

Immunity Enhancing Reported Medicinal Plants Which Can Be Helpful To Combat With Covid-19 Virus Infection: An Overview.

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Abstract

Currently there is much growing interest in the use of various medicinal plants as modulators of the complex immune system. A wide range of health-care practices is required to exploit the beneficial effects of Ayurveda, which is the most ancient system of medicines. Being the essence of herbal medicines, Indian medicinal plants manifest miraculous effects in curing a vast range of diseases and disorders among humans and can be better called as “elixirs of life. Through a number of vast researches conducted in the area, it is being explored that many of the chemicals in the form of alkaloids, flavonoids, terpenoids, polysaccharides, lactones, and glycoside products are responsible to cause alterations in the immunomodulatory properties. Keeping in mind, the tremendous potential of the medicinal plants and their derived drugs, herewith introducing this review with a purpose to globally popularize the Indian herbal medicinal plants as immunomodulatory action.

Keywords: Immunomodulators, Herbal Plants, Immunosuppressor.

Introduction

Biological products of animals and plants sources have been used by human for thousands of years either in the

pure forms or crude extracts to treat many diseases. Herbs are used as bases of medicine in many ways in human beings in their life. Research interest has focused on various herbs that possess immune-stimulating properties as a useful feature in helping diminish the risk of cancer. In different herbs, a wide-ranging of phytochemicals, have been identified such as the flavonoids, lignans, terpenoids, polyphenolics, sulfides, saponins, carotenoids, curcumins, plant sterols and phthalides. Several of these phytochemicals either inhibit nitrosation or the formation of DNA stimulate the activity of protective enzymes such as the phase II enzyme glutathione transferase. Many of plants contain potent antioxidant compounds that provide significant protection against chronic diseases. These compounds may defend LDL cholesterol from oxidation, inhibit cyclooxygenase and lipoxygenase enzymes, prevent lipid peroxidation, or have antitumor activity⁽¹⁻³⁾

It is an evident from the human history that medicinal plants have been the treatment regimen to cure a variety of diseases, including diseases caused by insects, fungi, bacteria, and viruses. The effects shown by the plants are due to the chemicals present in them and they work in the same manner as the conventional drugs. However, there are equally chances for these plants to have some potential

harmful and toxic effects also. These undesired side effects can be reduced by processing of the plant's crude product. Ethnobotany is the study of traditional plants for their medicinal properties and is an effective method to discover future medicines. According to 2015-16 data, more than 300 plants have been identified to have therapeutic potential.^[4]

Around 122 chemicals derived from plants have been identified as therapeutic substances which are also used in commercial drugs, for example, bark of willow tree is very rich in salicylic acid, which is also an active metabolite of aspirin, and this bark has been used from ancient times as a pain killer and antipyretic substance.^[5] Some of the drugs which are frequently used by the physicians are also derived from plant sources, for example, aspirin, digoxin, quinine and opium, etc.^[5] They have a long history of use as herbal drug. Currently, there is much growing interest to use these medicinal plants as modulators of the complex immune system. Through a number of researches conducted in the area have explored that many of the chemicals in the form of alkaloids, flavonoids, terpenoids, polysaccharides,^[6] lactones, and glycoside products are responsible to cause alterations in the immunomodulatory properties.^[6]

Immunity

The term immunity defines body's natural defense system against a vast array of diseases and disorders. Remarkably sophisticated and advanced among vertebrates, the complex immune system is capable to generate a limitless variety of cells and molecules to arrest enormous spectrum of infections and undesirable substances. Immunomodulators refer to those substances capable of inducing, amplifying, and inhibiting any component or phase of the immune system. Immunostimulators and immunosuppressant are two types of immunomodulators are known for use. In fact, immunopharmacology is a

newer branch of pharmacology concerned with immunomodulators.^[7] Administration of immunostimulators as in the case of AIDS and use of immunosuppressor in cases of an exaggerated response of an immune system is appreciating to reconstitute the normal immune system and increase the longevity of life. Immunomodulator intake along with antigen, the process is meant to boost the immune system, and the modulator is known as immune adjuvant.^[8] The two ways of defense of an immune mechanism involving short-term mechanism which is the first line of defense and the other highly advanced adaptive immune response marked by complexity, diversity, and memory.^[9] An adaptive immune response also consists of two subtypes of immune responses, humoral immune response concerned with β -lymphocytes and cell-mediated cytotoxic response mediated by T-cells.^[9] Well, all the component cells of the immune system originate from bone marrow through hematopoiesis from bone marrow-derived stem cells. They are either develop into mature cells or migrate to other peripheral sites for migration.^[9] Besides a vast range of specialized cells of immune cells, certain molecules called cytokines which are one of the important mediators of the immune system mediate the cross talk between the specialized cells of the immune system, thereby completely integrating the behavior and action responses of the cells.^[10]

Cytokine Modulation Caused By Herbal Plants

Through a number of in vitro and in vivo studies conducted to see the effect of the herbal medicine on cytokines have shown that they influence a large number of multiple cytokines. By nature, cytokines are a group of soluble extracellular proteins or glycoproteins in the form of interleukins (ILs), interferons, chemokines, etc., and are crucial to both innate and acquired types of immunity. These cytokines through intermolecular cross talks

maintain physiological stability through their secretions in all nucleated cells through inducible response to some injury.^[10] In fact, it is evident from knowledge of the medical literature of various diseases that these disease conditions are in connect with cytokine secretions. In diseases of the central nervous system, these cytokines have a predominant role as in the variety of psychiatric disorders, and abnormal secretions of these chemicals have been demonstrated. Various neurochemicals, neuroendocrine, and neuroimmune substances have appeared at the command of cytokines. Their role has been marked in cases of depression,^[11] Alzheimer's disease,^[12] and schizophrenia;^[13] various behavioral shifts, positive and negative emotions, stress, infection, etc., have all been demonstrated to stimulate cytokine secretion.^[14]

All these hurdles in the way of therapeutic protocol make a challenge for cytokines. Adverse effects produced and experienced among the patients made us consider phytotherapy in modifying the cytokine expression. Plants such as *Astragalus membranaceus* also known as "spleen chi tonic" is a Chinese plant used in various diseases and wasting state of the body. The root extract of the plant was found to lower IL-6 in in vitro human model.^[15] IL-6 is inflammatory and impending deterioration marker.^[17] Very well-known plant of garlic or *Allium sativum* used in most of the Indian houses is found to lower IL-1 and IL-6, acting as anti-inflammatory, hypocholesterolemic, antioxidant, and also angiotensin-converting enzyme inhibitor.^[16] It has great potential as anti-inflammatory due to an inhibitory effect on IL-1, IL-6, TNF, IL-8 and boosting effect on IL-10 which is an antagonist to pro-inflammatory cytokines.^[16] Besides anti-inflammatory, it also manifests antimicrobial potential. Garlic use has been suggested in inflammatory bowel diseases. Its use is also indicated in Alzheimer's disease due to IL-10 modulation. Spelman et al. have reported in his review,

immunomodulatory activity of more than 18 herbal plants including *Acanthopanax gracilistylus*, *A. sativum*, *Ananas comosus*, *Cissampelos sympodialis*, *Coriolus versicolor*, *Curcuma longa*, *Tinospora cordifolia*, and *Withania somnifera*.^[17] Aloe vera, a very popular plant which grows in arid climate, is claimed to have wound and burn healing properties due to its anti-inflammatory nature. It has been found to reduce TNF- α and IL-6 in various animal models.^[18]

Effect of Medicinal Plants On Innate And Acquired Immune Components

Various herbal medicines have been found to modulate various components of innate and acquired immune system. In fact, based on proper understanding of various immunomodulatory activities of herbal plants, plants derived the secondary metabolites in natural products can be the lead molecules for the future development of immunomodulators for therapeutic use. Various immunomodulators have been suggested in various allergic diseases including asthma, allergic rhinitis, and eosinophilic esophagitis on the basis of experiments performed on various animal models.

Effect on Acquired Immune System

Patil et al. explained that ethanolic extract of *Ficus carica* produces stimulatory effect on humoral and cell-mediated immune response in experimental animals and suggested its therapeutic use in immunological disorders.^[19] *Chlorophytum borivilianum* root extract, an effective immunomodulatory, not only potentiates non-specific immune response but also improves humoral as well as cell-mediated immunity. It may use in infection condition, enhancement of immunological response against foreign particles or antigens, and improving defensive response under normal circumstances.^[20] Ethanolic extract and aqueous extract of *Picrorhiza kurroa* have the ability to stimulate humoral response by acting various level of

immune mechanism such as antibody production, release of mediators of hypersensitivity reactions, and tissue responses to these mediators in the target organs.^[21]

1. Reishi (*Ganoderma tsugae*, *G. lucidum*, *G. curtisii*, *G. martinicense*, *Ganodermataceae*)

Parts Used: Mushroom fruiting body

Preparations: Long decoction, syrup, preserved concoction

Herbal Actions: Immune tonic Immunomodulator, Antiviral, Antibacterial, Adaptogen, Anti-inflammatory, Antioxidant, Anti-anxiety, Cardiotonic, Hepatic



Known as the ‘mushroom of immortality’, reishi is an herbal immune tonic and immunomodulator. Taken regularly, it can enhance and fine-tune the body’s immune response. It’s especially helpful as a daily remedy for those who have weak lungs or who frequently succumb to respiratory infections. It strengthens the circulatory system and is a legendary adaptogen, making it a supreme ally for increasing overall resilience. Reishi is also a traditional tonic for anxiety and can help impart calmness in a slow and sustained manner.

Reishi is better prepared as a tea than a tincture, as some of its medicinal properties are destroyed by high percentages of alcohol. Simmer the mushrooms for a few hours to fully extract its polysaccharide compounds, which are the active immunomodulation compounds. Its flavor is slightly bitter, so I like combining it with pleasant-tasting herbs like astragalus (*Astragalus*

propinquus), licorice (*Glycyrrhiza glabra*)*, and cinnamon (*Cinnamomum verum*)—it’s particularly delicious in herbal chai blends. I also add a handful or two of dried reishi slices to bone or vegetable broth when I have a pot simmering. Reishi can be purchased online or at local health food stores, cultivated at home, or gathered from the wild. There are a number of medicinal species in the genus. We use our local hemlock reishi (*Ganoderma tsugae*) and artist’s conk (*Ganoderma applanatum*). If you’d like to try foraging this mushroom, please research which *Ganoderma* species grows near you—and if they’ve been used medicinally—along with referencing a good mushroom field guide or reliable online source.^[21-25]

2. Elderberry (*Sambucus nigra* var. *canadensis* and *S. nigra*, *Adoxaceae*)

Parts Used: Berries and flowers

Preparations: Syrup, tincture, infusion (flowers), decoction (berries), infused honey

Herbal Actions:

Berries: Immune stimulant, Immune tonic, Antibacterial, Antiviral, Antioxidant, Diaphoretic, Anticatarrhal Anti-inflammatory.

Flowers: Immune tonic, Antiviral Anti-inflammatory, Diaphoretic, Anticatarrhal (decongestant), Astringent



The berries of elder are one of our most treasured immune tonics—they are effective, nourishing, and delicious when prepared as a dark purple syrup.

Taken daily throughout the fall and winter, elderberry offers us protection against colds, flu, and other viral infections. One study demonstrated elderberry's antimicrobial effects against two strains of the influenza virus and several bacteria that are commonly responsible for secondary, or concomitant, sinus infections with the flu.

And in the case of an illness, elderberry is immune stimulating, diaphoretic (helps to break a fever), and antitarrhal (decreases mucus in the respiratory passages). Studies show a lessening in the duration and severity of cold symptoms as well as the flu.

I prepare elderberry syrup by combining equal parts elderberry tincture, elderberry tea, and elderberry-infused honey. Children love this remedy, which can be made alcohol-free if you prefer (you can substitute a vinegar extraction for the alcohol-based tincture). Doses can be liberal (by the tablespoon), several times per day. Do not give elderberry honey or syrup containing the honey to babies younger than one-year-old.

Elder flowers also demonstrate strong antiviral activity against influenza, and can be integrated into your elderberry syrup along with other immune-boosting herbs like cinnamon (*Cinnamomum verum*) and ginger (*Zingiber officinale*). Curious to see a step-by-step demonstration on making herbal syrups? Visit our video tutorial and download our syrup guide!

Dried elderberries can be purchased online from sources like Mountain Rose Herbs, and fresh, frozen elderberries can be purchased from organic farms (you'll need to do an online search for these). However, elder is also a classic garden-grown medicinal and forageable herb. If you plan to forage elder from the wild, you will need to do some serious botanical detective work.

There are several deadly poisonous look-alikes, including water hemlock (*Cicuta* spp.).^[26-27]

3. Garlic (*Allium sativum*, Amaryllidaceae)

Parts Used: Bulb

Preparations: Raw, tincture, fire cider and other infused vinegars, honey

Herbal Actions:

Immune tonic, Immune stimulant, Antimicrobial, Diaphoretic, Hypotensive (lowers blood pressure) Antitarrhal (decongestant)

This beloved spice has been used medicinally for over 5,000 years; one of the first accounts of its use was to sustain the health of the Egyptian laborers who built the pyramids.¹ Later, it was a powerful field remedy in World War I, saving thousands of lives and limbs through its infection-fighting capabilities.²

Garlic is an essential staple in my kitchen as a potent immune system tonic and antimicrobial herb. It can be highly effective in preventing infections such as the common cold and flu, as well as infections of the digestive tract. The volatile oils in garlic are excreted through the lungs, making it especially beneficial for infections of the respiratory system. One randomized controlled study showed that garlic reduced the incidence of common cold. Here's a review of garlic's demonstrated activity against various pathogenic bacteria, fungi, and protozoans.

Our family prepares a special garlic sauce every week made of raw garlic, extra-virgin olive oil, sea salt, and nutritional yeast. The sauce goes on avocado toast, eggs, pasta, chili, soup, baked potatoes, you name it. We keep it in the refrigerator (important, as garlic oil can harbor botulism and has made people sick) and literally pull it out at every meal. Our family of three goes through a quart a week and we rarely catch colds.

Garlic is easy to add to the diet as a culinary herb, and I always save my garlic skins to toss into broths. The suggested daily dosage is one clove per day, added to food. My favorite garlicky preparation is fire cider—a sweet and spicy tonic made with apple cider vinegar. I recommend trying our ruby-red recipe for Hibiscus Pomegranate Fire Cider. To fully capitalize on garlic's antimicrobial and blood thinning qualities, it should be eaten raw.

Contraindications: Garlic can aggravate heartburn and gas, especially if ingested raw or in large quantities. It can also aggravate peptic ulcers. Coating garlic with olive oil or preparing it in an oil-based sauce helps minimize these effects. Avoid high doses of raw garlic one week before surgery due to its blood-thinning qualities. If taking blood thinners, consult a cardiologist before taking high doses of raw garlic.



Garlic is a superfood, used to treat numerous health-related issues. The pungent-smelling herb, found in almost every kitchen has antimicrobial, antibiotic, and anti-inflammatory properties. Ginger contains compounds that increase the number of white blood cells in the body, which kills foreign bacteria and virus. You can increase the amount of garlic in your food to uplift your immune system.[28-29]

4.Astragalus (*Astragalus propinquus*, Fabaceae [formerly *Astragalus membranaceus*])

Parts Used: Root.

Preparations: Decoction, powder, soup and stew stock, goo balls

Herbal Action: Immunetonic, Immunomodulator, Antiviral, Antibacterial,

Adaptogen,Antioxidant,CardiotonicHepatic,Astragalus has become a renowned tonic in Western herbalism over the past two decades, primarily for its adaptogenic and tonic immune qualities. Scientific studies



because demonstrate that astragalus regulates white blood cell (immune cell) activity and stimulates our natural killer cells (NK cells) to present a strong front against pathogens. Astragalus has also demonstrated increased interferon production (an antiviral and immune-signaling agent produced by the body).

Astragalus is best used as a daily remedy to build immune strength—its medicine is slow and sustained, with full benefits reached after weeks of daily ingestion. In Traditional Chinese Medicine, astragalus augments the Wei Qi, which can be likened to a protective sphere, shielding the body from harmful external pathogens.

Because astragalus is a food herb, it's safe to take relatively large amounts regularly. I love adding a handful

to broth, integrating the fine-flavored root into herbal chai, and mixing the powder into goo balls, cookies, and other treats. Tincture is not recommended because alcohol doesn't optimally extract astragalus' immune-enhancing polysaccharides. These polysaccharides are water soluble and more readily extracted with prolonged decoctions or simmering.

Astragalus root has a sweet, beany flavor (it is in the legume, or bean, family, after all), making it easy to sneak into the diets of picky eaters, including kids. Toss a few of the pressed roots (these look like tongue depressors, and are pictured above) into any simmering stew, soup, or sauce, and it will impart only the tiniest of flavor imprints! The roots can be pulled out of the dish, much as you would pull out a bay leaf, right before serving.

Contraindications: Because astragalus stimulates immune activity, it could potentially weaken the effects of immunosuppressive pharmaceuticals, such as cyclosporine and corticosteroids. This adverse reaction is theoretical in humans but has been verified in animal studies. In high doses (30 grams or more) and via injection, astragalus has caused itching and allergic skin reactions. Symptoms of overdose may include headaches, insomnia, dizziness, hot flashes, and hypertension.^[30-31]

5. Turkey Tail (*Trametes versicolor*, Polyporaceae)

Parts Used: Mushroom fruiting body

Preparations: Long decoction, soup stock

Herbal Actions: Immune tonic, Immune stimulant, Antiviral, Antitumor, Antioxidant

Turkey tail is a medicinal mushroom and immune tonic par excellence, with significant antiviral and immune-balancing qualities.⁵ It's beneficial for anyone who wants to prime their immune system, but especially for those who experience general immune weakness or frequent upper respiratory infections. In addition to boosting immunity, some herbalists believe turkey tail enhances the

effects of antimicrobial herbs.⁶ Turkey tail is a foundational herb for supporting the immune system in alternative cancer therapy and prevention.⁷

Like other medicinal mushrooms, turkey tail is best taken as a decoction or added to broth blends. Again, this is a perfect time to incorporate the warming flavors of chai. Turkey tail is mildly bitter—combine it with other medicinal mushrooms that are pleasant in flavor, such as shiitake (*Lentinula edodes*), maitake (*Grifola frondosa*), or lion's mane (*Hericium erinaceus*).

I make an herbal broth over the winter that contains astragalus, reishi (just a little, so it's not too bitter), shiitake, turkey tail, calendula (*Calendula officinalis*), and seaweed. We add the broth to soups, stews, and marinades, and my picky daughter doesn't notice the herbal flavor. However, her immune system certainly takes note!

Turkey tail is one of the most common woodland mushrooms in the world—it's likely growing near you! It can be found exclusively on dead hardwood trees, stumps, and branches (and sometimes on dead conifers).

Turkey tail does have some look-alikes, and proper identification is essential. That being said, many people successfully learn to know and recognize turkey tail. Its fruiting body is fan-shaped—bearing a likeness to a turkey's opened tail feathers—with colored bands of blue, brown, red, gray, and white. Its undersides are white or tan in color and spotted with tiny pores (NOT gills). False turkey tail mushrooms (*Stereum* spp.) have a matte, tawny underside with no visible pores.^[32-33]



6. Giloy

Giloy is a versatile herb used to make Ayurvedic medicines for a long time. It helps to remove toxins from the body, purifies the blood and fights disease-causing bacteria. Giloy contains anti-oxidant properties that improve health, boosts immunity and digestion. Mix 15-30 ml of Giloy juice in a glass of water and consume it on an empty stomach in the morning. [34-35]



7. Chia seeds

The small chia seeds are rich in antioxidants and omega-3 fatty acids, which is beneficial for enhancing immunity. It also reduces inflammation and regulates inflammatory responses in the body. You can make chia seeds pudding to increase your intake.



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8. Pumpkin seeds



Loaded with zinc, iron and vitamin E, pumpkin seeds are good for boosting the immune function. Pumpkin seeds also have anti-fungal and anti-viral properties. It helps in cell growth, improves your mood and is even better for quality sleep. Sprinkle some pumpkin seeds on your salad to reap its amazing health benefits.[38-39]

9. Sunflower seeds

Sunflower seeds are a rich source of vitamin E and nutrients. The small crunchy seeds contain selenium which helps to body fight certain type of cancer and helps to build your immunity. The antioxidant and vitamin E in the sunflower seeds fight free radicals and are even good for your skin. Add it in your salad or oatmeal.[40-41]



10. Turmeric

The bright yellow-spice is common in Indian cuisine as well as treating numerous health ailments. Curcumin, which is the main compound of turmeric has immunity-boosting potential. The compound activates white blood cells in the body, which in turn enhances its antibody response[42-43]



11. Cinnamon

Cinnamon has also been used for its medicinal properties for thousands of years. It fights inflammation, ward of infection and heals damaged tissues. Cinnamon is high in immune-boosting antioxidants, have anti-diabetic effects and even help to cut the risk of heart disease.[44-45]



12. Clove

Cloves (*Syzygium aromaticum*) are one of the most loved and well-utilized spices in the entire world. Its distinct

sweet and spicy aroma lends dishes and pastries a unique depth in flavor that you can pinpoint once you take a bite. But while cloves are usually relished for their taste and fragrance, they are also packed with vitamins, minerals and other nutrients that are absolutely essential for the body.



Cloves are the dried flower buds of the *Syzygium aromaticum* tree, an evergreen that grows up to about 30 feet. Its name originates from the Latin word “clavus,” which means “nail,” because of the shaft and head that it closely resembles. *Syzygium aromaticum* trees usually grow in warm and humid climates, typically in Indonesia, Sri Lanka and Brazil. In the current trade of cloves, Tanzania leads the market, producing about 80 percent of the world’s clove supply.

Like other spices, the story of how cloves were distributed throughout the world spans over hundreds of years, starting with the establishment of the trade routes. Together with pepper, cinnamon and hazelnut, cloves were one of the spices that were highly sought-after in both Europe and the Americas, especially by noblemen. These four spices were known to be the “Big Four” because of their rarity and value.

In the Moluccas, or the Spice Islands, clove spice trees were used to represent the lives of each child born into a family, an important symbolism that reflected their children’s survival. When the Portuguese and the Dutch learned of the existence of spices, they sought to control the monopoly of the trade. This led to the Dutch burning

down clove trees to raise its price, which then triggered to numerous wars and battles against the locals.

However, the high demand for the spice eventually died down once the spices were successfully cultivated in other parts of the world.⁵ While cloves are now easily available in the market and doesn't require the thousand-mile journey to reach our shores, it remains to be one of the most expensive spices in the world, placing fourth behind saffron, vanilla and cardamom. Because of its numerous health benefits and medicinal uses, it's a wise decision to invest in a small container of cloves to use for your food and in your home.^[46-47]

13 Tulsi

Tulsi is an aromatic shrub in the basil family Lamiaceae (tribe ocimeae) that is thought to have originated in north central India and now grows native throughout the eastern world tropics.^[48] Within Ayurveda, tulsi is known as “The Incomparable One,” “Mother Medicine of Nature” and “The Queen of Herbs,” and is revered as an “elixir of life” that is without equal for both its medicinal and spiritual properties.^[49] Within India, tulsi has been adopted into spiritual rituals and lifestyle practices that provide a vast array of health benefits that are just beginning to be confirmed by modern science. This emerging science on tulsi, which reinforces ancient Ayurvedic wisdom, suggests that tulsi is a tonic for the body, mind and spirit that offers solutions to many modern day health problems. Tulsi is perhaps one of the best examples of Ayurveda's holistic lifestyle approach to health. Tulsi tastes hot and bitter and is said to penetrate the deep tissues, dry tissue secretions and normalize kapha and vata. Daily consumption of tulsi is said to prevent disease, promote general health, wellbeing and longevity and assist in dealing with the stresses of daily life. Tulsi is also credited with giving luster to the complexion, sweetness to the voice and fostering beauty, intelligence, stamina and a

calm emotional disposition.^[49-52] In addition to these health-promoting properties, tulsi is recommended as a treatment for a range of conditions including anxiety, cough, asthma, diarrhea, fever, dysentery, arthritis, eye diseases, otalgia, indigestion, hiccups, vomiting, gastric, cardiac and genitourinary disorders, back pain, skin diseases,



Considered as a potent adaptogen, tulsi has a unique combination of pharmacological actions that promote wellbeing and resilience. While the concept of an “adaptogen,” or herb that helps with the adaptation to stress and the promotion of homeostasis, is not widely used in Western medicine, Western science has revealed that tulsi does indeed possess many pharmacological actions that fulfill this purpose.

The medicinal properties of tulsi have been studied in hundreds of scientific studies including in vitro, animal and human experiments. These studies reveal that tulsi has a unique combination of actions that include: Antimicrobial (including antibacterial, antiviral, antifungal, antiprotozoal, antimalarial, anthelmintic), mosquito repellent, anti-diarrheal, anti-oxidant, anti-cataract, anti-inflammatory, chemopreventive, radioprotective, hepato-protective, neuro-protective, cardio-protective, anti-diabetic, anti-hypercholesterolemia, anti-hypertensive, anti-carcinogenic, analgesic, anti-pyretic, anti-allergic, immunomodulatory, central nervous system depressant, memory enhancement, anti-asthmatic, anti-tussive, diaphoretic, anti-thyroid, anti-fertility, anti-

ulcer, anti-emetic, anti-spasmodic, anti-arthritis, adaptogenic, anti-stress, anti-cataract, anti-leukodermal and anti-coagulant activities.^[50-53] These pharmacological actions help the body and mind cope with a wide range of chemical, physical, infectious and emotional stresses and restore physiological and psychological function.

14. Honey

Nutritional and nonnutritional components of honey:

Today, approximately 300 types of honey have been recognized.^[54] These varieties are related to the different types of nectar that are collected by the honeybees. The main composition of honey is carbohydrates that contribute 95–97% of its dry weight. Furthermore, honey includes main compounds, such as proteins, vitamins, amino acids, minerals, and organic acids.^[55-56] Pure honey also consists of flavonoids, polyphenols, reducing compounds, alkaloids, glycosides, cardiac glycosides, anthraquinone, and volatile compounds.^[57-59] Monosaccharides (fructose and glucose) are the most important sugars of honey and may be contributed to the most of the nutritional and physical effects of honey.^[60] In addition to monosaccharides, smaller quantities of disaccharides (sucrose, galactose, alpha, beta-trehalose, gentiobiose, and laminaribiose), trisaccharides (melezitose, maltotriose, 1-ketose, panose, isomaltose glucose, erlose, isomaltotriose, theanderose, centose, isopanose, and maltopentaose), and oligosaccharides are present in honey.^[61-62] Many of these sugars are formed during the honey ripening and maturation times. Gluconic acid, a product of glucose oxidation, is the main organic acid that is present in honey; in addition, small amounts of acetic, formic, and citric have been found.^[63] These organic acids are responsible for the acidic (pH between 3.2 and 4.5) property of honey.^[64] Honey also consists of some important amino acids, such as all nine essential amino acids and all nonessential amino acids except for

asparagine and glutamine. Proline was reported as the primary amino acid in honey, followed by other types of amino acids.^[65] Enzymes (diastase, invertase, glucose oxidase, catalase, and acid phosphatase) constitute the main protein ingredients of honey.^[66] The vitamin level in honey is low and does not close to the recommended daily intake. All of the water-soluble vitamins exist in honey, with Vitamin C being the most frequent. Approximately 31 variable minerals have been found in honey, including all of the major minerals, such as phosphorus, sodium, calcium, potassium, sulfur, magnesium, and chlorine. Many essential trace components are detected in honey, such as silicon (Si), rubidium (RB), vanadium (V), zirconium (Zr), lithium (Li), and strontium (Sr). However, some heavy metals such as lead (Pb), cadmium (Cd), and arsenic (As) are present as pollutants.^[67] Previous studies have detected the approximately 600 volatile compositions in honey that contribute to its potential biomedical effects.^[68]



The volatile compounds of honey are generally low but include aldehydes, alcohols, hydrocarbons, ketones, acid esters, benzene and its derivatives, pyran, terpene and its derivatives, norisoprenoids, as well as sulfur, furan, and cyclic compounds.^[69-70] Flavonoids and polyphenols, which act as antioxidants, are two main bioactive molecules present in honey. Recent evidence has shown the presence of nearly thirty types of polyphenols in honey.^[71-72] The existence and levels of these polyphenols in honey can vary depending on the floral source, the climatic and geographical conditions. Some bioactive

compounds, including galangin, quercetin, kaempferol, luteolin, and isorhamnetin, are present in all types of honey whereas naringenin and hesperetin are found only in specific varieties. In general, the most phenolic and flavonoid compounds in honey consist of gallic acid, syringic acid, ellagic acid, benzoic acid, cinnamic acid, chlorogenic acid, caffeic acid, isorhamnetin, ferulic acids, myricetin, chrysin, coumaric acid, apigenin, quercetin, kaempferol, hesperetin, galangin, catechin, luteolin, and naringenin^[71-72] The ingredients of honey have been reported to exert antioxidant, antimicrobial, anti-inflammatory, antiproliferative, anticancer, and antimetastatic effects.

15. Orange peel

Citrus fruits are good sources of nutrition with an ample amount of vitamin C. Besides, the fruits are abundant in other macronutrients, including sugars, dietary fiber, potassium, folate, calcium, thiamin, niacin, vitamin B6, phosphorus, magnesium, copper, riboflavin and pantothenic acid^[73]. However, secondary metabolites are an especially popular topic in the present research. These constituents, also known as phytochemicals, are small molecules that are not strictly necessarily for the survival of the plants but represent pharmacological activity. Citrus fruits contain a number of secondary metabolites, such as flavonoids, alkaloids, coumarins, limonoids, carotenoids, phenol acids and essential oils. These active secondary metabolites show several bioactivities of vital importance to human health, including anti-oxidative, anti-inflammatory, anti-cancer, as well as cardiovascular protective effects, neuroprotective effects, etc. In addition, Citrus fruits have been used as traditional medicinal herbs in several Asian countries, such as China, Japan and Korea. Nine traditional Chinese medicines have been recorded in the Chinese Pharmacopoeia for appropriate medical use from

six Citrus species^[74]: *C. reticulata* Blanco, *C. medica* L. var., *C. medica* L., *C. wilsonii* Tanaka, *Citrus aurantium* L. and *C. sinensis* Osbeck. These peels or whole fruits (mature or immature) are known to treat indigestion, cough, skin inflammation, muscle pain, and ringworm infections, as well as to lower blood pressure.



Conclusion

As reported from the ancient time herbal properties are responsible for the immunomodulatory action. Many of the chemicals in the form of alkaloids, flavonoids, terpenoids, polysaccharides, lactones, and glycoside products are responsible to cause alterations in the immunomodulatory properties.

References

1. Craig WJ. Health-promoting properties of common herbs. *Am J Clin Nutr.* 1999;70:491s-9s.
2. Kyo E, Uda N, Kasuga S, Itakura Y. Immunomodulatory Effects of Aged Garlic Extract. *J Nutr.* 2001;131:1075S-9S.
3. Gebreyohannes G, Gebreyohannes M. Medicinal values of garlic: a review. *Int J Med Sci.* 2013;5:401-8.
4. Ramalingum N, Mahomoodally MF. The therapeutic potential of medicinal foods. *Adv Pharmacol Sci.* 2014;2014:354264.

5. Dias DA, Urban S, Roessner U. A historical overview of natural products in drug discovery. *Metabolites*. 2012;2(2):303-36.
6. Wadood A, Ghufuran M, Jamal SB, Naeem M, Khan A, Ghaffar R, et al. Phytochemical analysis of medicinal plants occurring in local area of Mardan. *Biochem Anal Biochem*. 2013;2(4):1-4.
7. Patil US, Jaydeokar AV, Bandawane DD. Immunomodulators: A pharmacological review. *Int J Pharm Pharm Sci*. 2012;4 Suppl 1:30-6.
8. Dutt SB. PA02. 10. A review on immunomodulator activity of some indigenous medical plants. *Anc Sci Life*. 2013;32 Suppl 2:S55.
9. Available from: https://www.en.wikipedia.org/wiki/Immune_system. [Last accessed on 2017 Jan 04]. 10. Mogensen TH. Pathogen recognition and inflammatory signaling in innate immune defenses. *Clin Microbiol Rev*. 2009;22(2):240-73.
10. Wilson DR, Warise L. Cytokines and their role in depression. *Perspect Psychiatr Care*. 2008;44(4):285-9.
11. Rubio-Perez JM, Morillas-Ruiz JM. A review: Inflammatory process in Alzheimer's disease, role of cytokines. *Scientific World Journal*. 2012;2012:756357.
12. Mansur RB, Zugman A, Asevedo EM, da Cunha GR, Bressan RA, Brietzke E. Cytokines in schizophrenia: Possible role of anti-inflammatory medications in clinical and preclinical stages. *Psychiatry Clin Neurosci*. 2012;66(4):247-60.
13. Fredrickson BL. The role of positive emotions in positive psychology. The broaden-and-build theory of positive emotions. *Am Psychol*. 2001;56(3):218-26.
14. Denzler KL, Waters R, Jacobs BL, Rochon Y, Langland JO. Regulation of inflammatory gene expression in PBMCs by immunostimulatory botanicals. *PLoS One*. 2010;5(9):e12561.
15. Singh UP, Prithiviraj B, Sarma BK, Singh M, Ray AB. Role of garlic (*Allium sativum* L.) in human and plant diseases. *Indian J Exp Biol*. 2001;39(4):310-22.
16. Spelman K, Burns J, Nichols D, Winters N, Ottersberg S, Tenborg M. Modulation of cytokine expression by traditional medicines: A review of herbal immunomodulators. *Altern Med Rev*. 2006;11(2):128-50.
17. Liu P, Chen D, Shi J. Chemical constituents, biological activity and agricultural cultivation of *Aloe vera*- A review. *Asian J Chem*. 2013;25(12):6477.
18. Patil VV, Bhangale SC, Patil VR. Studies on immunomodulatory activity of *Ficus carica*. *Int J Pharm Pharm Sci*. 2010;2(4):97-9.
19. Thakur M, Bhargava S, Dixit VK. Immunomodulatory activity of *Chlorophytum borivilianum* Sant. F. *Evid Based Complement Alternat Med*. 2007;4(4):419-23.
20. Hussain A, Shadma W, Maksood A, Ansari SH. Protective effects of *Picrorhiza kurroa* on cyclophosphamide-induced immunosuppression in mice. *Pharmacognosy Res*. 2013;5(1):30-5.
21. Liu B, Bau YS (1994) *Fungi Pharmacopoeia (Sinica)*. Oakland: Kinoko: 297.
22. Unschuld P (1986) *Medicine in China: A History of Pharmaceutics*. Berkeley: Univ California Press: 366.
23. Yang SZ (1997) *The Divine Farmer's Materia Medica*. Boulder (CO): Blue Poppy. Translation of: *ShenNongBenCao Jing*: 198.
24. *American Herbal Pharmacopoeia* (2006) *Reishi Mushroom Ganoderma lucidum Standards of Analysis, Quality Control, and Therapeutics*. In: Anonymous. *American Herbal Pharmacopoeia and Therapeutic Compendium*. American Herbal Pharmacopoeia: Scotts Valley, CA, USA: 10-12.

25. Broekaert WF, Nsimb Lubaki M, Peeters B, Peumans WJ. Alectin from elder (Sambucus nigra L.) bark. *Biochem J.* 1984;221(1):163–169.
26. Cao G, Prior RL. Anthocyanins are detected in human plasma after oral administration of an elderberry extract. *Clin Chem.* 1999;45(4):574–576.
27. Kasuga S, Ushijima M, Morihara N, Itakura Y, Nakata Y (1999). Effect of aged garlic extract (AGE) on hyperglycemia induced by immobilization stress in mice. *Nippon Yakurigaku Zasshi.* 114:191-197.
28. Lanzotti V (2006). The analysis of onion and garlic. *J. Chromat.A.* 12(1):3-22.
29. Chou, M.-X., Wei, X.-Y., Chen, D.-S., Zhou, J.-C. (2007): A novel nodule-enhanced gene encoding a putative universal stress protein from *Astragalus sinicus*. – *J. Plant Physiol* 164: 764-772.
30. Du, S. H., Meng, Z. (2004): The treatment of *Astragalus membranaceus* (Fisch.) Bunge. for nephrostenia syndrome and headache. – *J Trad. Chi. Med.* 45: 250.
31. Cui J. and Chisti Y. 2003. Polysaccharopeptides of *Coriolus versicolor*: physiological activity, uses, and production. *Biotechnol Adv*, 21, 109–122.
32. Deufel P., Schön A., and Hertel W. 1978. Use of polysaccharides containing nitrogen for promoting the drug-sensitivity antibiotic-resistant bacteria. *Kureha Chemical Industry Co.* (German patent 2,816,087); CA 90:12294v.
33. AV Raghu ; SP Geetha ; G Martin ; I Balachandran ; PN Ravindran , *In vitro cell. Dev. Biol. – Plant*, 2006, 42, 584-588.
34. BV Shetty ; V Singh. *Flora of Rajasthan*. 1st edition, Merrut publishers and Distributors, Merrut. Vol 1: 756-100.
35. W. Jamboonsri, T. D. Phillips, R. L. Geneve, J. P. Cahill, and D. F. Hildebrand, “Extending the range of an ancient crop, *Salvia hispanica* L.—a new source,” *Genetic Resources and Crop Evolution*, vol. 59, no. 2, pp. 171–178, 2012.
36. P. G. Peiretti and F. Gai, “Fatty acid and nutritive quality of chia (*Salvia hispanica* L.) seeds and plant during growth,” *Animal Feed Science and Technology*, vol. 148, no. 2–4, pp. 267–275, 2009.
37. Stevenson D, Eller F, Wang L, Jane J, Wang T, Inglett G. Oil and Tocopherol Content and Composition of Pumpkin Seed Oil in 12 Cultivars. *J Agric Food Chem* 2007; 55(10): 4005- 4013.
38. Applequist W, Avula B, Schaneberg B, Wang Y, Khan I. Comparative fatty acid content of seeds of four *Cucurbita* species grown in a common (shared) garden. *J Food Compost Anal* 2006; (19): 606-611.
39. Moyers S. *Garlic in Health, History, and World Cuisine*. Suncoast Press; 1996
40. Bergner P. *The Healing Power of Garlic: The Enlightened Person’s Guide to Nature’s Most Versatile Medicinal Plant*. Prima Lifestyles; 1995.
41. Denzler K, Moore J, Harrington H, et al. Characterization of the Physiological Response following In Vivo Administration of *Astragalus membranaceus*. *Evid Based Complement Alternat Med.* 2016.
42. Chu DT, Wong WL, Mavligit GM. Immunotherapy with Chinese medicinal herbs. I. Immune restoration of local xenogeneic graft-versus-host reaction in cancer patients by fractionated *Astragalus membranaceus* in vitro. *J Clin Lab Immunol.* 1988. <http://www.ncbi.nlm.nih.gov/pubmed/3260960>
43. <http://www.ncbi.nlm.nih.gov/pubmed/3260960>
44. Hobbs C. *Medicinal Mushrooms: An Exploration of Tradition, Healing, and Culture*. Book Publishing Company; 2002.

45. Rogers R. The Fungal Pharmacy: The Complete Guide to Medicinal Mushrooms and Lichens of North America. North Atlantic Books; 2011.
46. Patel, S, Goyal, A. Recent Developments in Mushrooms as Anti-Cancer Therapeutics: A Review. 3 Biotech. 2012. restore physiological and psychological function.
47. Bast F, Rani P, Meena D. Chloroplast DNA phylogeography of holy basil (*Ocimum tenuiflorum*) in Indian subcontinent. *ScientificWorldJournal*. 2014;2014:847–482. [PMC free article] [PubMed] [Google Scholar]
48. Singh N, Hoette Y, Miller R. *Tulsi: The Mother Medicine of Nature*. 2nd ed. Lucknow: International Institute of Herbal Medicine; 2010. pp. 28–47. [Google Scholar]
49. Mahajan N, Rawal S, Verma M, Poddar M, Alok S. A phytopharmacological overview on *Ocimum* species with special emphasis on *Ocimum sanctum*. *Biomed Prev Nutr*. 2013;3:185–92. [Google Scholar]
50. Mohan L, Amberkar MV, Kumari M. *Ocimum sanctum* linn. (TULSI)-an overview. *Int J Pharm Sci Rev Res*. 2011;7:51–3. [Google Scholar]
51. Pattanayak P, Behera P, Das D, Panda SK. *Ocimum sanctum* Linn. A reservoir plant for therapeutic applications: An overview. *Pharmacogn Rev*. 2010;4:95–105. [PMC free article] [PubMed] [Google Scholar]
52. Mondal S, Mirdha BR, Mahapatra SC. The science behind sacredness of Tulsi (*Ocimum sanctum* Linn.) *Indian J Physiol Pharmacol*. 2009;53:291–306. [PubMed] [Google Scholar].
53. Lay-flurrie K. Honey in wound care: Effects, clinical application and patient benefit. *Br J Nurs*. 2008;17:S30, S32–6. [PubMed] [Google Scholar]
54. Betts J. The clinical application of honey in wound care. *Nurs Times*. 2008;104:43–4. [PubMed] [Google Scholar]
55. Helmy N, El-Soud A. Honey between traditional uses and recent medicine. *Maced J Med Sci*. 2012;5:205–14. [Google Scholar]
56. White JW. *Composition of American Honeys*. Washington, DC, USA: Agricultural Research Service, USDA; 1962. [Google Scholar]
57. White JW., Jr Detection of honey adulteration by carbohydrate analysis. *J Assoc Off Anal Chem*. 1980;63:11–8. [PubMed] [Google Scholar]
58. Islam A, Khalil I, Islam N, Moniruzzaman M, Mottalib A, Sulaiman SA, et al. Physicochemical and antioxidant properties of Bangladeshi honeys stored for more than one year. *BMC Complement Altern Med*. 2012;12:177. [PMC free article] [PubMed] [Google Scholar]
59. Manyi-Loh CE, Clarke AM, Ndip RN. Identification of volatile compounds in solvent extracts of honeys produced in South Africa. *Afr J Agric Res*. 2011;6:4327–34. [Google Scholar]
60. Sato T, Miyata G. The nutraceutical benefit, part iii: Honey. *Nutrition*. 2000;16:468–9. [PubMed] [Google Scholar]
61. Siddiqui I, Furgala B. Isolation and characterization of oligosaccharides (Disaccharides) from honey. *J Apic Res*. 1967;6:139–45. [Google Scholar]
62. Siddiqui IR, Furgala B. Isolation and characterization of oligosaccharides (Trisaccharides) from honey. *J Apic Res*. 1968;7:51–9. [Google Scholar]
63. Mato I, Huidobro JF, Simal-Lozano J, Sancho MT. Significance of nonaromatic organic acids in honey. *J Food Prot*. 2003;66:2371–6. [PubMed] [Google Scholar]

64. French VM, Cooper RA, Molan PC. The antibacterial activity of honey against coagulase-negative staphylococci. *J Antimicrob Chemother.* 2005;56:228–31. [PubMed] [Google Scholar]
65. Iglesias MT, De Lorenzo C, Del Carmen Polo M, Martín-Alvarez PJ, Pueyo E. Usefulness of amino acid composition to discriminate between honeydew and floral honeys. Application to honeys from a small geographic area. *J Agric Food Chem.* 2004;52:84–9. [PubMed] [Google Scholar]
66. Vorlova L, Pridal A. Invertase and diastase activity in honeys of Czech provenience. *Acta Univ Agric.* 2002;5:57–66. [Google Scholar]
67. Ajibola A, Chamunorwa JP, Erlwanger KH. Nutraceutical values of natural honey and its contribution to human health and wealth. *Nutr Metab (Lond)* 2012;9:61. [PMC free article] [PubMed] [Google Scholar]
68. Manyi-Loh CE, Ndip RN, Clarke AM. Volatile compounds in honey: A review on their involvement in aroma, botanical origin determination and potential biomedical activities. *Int J Mol Sci.* 2011;12:9514–32. [PMC free article] [PubMed] [Google Scholar]
69. Barra MP, Ponce-Díaz MC, Venegas-Gallegos C. Volatile compounds in honey produced in the central valley of Ñuble province, Chile. *Chil J Agric Res.* 2010;70:75–84. [Google Scholar]
70. Nurul Syazana MS, Gan SH, Halim AS, Shah NS, Gan SH, Sukari HA. Analysis of volatile compounds of Malaysian Tualang (*Koompassia excelsa*) honey using gas chromatography mass spectrometry. *Afr J Tradit Complement Altern Med.* 2012;10:180–8. [PMC free article] [PubMed] [Google Scholar]
71. Carlos AU, David H, Carmen G. Role of honey polyphenols in health. *J ApiProduct ApiMedical Sci.* 2011;3:141–59. [Google Scholar]
72. Economos C, Clay WD. Nutritional and health benefits of citrus fruits. *Food Nutr Agric.* 1999;24:11–18. [Google Scholar]
73. Committee NP. *Pharmacopoeia of People’s Republic of China.* Beijing: China Medicinal Science and Technology Press; 2010. [Google Scholar]
74. Moyers S. *Garlic in Health, History, and World Cuisine.* Suncoast Press; 1996
75. Bergner P. *The Healing Power of Garlic: The Enlightened Person’s Guide to Nature’s Most Versatile Medicinal Plant.* Prima Lifestyles; 1995.
76. Denzler K, Moore J, Harrington H, et al. Characterization of the Physiological Response following In Vivo Administration of *Astragalus membranaceus*. *Evid Based Complement Alternat Med.* 2016
77. Chu DT, Wong WL, Mavligit GM. Immunotherapy with Chinese medicinal herbs. I. Immune restoration of local xenogeneic graft-versus-host reaction in cancer patients by fractionated *Astragalus membranaceus* in vitro. *J Clin Lab Immunol.* 1988. <http://www.ncbi.nlm.nih.gov/pubmed/3260960>.
78. Hobbs C. *Medicinal Mushrooms: An Exploration of Tradition, Healing, and Culture.* Book Publishing Company; 2002.
79. Rogers R. *The Fungal Pharmacy: The Complete Guide to Medicinal Mushrooms and Lichens of North America.* North Atlantic Books; 2011.
80. Patel, S, Goyal, A. Recent Developments in Mushrooms as Anti-Cancer Therapeutics: A Review. *3 Biotech.* 2012.

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