systemic lupus erythematosus, and renal illness are also treated [18].

Bacopa Monnieri

It's also known as Brahmi; it grows well in moist and humid areas, and its propensity to flourish in water makes it a desirable aquarium plant. It's used for a

variety of things, including memory enhancement, anxiety reduction, and epilepsy treatment. It has anticancer characteristics, as well as the ability to alleviate ADHD symptoms and control blood pressure [19].

Khus

The flowers of poppy seeds are called as khus. The seeds are tiny and hard with a western type in slate blue colour while creamy off-white is Indian one. It is used in ayurvedic preparations for treating inflammation,prevents sleep disorders, improves immunity, zinc present in khus that facilitates stronger immunity in the body by resisting foreign bodies and building a strong metabolism, also improves heart's function, prevents kidney stones, improves digestion, prevents respiratory problems etc [20].

Haritaki

It is a miraculous ayurvedic fruit that is extensively used for a wide range in traditional remedies. Chebulic myrobalan is one of the three musketeers that constitute the potent rejuvenate triphala formulation. It improves immune system and fight against microbes & various infections. It also inherently portrays the presence of strong antiviral, antibacterial, and antifungal properties, which effective in preventing infections. They are also preventing diabetics, improves cognitive functions, heals wounds and infections [14].

Tinospora Cordifolia

It is also called as amrita Valli in Sanskrit, it is a shrub that grows in India.They are highly valued in ayurveda for it revitalise immune boosting and other benefits like detoxify the body, and reduces stress & anxiety, also having anti-inflammatory properties. The chemicals present in this might have activity against cancer cells in test animals [13].

Conclusion

Immunomodulators (more accurately, immunostimulants), like Ras Ayana, and adaptogen actions have all been linked to some of their constituents. High molecular weight polysaccharide components, as well as glycolipids and peptides, have been linked to immunostimulant activity. Macrocyclic lactones, quinones, alkaloids, alkylamines, sesquiterpenes, di-, and triterpenoids are low molecular weight compounds with a high percentage of immunostimulant activities. Tinospora cordifolia, Asparagus racemosus, Reishi, haritaki, and other plants have been extensively studied for immunostimulant activity. By preparing new formulations using these natural modulators, we can overcome many variants in corona as well as other new infections that may be caused by our lifestyle and eating habits. Immune function is the result of a complicated chain of events including effective communication between all of the body's tissues. Many common illnesses are caused or progressed by changes in immune function balance. Natural chemicals will aid in the body's immune system's optimal function as well as the management of undesired inflammatory reactions. Nature's Immune Stimulator is a combination of well-researched natural herbs that have been shown to boost and improve the immune system, fight infections, aid in the healing of infections-related injuries, and regulate other disorders that can lead to illness.

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