



A REVIEW ON NATURE'S IMMUNE BOOSTERS

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ABSTRACT

The immune system is one of nature's most fascinating inventions. It is an amazing protection mechanism designed to defend us against millions of bacteria, viruses, fungi, toxins and parasites. The immune system is very complex. It is made up of several types of cells and proteins that have different jobs to do in fighting against foreign invaders. If our immune system is working properly we are protected from dangers caused by microbes. If not, we suffer sickness and disease. It is possible to intervene in this process and make our immune system stronger using immune boosters. Immune boosters work in many ways. They increase the number of white blood cells in the immune system army, train them to fight against microbes causing diseases. This review article gives an overall view about some natural herbs like *Echinaceae purpurea* [Cone flower], *Panax ginseng* [Asian ginseng], *Astragalus membranaceus* [Milk vetch], *Uncaria tomentosa* [Cat's claw] and *Withania somnifera* [Ashwagandha] that have been proven clinically for their strong immunostimulatory activities.

Keywords: Immune system, Microbes, Immune boosters, Natural herbs, Remedy.

INTRODUCTION

The immune system is the body's defense against infectious organisms and other invaders. Through a series of steps called the immune response, it attacks organisms and substances that invade body systems and cause disease. It is made up of a network of cells, tissues, and organs that work together to protect the body.¹ The cells involved are white blood cells, or leukocytes which are produced and stored in many locations in the body, including the thymus, spleen, bone marrow and lymph nodes. The leukocytes circulate through the body between the organs and nodes via lymphatic vessels and blood vessels. In this way, the immune system works in a coordinated manner to monitor the body for germs or substances that might cause problems.²

Cells of Immune system

Phagocytes and Granulocytes

Phagocytes are large white cells that can engulf and digest foreign invaders. They include monocytes, which circulate in the blood, and macrophages, which are found in tissues throughout the body, as well as neutrophils, that circulate in the blood but move into tissues where they are needed. Macrophages are versatile cells; that act as scavengers. They secrete a wide variety of powerful chemicals, and they play an essential role in activating T cells.³

Neutrophils are not only phagocytes but also granulocytes: they contain granules filled with potent chemicals. These chemicals, in addition to destroying microorganisms, play a key role in acute inflammatory reactions. Other types of granulocytes are eosinophils and basophils. Mast cells are granule-containing cells in tissue.⁴

T Cells

T cells contribute to the immune defenses in two major ways. Some help regulate the complex workings of the immune system, while others are cytotoxic and directly contact infected cells and destroy them.

Chief among the regulatory T cells are "helper/inducer" T cells. They are needed to activate many immune cells, including B cells and other T cells. Another subset of regulatory T cells acts to turn off or suppress immune cells.

Cytotoxic T cells help rid the body of cells that have been infected by viruses as well as cells that have been transformed by cancer. They are also responsible for the rejection of tissue and organ grafts.^{3,4}

B Cells

B cells are lymphocytes that play a major role in the humoral immune response. The principal functions of B cells is to produce antibodies against antigens, perform the role of antigen-presenting cells (APCs) and eventually develop into memory B cells after activation by antigen interaction. B cells are an essential component of the adaptive immune system.^{3,4}

Natural Killer Cells

At least two types of lymphocytes are killer cells - cytotoxic T cells and natural killer cells. To attack, "cytotoxic T cells" need to recognize a specific antigen, whereas natural killer or NK cells do not. Both types contain granules filled with potent chemicals, and both types kill on contact. The killer binds to its target, aims its weapons, and delivers a burst of lethal chemicals.



Complement

The complement system consists of a series of proteins that work to "complement" the work of antibodies in destroying bacteria via two cascade like path ways – classical and alternative complement pathway.

Cytokines

Cytokines are diverse and potent chemical messengers secreted by the cells of the immune system-and the chief tool of T cells. Lymphocytes, including both T cells and B cells, secrete lymphokines, while monocytes and macrophages secrete monokines. Cytokines encourage cell growth, promote cell activation, direct cellular traffic, and destroy target cells—including cancer cells. Because they serve as a messenger between white cells, or leukocytes, many cytokines are also known as interleukins. (e.g.: Il-1, Il- 2 etc).

Immune response

The immune response is how the body recognizes and defends itself against bacteria, viruses, and substances that appear foreign and harmful. The first requirement of a defense system is to recognize that a foreign substance [antigen] has entered into the body. The second requirement is to kill/eliminate the antigen out of the body. The resistance offered by the immune system can be categorized into two major divisions - Humoral immune response and Cell mediated immune response.

Humoral immune response

The humoral response, or antibody-mediated response uses specific immune-system structures called antibodies. The first stage is the ingestion (phagocytosis) of foreign matter by special blood cells called macrophages. The macrophages digest the infectious agent and then display some of its components on their surfaces. Cells called helper-T cells recognize this presentation, activate their immune response, and multiply rapidly. This is called the activation phase.

The next phase, called the effector phase, involves a communication between helper-T cells and B-cells. Activated helper-T cells use chemical signals to contact B-cells, which then begin to multiply rapidly as well. B-cell descendants become either plasma cells or B memory cells. The plasma cells begin to manufacture huge quantities of antibodies that will bind to the foreign invader (the antigen) and prime it for destruction. B memory cells retain a "memory" of the specific antigen that can be used to mobilize the immune system faster if the body encounters the antigen later in life. These cells generally persist for years.^{5,6}

Cell mediated immune response

Macrophages or antigen presenting cells engulf antigens, process them internally, then display parts of them on their surface together with Class II MHC Molecules. This sensitizes the T cells to recognize these antigens. Helper T cells (CD4+) serve as managers, directing the immune

response. They secrete chemicals called lymphokines that stimulate cytotoxic T cells and B cells to grow and divide, attract neutrophils, and enhance the ability of macrophages to engulf and destroy microbes. Cytotoxic or killer T cells (CD8+) release lymphotoxins, which cause cell lysis. Suppressor T cells inhibit the production of cytotoxic T cells once they are unneeded. Killer-T cells also produce T memory cells which "remember" a specific protein or antigen.

On the whole, immune system does a remarkable job of defending us against disease-causing microorganisms. But sometimes it fails. Many conditions such as age, poor nutrition, stress, environmental pollution, organ- or systemic malfunctions and unhealthy lifestyle can reduce an individual's immune status thus allowing a germ to invade successfully and cause infection and disease. In such conditions immune system can be enhanced using immuno stimulators. Modern research on remedies of natural origin has pointed that a number of herbs have complex actions on immune function and acts at many different sites in the overall cascade of immune events and can act as a strong immune stimulators.⁷⁻¹⁰ This review article gives an overall view about some natural herbs like *Echinaceae purpurea* [Cone flower], *Panax ginseng* [Asian ginseng], *Astragalus mambraneous* [Milk vetch], *Uncaria tomentosa* [Cat's claw] and *Withania somnifera* [Aswagandha] that have been proven clinically for their strong immunostimulatory activities.

ECHINACEA PURPUREA

Family: Asteraceae

Common names: Purple cone flower, Sampson, Snake root, Red sun flower.

Echinacea is a genus of herbaceous flowering plants in the daisy family, *Asteraceae*. They are endemic to Eastern and Central North America, where they are found growing in moist to dry prairies and open wooded areas. They have large, showy heads of composite flowers, purple in colour blooming from early to late summer. It has a faint aromatic smell, with a sweetish taste, leaving a tingling sensation in the mouth. Some species are used in herbal medicines and some are cultivated in gardens for their showy flowers.¹¹⁻¹³



Figure 1: *Echinaceae purpurea*

Primary chemical constituents of Echinacea are known to include mucopolycarbohydrides, echinacoside, echinaceine, isobutylamines, linoleic and palmitic acids, essential oils, glycosides, inulin, polyacetylenes, sesquiterpenes, betaine, and phenolics. Echinacea also contains small amounts of iron, iodine, copper, potassium, sulphur, vitamin A, vitamin E and vitamin C.¹⁴⁻¹⁶ Several species of the echinacea plant are used to make medicine from its leaves, flower, and root. Echinacea is widely used to fight infections, especially common cold and other upper respiratory infections.¹⁷ Some people take echinacea at the first sign of cold, hoping they will be able to keep the cold from developing. Other people take echinacea after cold symptoms have started, hoping they can make symptoms less severe.¹⁸⁻²¹ Research to date shows that echinacea can help treat a cold, but it won't prevent one. Echinacea is also used against many other infections including the urinary tract infections, vaginal yeast infections, genital herpes, bloodstream infections (septicemia), gum disease, tonsillitis, streptococcus infections, syphilis, typhoid, malaria and diphtheria. Echinacea is one of the most popular herbs and has been extensively studied for its effects on the immune system.²² It has been used as an immune stimulant for a variety of afflictions including colds and flu. Echinacea is widely promoted for its ability to "boost" the immune system.²³

Action on immune system

Echinacea is one of the strongest immune stimulators and enhancers known. It works in two main ways. First, it builds up the immune system by stimulating the body to produce more immune cells and immune chemicals. Secondly, it stimulates these cells into action and heightened activity levels. These actions will help combat any infection or disease more effectively and also protect from future invasion and illness. Echinacea stimulates the 'non-specific' activity of the immune system. It increases the amount of T-cells and macrophages in the bloodstream. It also increases the amount of Interferon, Interleukin, Immunoglobulin and other important natural immune chemicals present in our blood.²³ A number of in vitro and animal studies have shown that Echinacea appears to increase immunologic activity by increasing levels of interferon and may increase phagocytosis, cellular respiratory activity, and lymphocyte activation through release of tumor necrosis factor, interleukin-1 and interferon β_2 .²⁴

The Polysaccharide constituents of Echinacea bind to carbohydrate receptors on the surface of T-lymphocytes and macrophages to produce immune stimulatory effects. It increases the ability of macrophages to engulf and destroy bacteria, viruses and foreign matter, through a process known as phagocytosis.²⁵⁻²⁷ It also destroys tumor cells. It promotes chemotaxis of monocytes and neutralizes viruses and causes bacteriolysis. Inulin another important component activates the alternative complement pathway.²⁸ This results in an influx of white

blood cells into areas of infections, thus destroying bacteria, viruses, and microorganisms. In addition, consumption of Echinacea is claimed to further heighten the alternate complement pathway by increasing levels of properdin - the natural immune system stimulant of the body.

Echinaceae is proven to have stimulating effect on another important cell of innate immunity, the Natural killer cells [NK cells].²⁹ In addition, it boosts the body's own production of the powerful antiviral compound interferon. Interferon works by attacking the genetic blueprint of germ cells, rendering them unable to reproduce, thus echinacea effectively limits the spread of the cold virus throughout the body by preventing the germ cells from multiplying. It is also instrumental in preventing bacteria from producing an enzyme called hyaluronidase, which allows the bacteria to penetrate cell membranes, thus being readily transported to many parts of the body and causing generalized infection.

In a double-blind, placebo-controlled studies enrolling a total of more than 1,000 individuals it was found that various forms and species of Echinacea can reduce cold symptoms and help to get over a cold faster.³⁰ In another double-blind, placebo-controlled trial, 80 individuals with early cold symptoms were given either an above-ground *E. purpurea* extract or placebo.³¹ The results showed that the people who were given Echinacea recovered significantly more quickly: just 6 days in the Echinacea group versus 9 days in the placebo group. And, symptom reduction with a whole plant formulation of *E. purpurea* was seen in a double-blind, placebo-controlled study of 282 people.³²

Another double-blind study suggests that Echinacea cannot only make colds shorter and less severe, it might also be able to stop a cold that is just starting.³³ In this study, 120 people were given *E. purpurea* or a placebo as soon as they started showing signs of getting a cold. Participants took either Echinacea or placebo at a dosage of 20 drops every 2 hours for 1 day, then 20 drops 3 times a day for a total of up to 10 days of treatment. The results were promising. Fewer people in the Echinacea group felt that their initial symptoms actually developed into "real" colds (40% of those taking Echinacea versus 60% taking the placebo actually became ill). Also, among those who did come down with "real" colds, improvement in the symptoms started sooner in the Echinacea group (4 days instead of 8 days). Both of these results were statistically significant.

PANAX GINSENG

Family: Araliaceae

Common names: Asiatic ginseng, Chinese ginseng, five-fingers, Japanese ginseng, jintsam.

Panax ginseng is a shade-loving, deciduous perennial herb found throughout East Asia, Russia and cooler regions of northern hemisphere. It reaches a height of about one foot. The ginseng plant has yellowish-green



umbrella-shaped flowers that grow in a circle around a straight stem, with its five leaflets joined together at one point. The fruit is a bright crimson berry containing one to three wrinkled seeds. The root of *Panax ginseng* is a thick structure that resembles a human-like form, which is responsible for its name in Chinese, jen shen, or "man-root." There are two distinct forms of *Panax ginseng*, red and white ginseng. The difference is the method of processing that result in different pigment compositions; white ginseng is produced by harvesting the root and drying it in the sun, while red ginseng is steamed after harvest and dried.

The content of ginsenoside compounds differs slightly between the red and white forms.³⁶⁻³⁹ The root is utilized medicinally, although active compounds are present in all other parts of plant.

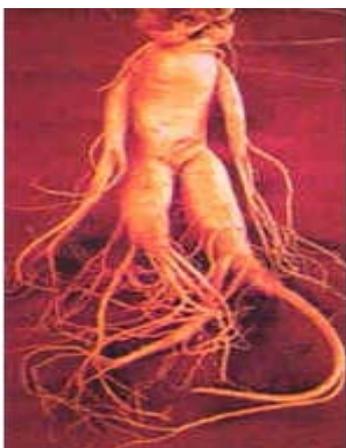


Figure 2: *Panax ginseng*

Panax ginseng contains triterpene glycosides, or saponins, commonly referred to as ginsenosides. Many active compounds can be found in all parts of the plant, including amino acids, alkaloids, phenols, proteins, polypeptides, and vitamins B1 and B2. Ginsenosides contain aglycone dammarol, panaxosides contain oleanolic acid as aglycone. Panaxosides gives oleanolic acid, panaxadiol and panaxatriol on decomposition.⁴⁰⁻⁴³

Ginseng has been used for a variety of purposes for about 5000 years. It has been used to increase physical endurance and lessen fatigue, to improve the ability to cope with stress, and to improve concentration. It is also used for anemia, diabetes, gastritis, neurasthenia, erectile dysfunction, impotence and male fertility, fever, hangover, and asthma. *Panax ginseng* is also used for bleeding disorders, loss of appetite, vomiting, colitis, dysentery, cancer, insomnia, neuralgia, rheumatism, dizziness, headache, convulsions, disorders of pregnancy and childbirth, hot flashes due to menopause, and to slow the aging process.⁴⁴⁻⁴⁶

Action on Immune system

Panax ginseng is often referred to as an adaptogen, which suggests it has varied actions and effects on the body that support nonspecific resistance to biochemical and physical stressors, improve vitality and longevity, and

enhance mental capacity.⁴⁷⁻⁵¹ In an attempt to prove ginseng's effect on the immune system, a 70% ethanolic extract of *P. ginseng* was subjected to a comprehensive testing battery capable of detecting subtle immune changes in mice, whose immune function was suppressed by cyclophosphamide, a common chemotherapeutic agent. The observation showed that the basal natural killer (NK) cell activity was stimulated, supporting an immunomodulatory property of ginseng.⁵² Research reviews postulate that extracts of *Panax ginseng* affect the hypothalamus-pituitary-adrenal axis and the immune system, which could account for many of the documented effects. Animal models and in vitro studies indicate that *Panax ginseng* enhances phagocytosis, natural killer cell activity, and the production of interferon.

A double-blind, placebo-controlled eight-week study examined the immune effects of 100 mg Ginsana[R] (G115), 100 mg liquid ginseng extract, or placebo twice daily in 60 healthy volunteers. Blood samples collected at baseline, week four, and week eight examined polymorphonuclear (PMN) cell chemotaxis, phagocytosis, total lymphocytes, T-helper and T-suppressor cells, and NK-cell activity. The groups receiving ginseng experienced consistent improvement in immune system activity at week four and statistically significant differences at week eight, evidenced by improvements in PMN cell chemotaxis, phagocytosis, and total number of T-helper and T-suppressor cells. The authors concluded ginseng extract stimulates the immune system and the standardized extract is more effective than the liquid ginseng extract.⁵³

Some of the same researchers examined the effects of *Panax ginseng* extract on the immune response to vaccination. The multicenter, 12-week, double-blind RCT compared immune response in 227 participants, measured as NK-cell activity, at weeks eight and 12, post influenza vaccine given at week four. The treatment group received 100 mg G115 twice daily. NK-cell activity for the ginseng group was double that of the placebo group ($p < 0.0001$) at weeks eight and 12. Serum antibody titers were 272 units in the ginseng group compared to 171 units in the placebo group. A significant decrease in the frequency of upper respiratory infections during weeks 4-12 was noted in the treatment group compared to placebo; 15 cases versus 42 cases, respectively. This study supports the role of ginseng in immune system modulation.⁵⁴

An RCT compared the effects of red *Panax ginseng* on HIV-1 infected patients ($n=61$). The purpose of this study was to determine the effects of red ginseng after accounting for HLA type (I or II and class A, B, and C), on CD4 counts, CD8 counts, and the trend toward decreased resistance to antiretroviral drugs. HLA type can be associated with an improved prognosis in HIV patients, based on an algorithm that also predicts risk of disease progression. The treatment group received 5.4 g red *Panax ginseng* daily. Blood samples were taken from the

control group (n=199) and HIV-1 infected patients every six months throughout the study. Data analysis revealed an inverse correlation between the HLA score and the decrease of CD4 T cells over time, a decrease in the decline of CD4 T cells associated with the intake of red Panax ginseng, and a significant ($p < 0.05$) decline of CD4 T cells, independent of the HLA class I effects on immune system cells. The authors concluded that red Panax ginseng and HLA type independently affect the slow depletion of CD4 T cells in HIV-infected patients.⁵⁵

ASTRAGALUS MEMBRANACEUS

Family: Fabaceae, Subfamily: Faboideae

Common names: Bay chi, bei qi, milk vetch, goat's thorn, huang qi.

Astragalus is a perennial plant native to the northern and eastern parts of China as well as Mongolia and Korea. It grows about 16 - 36 inches tall. It has hairy stems with leaves made up of 12 - 18 pairs of leaflets. The root is the medicinal part, and is usually harvested from 4-year-old plants.^{56,57}



Figure 3: *Astragalus Membranaceus*

Active constituents of Astragalus root have been identified and characterized. These components include: polysaccharide cycloartane glycoside fractions (astragalosides I-IV and trigonosides I-III), four major isoflavonoids (formononetin, ononin, calycosin, and its glycoside), saponins, several minor isoflavonoids, and other biogenic amines.⁵⁸⁻⁶¹ Astragalus also contains triterpenoids. Triterpenoids and saponins have a structural similarity to steroid hormone precursors. Astragalus protects body from diseases such as cancer and diabetes. It contains antioxidants,⁶² which protect cells against damage caused by free radicals, byproducts of cellular energy. Astragalus has antibacterial⁶³, and anti-inflammatory properties.⁶⁴ It is sometimes used topically for wounds. In addition, studies have shown that a Astragalus has antiviral properties and stimulates the immune system,⁶⁵ suggesting that it is indeed effective at preventing colds.

Action on immune system

This herb has long been used in traditional oriental medicine for conditions exhibiting fatigue and wasting. Astragalus's primary function is as an immune stimulator

supporting and enhancing the body's own defense system while controlling autoimmune issues. It increases the number of stem cells in bone marrow and lymph tissue and encourages their development into active immune cells.⁶⁶ It appears to help trigger immune cells from a "resting" state into heightened activity. Astragalus stimulates the production of T cell, Natural Killer (NK) cell, macrophages, immunoglobulins and interferons.⁶⁷ The herb contains at least 8 major polysaccharide fractions which have exhibited immuno-modulating activity. Fractions 3, 7, and 8 have been shown to stimulate interferon production, mononuclear cell proliferation (both granulocytic and lymphocytic series), accelerate phagocytosis and restore T-cell function in immunocompromised and immuno-suppressed individuals.⁶⁸

Studies on cyclophosphamide induced immuno-incompetent rats showed not only complete restoration of cellular immunity and T-cell function, but that restored immunity was greater than normal subjects. Furthermore, the same phenomenon has been observed in human cancer subjects who have been immuno-compromised by radiation, chemo- or combination therapy.⁷⁰ This may be due in part to its ability to prevent hepatotoxicity from radiation and chemotherapeutic agents as well as its documented ability to synergize recombinant interferon against chronic viral disease i.e., Varicella zoster, Herpes Simplex virus, Human Papilloma virus and Epstein-Barr virus. It increases the patient's energy, appetite and sense of well being.

In an open, randomized clinical trial, 115 patients with leukopenia received a high dose of a concentrated Astragalus preparation (equivalent to 30 g Astragalus daily) or a low dose (equivalent to 10 g Astragalus daily) over a period of eight weeks. In both groups there was a significant increase in average white blood cell counts after treatment ($p < 0.05$). On the basis of these findings, the author suggests Astragalus is an effective treatment for leukopenia.⁷¹

In another study viral myocarditis patients given an oral Astragalus extract, enhanced T3, T4 and T4/T8 cell ratios were demonstrated, suggesting improved immune response.⁷²

UNCARIA TOMENTOSA

Family: Rubiaceae

Common names: Cat's claw, una de gato

Cat's claw is a large woody vine found in the Amazon rain forest and other tropical parts of South & Central America. It got its name from the hook-like thorns that grow along its vine. These thorns enable the vine to attach itself around trees climbing to heights up to hundred feet. Leaves are elliptic with a smooth edge and grow in opposite whorls of two.⁷³⁻⁷⁵ The root which can develop to a size of watermelon and the inside of the bark have traditionally been used in herbal remedies. There are two main species of cat's claw used medicinally: *Uncaria guianensis* & *Uncaria tomentosa*. Research on



Uncaria tomentosa shows it to be more beneficial as a therapeutic agent.



Figure 4: *Uncaria Tomentosa*.

Cat's claw has several groups of active components that account for much of the plant's actions and uses. These include oxindole alkaloids (rhynchophylline, alloptropodine, alloisopteropodine, isopteropodine, and uncarine), quinovic acid, triterpenes, polyphenols, proanthocyanidins, phytosterols (beta-sitosterol, stigmasterol, and campesterol), and catechin tannins⁷⁶⁻⁷⁸. These compounds possess immune augmenting,^{79,80} anti-microbial, anti-tumor,⁸¹ anti-allergic, anti-ulcer, anti-oxidant,^{82,83} anti-inflammatory^{83,84} and adaptogen properties. Cat's claw is one of the most important herbs found in the rain forest and used as a cleansing and supportive herb of the immune system, cardiovascular system, and intestinal system. It is effective in treating the stiffness and swelling prevalent in arthritis, rheumatism, and joint pain.⁸⁵ While the stem bark of cat's claw has some medicinal properties, the root is three to four times more potent than the stem bark.

Action on Immune system

Cat's Claw is considered to be an excellent immune system booster. Alkaloids isolated from the bark and roots increase white blood cell activity and therefore activate the immune system.⁸⁶ Cat's claw's stimulates and strengthen white blood cell to attack, engulf and digest harmful micro-organisms or foreign matter, thus assisting the process of phagocytosis in the body. Increased white blood cell count is useful in fight off viral and respiratory infections. Research suggests that Cat's claw extracts exert a direct anti-proliferative activity on MCF7 cells - a breast cancer cell line.⁸⁷ This has led to its use as an adjunctive treatment for cancer and AIDS as well as other diseases that negatively impact the immunological system.⁸⁸ When used as a complementary treatment to chemotherapy and radiation, cat's claw has been shown to be effective in reducing side effects like hair loss, nausea, skin problems, infections, and weight loss.

The presence of glycosides, proanthocyanidins and beta sitosterol in Cat's Claw has anti-viral and anti-inflammatory activity. These alkaloids also have a beneficial effect on memory. Cat's claw is considered a remarkably potent inhibitor of TNF-alpha production.

⁸⁹The primary mechanism of anti-inflammatory actions appears to be immunomodulation via suppression of TNF-alpha synthesis. The alkaloid, rhynchophylline, has antihypertensive properties that may reduce heart rate, lower blood pressure, increase circulation, and lower blood cholesterol levels making it beneficial in lowering the risk of strokes and heart attacks.^{90,91}

Many studies have shown it to enhance immunity and heal digestive and intestinal disorders making it a choice among many for the treatment of Acquired Immune Deficiency Syndrome (AIDS) and Human Immunodeficiency Virus (HIV) infection; cancer;⁹² and other ailments including acne, allergies, arthritis, asthma, candidiasis, chronic fatigue, chronic inflammation, environmental toxicity and poisoning, depression, diabetes mellitus, Epstein-Barr virus (EBV), systemic lupus erythematosus (SLE), menstrual disorders and hormone imbalances, parasites, fibromyalgia, hemorrhoids, herpes, hypoglycemia, premenstrual syndrome (PMS), tumors, upper respiratory infections, viral infections, and wounds

WITHANIA SOMNIFERA

Family :Solanaceae

Common names: Ashwagandha, Indian ginseng, Indian Winter Cherry

Ashwagandha is an important ancient plant, the roots of which have been employed in Indian traditional systems of medicine, Ayurveda and Unani. It grows in dry parts of sub-tropical regions. It is a small, woody and erect shrub that grows up to 5 feet in height. It is well branched short shrub (35–75 cm) with a central stem from which branch extend radially in a star pattern and covered with a dense mat of woolly hairs. Leaves are alternate and ovate, up to 10 cm long and up to 5 cm wide. The flowers are small and green, while the ripe fruit is orange-red and has milk-coagulating properties.^{93,94} The plant also has long fleshy brown tuberous roots that are used for medicinal purposes.



Figure 5: *Withania somnifera*

The principle constituents of its roots, known as withanolides are believed to account for the multiple medicinal applications of ashwagandha. These molecules

are steroidal lactones with ergostane, which include withanone, withaferin, withanolides, withasomidenone, withanolide C and alkanoids^{3,4} about 0.2 % and bear a resemblance, both in their action and appearance, to the active constituents of Asian ginseng (*Panax ginseng*) known as ginsenosides.^{95,96} Ashwagandha has long been considered as an excellent rejuvenator,⁹⁷ a general health tonic and a cure for a number of health complaints. It is a sedative, diuretic,⁹⁸ anti-inflammatory,⁹⁹ immune stimulatory,¹⁰⁰ increases energy, endurance, and acts as an-adaptogen and an-anti-stress agent.^{101,102}

Ashwagandha is taken for treating cold and coughs, ulcers, emaciation, diabetes, conjunctivitis, epilepsy, insomnia, senile dementia, leprosy, Parkinson's disease, nervous disorders, rheumatism, arthritis, intestinal infections, bronchitis, asthma, impotence and a suppressant in HIV/AIDS patients.

Ashwagandha has profound effects on the hematopoietic system, acting as an immunoregulator and a chemoprotective agent. In a mouse study, administration of a powdered root extract from ashwagandha was found to enhance total white blood cell count.¹⁰³ In addition, this extract inhibited delayed-type hypersensitivity reactions and enhanced phagocytic activity of macrophages when compared to a control group. Recent research suggests a possible mechanism behind the increased cytotoxic effect of macrophages exposed to *W. somnifera* extracts.¹⁰⁴ Nitric oxide has been determined to have a significant effect on macrophage cytotoxicity against microorganisms and tumor cells. Iuvone et al demonstrated *Withania somnifera* increased NO production in mouse macrophages in a concentration-dependent manner.^{105,106} This effect was attributed to increased production of inducible nitric oxide synthase, an enzyme generated in response to inflammatory mediators and known to inhibit the growth of many pathogens.

The use of WS as a general tonic to increase energy and prevent disease may be partially related to its effect on the immune system. Glycowithanolides and a mixture of sitoindosides IX and X isolated from WS were evaluated for their immunomodulatory and central nervous system effects (antistress, memory, and learning) in Swiss mice (15-25 g, 5-6 months old) and Wistar strain albino rats (120-150 g and 250-300 g).¹⁰⁷ Both materials produced statistically significant mobilization and activation of peritoneal macrophages, phagocytosis, and increased activity of the lysosomal enzymes. Root extract of WS was tested for immunomodulatory effects in three myelosuppression models in mice: cyclophosphamide, azathioprin, or prednisolone. Significant increases ($p < 0.05$) in hemoglobin concentration, red blood cell count, white blood cell count, platelet count, and body weight were observed in WS-treated mice compared to untreated control mice. The authors also reported significant increases in hemolytic antibody responses

toward human erythrocytes which indicated immunostimulatory activity.

The major activity of WS may be the stimulation of stem cell proliferation. Administration of WS extract was found to significantly reduce leukopenia induced by cyclophosphamide (CTX) treatment in Swiss albino mice.¹⁰⁸ Total white blood cell count on the 12th day of the CTX-treated group was 3720/mm³; that of the CTX-plus-WS group was 6120/mm³. In the CTX-plus-WS mice, the cellularity of the bone marrow was significantly increased (13.1×10^6 /femur) ($p < 0.001$) compared to the CTX-alone treated group (8×10^6 /femur). Similarly, the number of alpha-esterase positive cells (1130/4000 cells) in the bone marrow of the CTX-plus- WS mice increased compared to the CTX alone mice (687/4000 cells). These studies indicated WS reduced CTX-induced toxicity and may prove useful in cancer chemotherapy. Further studies need to be conducted to confirm the hemopoetic effect with other cytotoxic agents and to determine its usefulness as an adjuvant in cancer chemotherapy.

CONCLUSION

Immune function involves a complex cascade of events involving intelligent communications between all tissues of the body. Alterations of the balance of the immune function are responsible for the cause or progression of many common diseases. Natural substances will help to deliver optimal immune function in the body and control unwanted inflammatory responses. Nature's Immune Stimulator is a blend of well-researched natural herbs known to support and boost the immune system, fight infections, help heal injuries resulting from infections and control other conditions that lay the foundation for disease. The five herbs, *Echinaceae purpurea*, *Panax ginseng*, *Astragalus membranaceous*, *Uncaria tomentosa* and *Withania somnifera* discussed above have various chemicals components which stimulate the immune system in many ways as follows-

- Strengthens the immune system
- Stimulates body's natural defenses to kill unfriendly microorganisms, viruses, bacteria, allergens, molds and parasites
- Increases immunoglobulin proteins in the intestinal tract to combat foreign invaders
- Acts as an antioxidant
- Promotes the repair of DNA

Thus nature's Immune Stimulator will strengthen the body as a whole, helping to enjoy a better quality of life.



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