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Review Article

**IMMUNITY MODULATING NATURAL HERBS IN THE
PREVENTION OF COVID-19****Suraj K Sonune¹, Vijay M Waghulkar¹, Abhay P Gawande¹**
Vidyabharti College of Pharmacy, C.K. Naidu camp Amravati**Abstract:**

The COVID-19 has spread all over the world and there is no single drug or medicine for the prevention and the treatment of this deadly disease. One can get prevention from this disease by boosting the immune system. Persons with weak immune system e.g. children, elder patients or patients with preexisting diseases affect rapidly due to coronavirus. This novel coronavirus attacks mainly on the person immunity. For the centuries the herbal medicinal plants have many beneficial effects against deadly viruses. Herbal medicines provide a rich resource for new antiviral drug development. These natural agents interact with the life cycle of virus such as virus entry, replication, assembly and release. In this review, the importance, immunomodulator, antiviral and pharmacological activities of some medicinal plants, namely, Aloe vera, Giloy, Echinacea purpurea, Shatavari, Liquorice, Punarnava, Chirata, Blackpepper, Harsingar, Amalki, Kutki, Drumstick plant, Almond, Broccoli are highlighted. These medicinal plants have many phytoconstituents like alkaloids, glycosides, terpenoids, flavonoids, lactones, polysaccharides, volatile oils, tannins, resins, etc which are helpful for boosting immunity and will help in the prevention and in the management of COVID-19. Several types of research attempted to use herbal medicines against COVID-19.

Keywords: COVID-19, Herbs Medicine, Immunomodulators, Phytoconstituent, Prevention.

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INTRODUCTION:

Plants are the invaluable, incredible and traditional sources for the curability of various diseases in the form of medicines.¹ Plants are the main source of drugs that being used from the ancient times as a herbal remedies for the health care, prevention and cure of various diseases and ailments². Plants secondary metabolites have been implicated for most plants therapeutic activities. Drug discovery from plants involves a multidisciplinary approach combining botanical, ethnobotanical, phytochemical and biological techniques. They continue to provide us new chemical entities (lead molecules) for the development of drugs against various pharmacological targets.³

Corona virus disease 2019 (COVID-19) is defined as illness caused by a novel corona virus (SARS- CoV-2; formerly called 2019-nCoV). COVID-19, is a transmissible disease which was spread from bats to human beings. Although COVID-19 originating from animals but it affects human beings. Corona virus transmitted in an identical way to the common cold, via influence with droplets of infected individual's upper respiratory tract secretions that is from coughing and sneezing. Being an unfamiliar virus type, immunopathogenesis of COVID-19 disease causation is not fully recognized and vaccines and medications against corona virus are still in trial. Thus, no effective medications and vaccines have been advised by higher regulatory authority. COVID-19 generally presents with respiratory and systemic manifestations. Individuals infected with corona virus are asymptomatic and can act as a carriers, signs and symptoms are non-specific such as fever (84-90%), cough (65-75%), fatigue (30-40%), sputum production (31-35%) and shortness of breath (15-25%). Immunity is a biological term that is defined as a state of having ample biological defences to avoid disease or other undesirable biological invasion and infections. The immune system provides protection to the host from pathogens or other foreign material while minimizing damage to own tissue. Immune system is the second line of body defence mechanism against pathogens or foreign material. The linked network of cells, proteins and lymphoid organs which are strategically placed to ensure maximum protection against infection is define as individuals immune system. Immune defence or response categorized into the two ways i.e., 1.innate immune response, 2.adaptive or acquired immune response. Innate immune response provides immediate shelter against an invading pathogen while Adaptive immune response which takes more time to develop but confers long lasting protection exquisite specificity.⁴

IMMUNOPATHOGENESIS OF COVID-19⁴

It has been shown that SARS-CoV-2 virus disrupts immune responses of infection patient, leading to an uncontrolled inflammatory responses and impaired immune system in patients with severe COVID-19 infection. These patients possess sign of lymphocyte activation and dysfunction, lymphopenia, granulocyte and monocyte abnormalities, an induction in level of immunoglobulin G (IgG), high cytokine levels, and elevated total antibodies in the patients . Coronavirus virions are enveloped particles with spherical to pleomorphic shaped, envelope contains projecting glycoproteins, and surrounds a core consisting of matrix proteins. The single strand of positive-sense RNA (Mr 6×10^6) associated with nucleoprotein is enclosed within inner core. For attachment to the host cells, the envelope glycoproteins are plays role and carry the main antigenic epitopes, and this epitopes are perceived by neutralizing antibodies .

Non-severe stage

The corona virus enters in to the host cell through airway epithelium via fuse with the host cell membrane . The virus enter lower airway and alveoli after proliferation inside host cell. In new grown-ups with good cellular and innate humoral immunity virus multiplication can be limited and viral abundance diminished reaching alveoli thus recovery can occur within 2–3 weeks of infection. Prevention of the viruses to penetrate new cells is done via humoral immunity of body while cellular immunity eradicating virus-infected cells. In these stage, a vigorous immune system can be advantageous in prevention of the proliferation of the virus thus reducing the COVID-19 infection severity.

Severe stage

Once the immune system is intruded, viral multiplication is their and reaches the alveoli and lower respiratory tract. Then the virus can permeate alveoli and reaches systemic circulation provoke "viremia". After that organs with ACE2 receptor proteins virus attaches there . During this stage, immunity particularly cellular immunity, becomes sturdy and starts releasing various pro-inflammatory cytokines (IFN- α , IFN- γ , IL-6, IL-1B, IL-12, IL-33, IL-

18, TNF- α , etc.) and chemokines (CCL2, 3, 5, CXCL8, 9, 10, etc.) inducing damage to multiple organs called as "Cytokine storm". So, for recovery to these stage we require to abolish the inflammation or lower down cytokines levels . Anti-inflammatory interleukin (IL10) and IL-6 receptor inhibitor (Tocilizumab) are exhibited therapeutic and beneficial role in the minimization of severity and lethality of

COVID-19. As there is increased risk of thromboembolic phenomena with COVID-19, prophylactic antithrombotic medications are advised during this stage.

PRIMARY PREVENTIVE MEASURE ⁵

During home quarantine, the adaptation of various traditional practices may strengthen the body's immunity and are considered first-line preventive measures against COVID-19. The Ministry of Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homoeopathy (AYUSH) recommend some self-care guidelines (AYUSH, 2020) which are as follows:

- a) Drink warm water in the morning and after 1–2 hours gap, throughout the day.
- b) Practice Yogasana, Pranayama, and meditation for at least 30 min daily to build body immunity.
- c) Consume homemade food with applied spices such as turmeric (*Curcuma longa*), cumin (*Cuminum cyminum*), coriander (*Coriandrum sativum*), and garlic (*Allium sativum*), will increase immunity.
- d) Drink hot herbal tea containing tulsi, cinnamon, black pepper, dried ginger, and raisins once or twice a day.
- e) Drink hot milk mixed with half teaspoon turmeric powder, once or twice a day.
- f) Apply a few drops of sesame oil, coconut oil, or ghee in both the nostrils each day in morning and evening.
- g) Steam inhalation of extremely hot water infused with fresh mint leaves or caraway seeds before bed at night.
- h) Clove powder mixed with honey taken 2–3 times a day to reduce cough or throat infections. Other important traditional applications which are easy to follow in the home include:

- Ingestion of cinnamon powder with honey in the morning to strengthen the immune system.
- Ingestion of one glass of hot water mixed with one spoon of ginger juice to improve throat infections and overall immunity.
- Ingestion of half a spoon of black pepper powder mixed with ginger paste, combined with one spoon of ghee in hot rice for cough, cold, and throat infection.
- Combine one spoon of honey and garlic in the morning to increase immunity.
- Ingest one glass of hot water mixed with one spoon of lemon juice to increase immunity.
- Take one spoon of honey mixed with one spoon of turmeric powder, half spoon of cinnamon powder and black pepper powder each day for cough, and to soothe a scratchy throat.
- Take one glass of hot milk with half a spoon of turmeric and half a spoon of almond powder once daily after dinner to strengthen immunity.

- Take black jeera (black cumin) powder with coleus leaf extract one spoon daily in the morning to strengthen immunity.
- Take one spoon of tulsi leaf juice with half spoon of honey for throat infections and respiratory tract issues.
- Ingest hot milk with 2–3 saffron petals mixed with half spoon almond seed powder after dinner will boost immunity.

Prevention of Covid -19⁶

Traditional Chinese medicine seems to have revealed encouraging results in reducing the rate of mild, severe, overall mortality, and shortening total disease duration. When combined with modern biomedicine, herbal medicines could exert antiviral, relieve chronic obstructive pulmonary disease and hypoxemia, immune regulatory, and anti-inflammatory, activities. Similarly, traditional medicines are used for the management of COVID-19 parallel with modern medicine and vaccinations in India.

Based on the sign and symptoms of COVID-19 infection can be classified as "wet, heat, congestion", in the respiratory system. According to Chinese traditional medicine, lung function is the first affected part of the body. "Wet" refers to the factor with sticky and high turbidity that can lead to prolong the disease severity and damage the body function. "Hot" refers to the factor with hot, dry, and rising turbidity that can lead to the virus. "Congestion" is a contributing factor that can affect blood circulation and cause symptoms such as pain. China to protect respiratory function, a kind of prevention value is chosen because of the nature of viral condition by using Yupingfeng San. It is an ancient herbal medicine in China that contains three types of plants: Astragalus can (improve lung function), Fangfeng (to relieve the pathogen), and Atractylodes (enhance the spleen function and digestion and absorption of our body function). Studies have shown that Yupingfeng San could optimally regulate the body's immune function.

In this background, home preparations, like the use of medicinal plants supported by the relevant establishments can serve as an alternative option to combat COVID-19 in Ethiopia. Some medicinal products such as garlic, ginger, turmeric, chili, lemon, hot water with salt would be used for viral suppression.

Herbal Immunomodulators⁷

There are some points to know immunomodulators: Immune stimulants cause our immune defences to be stimulated in a non-specific way. They have little influence on our immune memory cells, and their pharmacological effects disappear fast, therefore they

must be given at regular intervals or on a continual basis. These herbs are more equivalent to traditional antibiotics, and they're useful for boosting the body's innate immune processes in immunocompromised patients and those with autoimmune illness.

This review's ability to provide an accurate portrait of the immunomodulatory activities of herbal preparations used by millions around the world is based on an inconsistent understanding of bioactive components and the delivery of effective human clinical trial performance. The immune system is a well-functioning network of cellular elements and chemicals that protects the organism's integrity from external slurs. Its proper functioning and balance are essential for preventing a variety of diseases. Evidence from the literature suggests that immunological diseases are on the rise, and much emphasis has been placed on the development of molecules that can modulate the immune response.

Based on the preceding explanation, we conclude that these herbal medicines may be able to regulate the production and release of proinflammatory cytokines, interfere with virus development in host cells, and modify certain RAA-related molecular pathways. Herbal agents may be effective COVID-19 treatments. Finally, it is still not recommended for patients to take a supplement containing one of these compounds to prevent COVID-19.

Herbal Kadha for Immunity: In the current pandemic scenario, taking precautions and boosting immunity are two of the best options for avoiding COVID19 infection. According to our findings, the use of spices and herbs may play an important role in the prevention of viral infections. We discovered that cinnamon, black pepper, basil, and turmeric are effective against SARSCoV2 (COVID19) and other viral infections,

which is supported by another recent research. Since ancient times, people in India have used spices and herbs for their taste, antiviral, antimicrobial, antioxidant, and immunity boosting properties.

Since the outbreak of the novel Coronavirus (SARS-CoV-2) infection in Wuhan, China in December 2019, it has spread to over 205 countries. The ever-expanding list of corona virus19 disease (COVID-19) patients has demonstrated the disease's high transmission rate among the human population. There are currently no FDA-approved drugs or vaccines to prevent or treat SARS-CoV-2 infection. Given the current state of affairs, there is an urgent unmet medical need to identify novel and effective approaches for the prevention and treatment of COVID-19 through re-evaluating traditional medicine knowledge and drug repurposing.

The Government of India's Ministry of AYUSH has provided "Ayush Kwath" to improve the immune system and stabilise the situation. (Chandurkar et al., 2021) It is recommended that people use herbs and traditional medicinal products to boost their immunity and build their livelihood. Herbal kadha and chawanprash protect public health by increasing immunity and possibly resisting viral attacks in the body. In this survey, we attempted to understand the views of the people of Bhopal, MP, India on the use of herbs and spices such as tulsi, turmeric, ginger, giloy, ashwaghandha, cinnamon, and so on. boost their immunity in the face of a pandemic attack.

The Indian ayurvedic system is a natural source of ayurvedic medicine, as we all know. Corona plays an important role. "Prevention is preferable to cure" in relation to corona. Ayurvedic medicines are widely available, have no side effects, and are inexpensive.

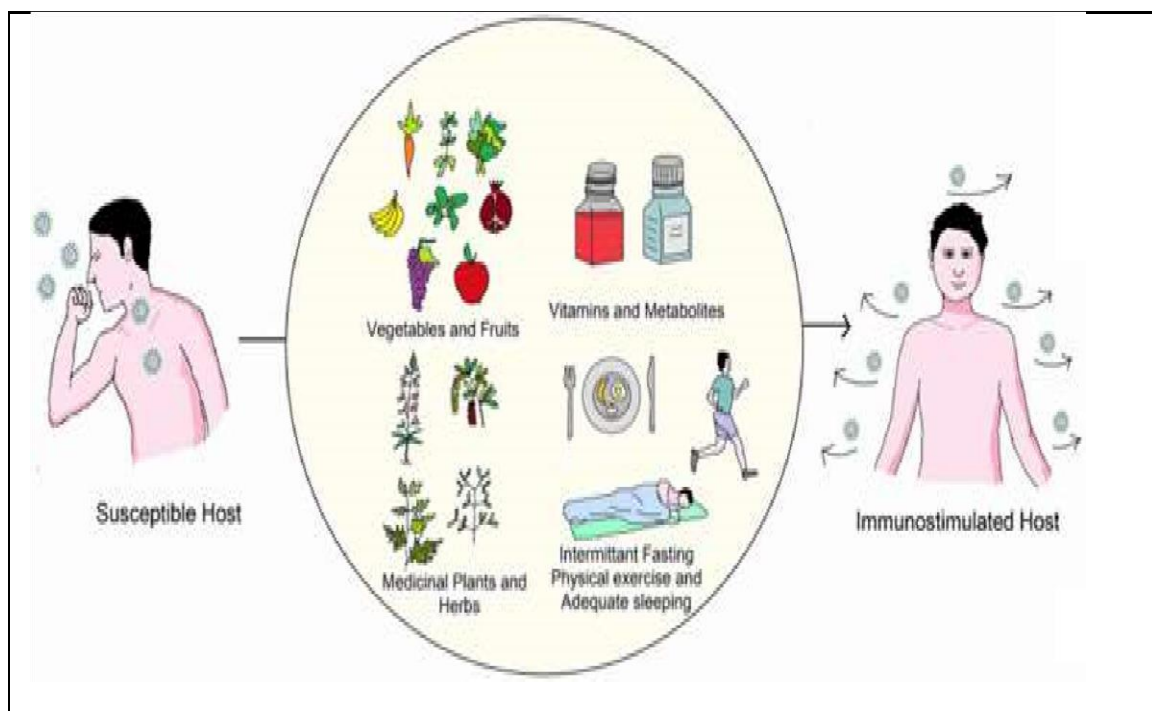


Fig no. 1 Immune System

Role of Immune System Against COVID-19 Infection

The immune system is the greatest defence line against any infection; it supports to human natural capacity to protect against pathogens (e.g., viruses, bacteria, fungi, protozoans, and worms) and resists infections. COVID-19 infections are undiagnosed as long as the immune system is functioning properly. Although innate immunity (quick response), adaptive immunity (delayed response), and passive immunity are the three types of defense mechanisms that work against infections, this review focuses on factors that improve innate immunity, as well as the importance of developing an effective vaccine and antiviral drugs. The key role of the immune system against COVID-19 is precise to certain structural features of SARS-CoV-2. Particular proteins and specific sequences of the viral genome known as pathogen-associated molecular patterns (PAMPs) induce the immune response against the viruses. Viral double-stranded RNA, nucleocapsid, membrane protein, and surface glycoprotein are some of the significant viral PAMPs.

These PAMPs are accepted by specific intracellular pattern recognition receptors (PRRs) present in the human body. Upon recognizing of PAMPs, PRRs trigger the expression of certain interferon's, cytokines, and antiviral interferon-producing genes, like- *IFN3*, *IFN7*, and the plethora of interleukins (IL). Together, they inhibit viral replication and prevent viral spread.

All the vital immune cells mentioned above produce cytokines and have an efficient immune response against COVID-19 that is highly dependent on the nutritional status of the host and the presence of certain vitamins and metabolites. Moreover, some external factors like- physical exercise, intermittent fasting, and adequate sleeping have also been reported to facilitate and enhance immune response. Hence, the role of the immune system against COVID-19 is very vital, and it can only be replenished by maintaining some simple lifestyle practice until fully-functional vaccines and specific anti-viral drugs have been developed and reached to all the people in the world.⁸

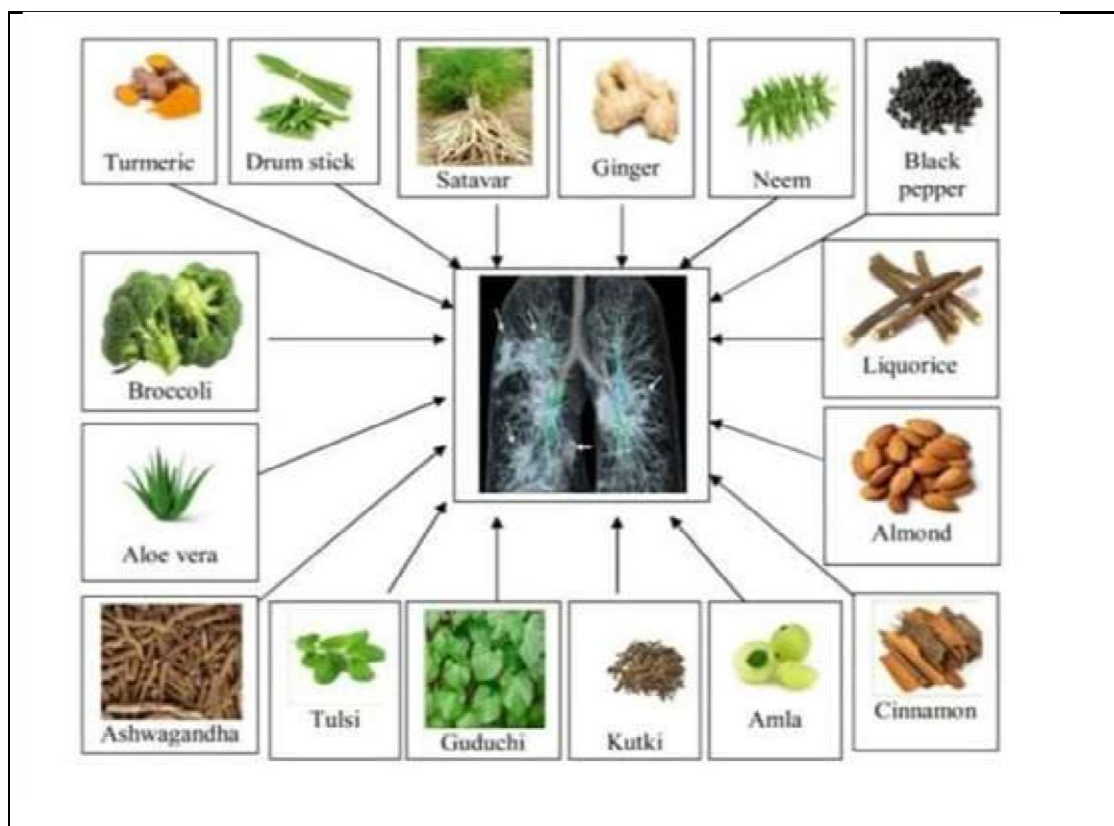


Fig no 2 - Herbal plant as immunomodulator against covid 19

HERBAL IMMUNOMODUPATOR PLANTS

Aloe Vera (Acemannan)

Aloe vera (*Aloe barbadensis*), is a perennial plant of Liliacea family, commonly known as Ghritakumari. On dry drug basis, aloe gel consists of polysaccharides, minerals, sugar, proteins, lipids and phenolic compounds. The curative potential of plant credited to polysaccharides present in the inner leaf parenchymatous tissue of leaf extracts. Various range of effective secondary metabolites possessed by plant that includes tricyclic aromatic quinine structure with anthraquinone base. Aloe-emodin and chrysophanol are main naturally developing anthraquinone compounds from aloe vera. Two types of exudates are secreted by aloe leaves, one is transparent and

resembles colorless gelatin and another that is bitter reddish yellow juice due to the presence of aloe-emodin, aloin and related compounds. Aloe vera possess wound healing, antiinflammatory, anticancer, antidiabetic, antiulcer, antihyperlipidemic activity, antioxidant effects and Immunomodulatory activity. Immunomodulatory properties of extracts of Amla and its interaction with Aloe vera in immunocompromised states.⁴ Aloe vera is a medicinal plant species of the genus *Aloe* with a long history of traditional therapeutic use around the world. Acemannan, the main bioactive polysaccharides of Aloe vera possesses several pharmacological activities among which immunomodulation are considered as the most vital one.⁹

| Sr.no | Name | Dose | Price |
|-------|---|-------------------------------|--------|
| 1 | Vitro Aloe vera juice | Twice in day 1 to 2 spoon | 379.00 |
| 2 | Nourishvitals pure aloe vera juice | Twice in day 1 to 2 spoon | 349.00 |
| 3 | Kapiva Aloe vera immunity booster capsule | 1 to 2 capsule Twice a day | 123.00 |
| 4 | Baidyanath vansar Aloe vera tablet | 2 tablet twice a day | 187.00 |

Giloy (Tinospora cordifolia) (Gudwell)

Giloy or Guduchi or Amruta is a large climbing shrub belonging to the family Menispermaceae. It is found throughout India. *Tinospora cordifolia* has importance in traditional Ayurvedic medicine and used for the treatment of chronic diarrhoea, dysentery, cancer, jaundice, bone fracture, pain, asthma, skin disease, poisonous insect, snake bite and eye disorders¹⁰. It gives relief from chronic cough, breathlessness, tuberculosis, syphilis, gonorrhoea and leprosy in Unani medicine¹¹. It also improves learning and memory power¹². Giloy has many medicinal properties like anti-inflammatory, antiosteoporotic, anti-arthritis, antioxidant, anti-allergic, antihyperglycemic, immunomodulatory, antipyretic, anti-infective, hepatoprotective, antileprotic, antifertility, antimutagenic, antiobesity, antineoplastic and radioprotective activity¹³. Different classes of chemical constituents are present in Giloy are lactones, alkaloids, glycosides, sesquiterpenoids, diterpenoids, steroids, phenolics, essential oils, polysaccharides, aliphatic compounds and flavonoids. The chief constituents are tinosporone, tinosporine, tinosporic acid, cordifolisides A to E, syringe, berberine and giloin¹⁴.

Giloy also contains high fibre content (15.8%), protein (4.5%-11.2%), carbohydrate (61.66%), and low fat (3.1%), high chromium (0.006%), potassium (0.845%), sufficient iron (0.28%) and sufficient calcium (0.131%). Nutritive value of *T. cordifolia* nutritive is 292.54 calories per 100 grams¹⁴. Researchers have found that methanolic extract of

Giloy is found to have broadspectrum antimicrobial effectiveness against various strains which are *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Shigella flexneri*, *Salmonella paratyphi*, *Salmonella typhimurium*, *Salmonella typhi*, *Enterobacter aerogene*, *Serratia marcescens* and *Proteus vulgaris*.¹⁶

1, 4-alpha-D-glucan which is one of the constituent of *Tinospora cordifolia* found to activate macrophages, NFκB translocation and cytokine production, and hence activates the immune system¹⁶. Favorable effects of *Tinospora cordifolia* was seen in HIV positive patients when it was used with conventional antiviral treatment.¹⁸ Tinosporin is effective against HIV and other viral diseases as immunomodulatory and selective inhibition of the virus to target T helper cell. Sanshamani Vati (also called Guduchi ghana vati) which is made from the aqueous extract of *T. cordifolia* can be administered as 500mg twice a day, 15 days with warm water as a preventive and prophylactic drug for COVID-19.¹⁹

The combined herbal formulation of Giloy, six leaves of tulsi, one or two tablespoon of ginger juice and four to six seeds of black pepper receiving enormous popularity and found to be helpful for preventing COVID-19 disorder. This mixture is crushed or grind into a fine powder and use it as herbal tea or consume with honey. It can control fever, cough and support immunity.²⁰

| Sr. no. | Name | Dose | Price |
|---------|---|---|-----------|
| 1 | Apollo Life Giloy Tulsi Plus Juice 500ml | 10ml (for children) 30ml (for Adult) | Rs.166.50 |
| 2 | Patanjali Giloy Ghanvati 60 tablet | 1 tab twice daily (for adult) ½ tablet (for children) | Rs.100.00 |
| 3 | Dabur Samshamani Vati Giloy 100 tablet | 1 or 2 tablets twice a day | Rs.185 |
| 4 | Baidyanath Giloy Juice 500ml | 10ml (for children) 30ml(for adult) | Rs.120 |
| 5 | Zandu Giloy Immunity Booster 60 veg capsule | 1-2 casules twice a day | Rs .125 |

Echinacea purpurea-(Coneflower)

The genus *Echinacea* (coneflower, family Asteraceae) is indigenous to North America. *Echinacea* preparations are commonly used as immunostimulants and prevent cold and other respiratory infections and conditions associated with respiratory discomfort. These preparations widely used as dietary supplements in Europe and the United States. In Germany, *Echinacea* containing products have the greatest popularity and approved for supportive treatment of respiratory and urinary infections.²¹

Preparations of *Echinacea purpurea* can be made in the form of tinctures, extracts and sprays. *Echinacea purpurea* preparations stimulate phagocytosis of neutrophils both in vitro and in vivo and activate cellular immunity. It contains chemical constituents

like caffeic acids, polysaccharides, chicoric acid, alkylamides, essential oils, hydroxycinnamic acids, tannins, saponins, flavonoids, echinacin, echinacoside, echinolone, organic acids, resins and phenolcarboxylic acids.²²

The extract of *E. purpurea* has antiviral activity against virus-induced diseases. It is effective against herpes simplex virus, influenza and rhinovirus. Depending on different studies, it can be concluded that *E. purpurea* can be used for the prevention and treatment of COVID-19.²³

Echinacea species particularly *Echinacea purpurea* (*E. purpurea*), one of the most clinically studied herbal medicines, have been suggested to be an important and useful antiviral agents that modulate virus entry, internalization, and replication.²⁴

| Sr.no | Name | Dose | Price |
|-------|-----------------------------------|--------------------------|---------|
| 1 | Lung Detox 60 capsules | 1 capsule per day | Rs.1299 |
| 2 | Lungs Pure 60 capsules | 1-2 capsule before meal | Rs .627 |
| 3 | Echinacea 400mg 100 capsule | 1 capsule twice in a day | Rs 1256 |
| 4 | Indian Echinacea 500mg 60 capsule | 1 capsule twice in a day | Rs 1215 |

Shatavari (*Asparagus racemosus*)

Commonly known as satavar, shatavari and shatamull having a place in the family Asparagaceae. Traditionally it was used as galactagogue, aphrodisiac, Rasayana, antiepileptic, adaptogenic, general health tonic and in numerous female reproductive system problems. Punarnava contains specific steroids, flavonoids, phenolic compounds and glycosides as chemical constituents. Extract of different parts of the plant has been approved for its both in vitro and in vivo activities. Shatavari has a potent immunomodulatory property by altering the function of macrophages. It has immunomodulatory, antidiabetic, antioxidant, anticancer, hepatic, and neuroprotective effect, antimicrobial, antiurolithiatic, aphrodisiac, memory enhancing the property, antitussive effect, etc.⁴ Shatavari is an important Ayurvedic rejuvenating tonic for the female, as Ashwagandha (*Withania somnifera*) for the male. It has immune adjuvant potential with Diphtheria, Tetanus, Pertussis (DPT) vaccine by significant up-regulation of Th-1, Th-2 and cytokines and

immunostimulation property by significant increase of CD4/CD8 along with T cell activation.²⁵

Apart from the bioactive components, the plant parts are also imbued with an excellent source of healthful nutrients and minerals such as manganese, copper, zinc, cobalt, potassium, selenium, calcium, and magnesium. Besides containing vitamins like Vitamin A and ascorbic acid, the plant also shows presence of essential fatty acids like gamma-linolenic acid that hold high significance in treating conditions like hypercholesterolemia, heart disease, depression, diabetes and arthritis.²⁶

Shatavari has been reported for its anti-bacterial, anti-candidal, anti-viral activities. Recent studies have reported that, the drug under investigation, if possess a potent immunomodulatory, anti-inflammatory and antioxidant potential could prove an effective agent in treatment of COVID 19. Further, all these suggested properties are well equipped by the phytoconstituents from *Asparagus racemosus*.²⁷

| Sr.no | Name | Dose | Price |
|-------|----------------------------------|-------------------------------------|-----------|
| 1 | Shatavari Tablet | 1 to 2 Tablet Twice in a day | Rs.1299 |
| 2 | Extra Strength Shatavari Capsule | 1 to 2 Capsule Twice in a Day | Rs .15.49 |
| 3 | Shatavar churna 100 g | 1\4-1\2 tea spoon Twice in a Day | Rs 160 |
| 4 | Himalaya shatavari powder 100 g | 1\4-1\2 tea spoon Twice in a Day | Rs 320 |

Liquorice (*Glycyrrhiza glabra*)

Yashtimadhu or Liquorice which contain glycyrrhizin, glycyrrhizic acid, glycyrrhetic acid and glabrine etc. as major chemical constituents. Natural triterpenoid saponin derived from the root of liquorice (*Glycyrrhiza glabra*) that is Glycyrrhizin has shows numerous pharmacologic actions, including antiinflammatory, antibacterial, antioxidant, antitumor, antiviral and immunomodulatory activities. Stimulation of IL-12 and suppression of IL-10 production and NO production from macrophages, up regulation of costimulatory molecules on dendritic cells, augmentation of NK cell activity, increase in T cell proliferation and Th1 directed immune response, are the most Journal of Ayurvedic and Herbal Medicine|April|June|2021 129 known immunomodulatory activities possess by glycyrrhizin. *Glycyrrhiza glabra* mentioned in Ayurveda as “Rasayana”.⁴ Glycyrrhizin, also called glycyrrhizic acid (GLR), is a triterpenoid saponin mainly isolated

from the roots (*Glycyrrhizae Radix*) of the plant *Glycyrrhiza*. GLR effectively inhibited the replication of two clinical isolates of SARS associated coronavirus (FFM-1 and FFM-2). The drug was found to inhibit the cytopathic effect of the virus with an EC₅₀ of 300 mg/ml while being non-cytotoxic to the host cells. GLR inhibited virus replication but also the penetration and adsorption of the virus into cells. The mechanism of action at the origin of this activity was not known at that time but a drug-induced production of nitrous oxide synthase was mentioned, signifying that nitrous oxide could be accountable for the inhibition of virus replication. GLR also showed active when it was tested against 10 clinical isolates of SARS coronavirus in infected Vero-E6 cells but the activity was limited in time. The rapid metabolism of the drug limits the drug exposure, not permitting it to reach an effective concentration. The modification of the GLR structures, particularly to make amino-acid conjugates and amide.³⁰

| sr.no. | Name | Dose | Price |
|--------|-----------------------------|----------------------------------|--------|
| 1 | Organic liquorice powder | 1 teaspoon with milk twice a day | 299.00 |
| 2 | Inlife liquorice capsule | 1 capsule /day | 374.25 |
| 3 | Yastimadhu liquorice tablet | 1 tab/day | 142.00 |

Punarnava (*Boerhaavia diffusa*)

Punarnava is a well known medicinal plant packed with essential nutrients, vitamins such as vitamin C and other constituents. It might also be useful for managing liver problems due to its antioxidant activity which prevents liver cell damage caused by free radicals. Punarnava has immunomodulatory effects due to its immunosuppressive and immunostimulatory activity. Administration of Punarnava consequently decrease down the enhanced level of proinflammatory cytokines such as TNF α , IL-1 β , and IL-6 in experimental animals. These

outcome point out the immunomodulatory action of Punarnava. Extracts of *B. diffusa* roots have anti-inflammatory activity by inhibiting natural killer (NK) cell, cytotoxicity, production of nitric oxide in human and very high antiviral activity.⁴ Bronchial asthma is a condition which occurs due to an imbalance of Kapha dosha which results in the accumulation of mucus in the respiratory pathway. This lead to blockage in the air passages making breathing uncomfortable. Punarnava helps prevent the production of mucus and reduces the symptoms of asthma, resulting in easy breathing due to its

Kapha balancing and Rasayana (rejuvenation) properties. The phytochemicals extracted from *B. diffusa* belongs to the novel class of isoflavonoids known as rotenoids, flavonoids, flavonoid glycosides, xanthenes, purine nucleosides, lignans, ecdysteroids and steroids. A mitochondrial inhibitor called rotenone is a prototype compound for the isoflavonoid derivative called Rotenoid. Identification of these compounds, its isolation and characterization were only possible after the rapid quantitative estimation methods for boeravinones of *B. diffusa* developed recently. The roots and in some tribes the entire plant is used as a culinary ingredient accounting to its Vitamin C, Vitamin B3, Vitamin B2 as well as calcium content in roots alone. *B. diffusa* also has been reported to contain 15 amino acids

among which 6 are essential in the entire plant and 14 amino acids among which 7 are essential in the roots alone. The roots are also known to contain isopalmitate acetate, behenic acid, arachidic acid and saturated fatty acids. The present study involves selection of 9 major phytochemicals of *B. diffusa* namely 2-3-4 beta-Ecdysone, Bioquercetin (Quercetin-3-O-robinobioside), Biorobin (Kaempferol-3-O-robinobioside), Boeravinone J, Boerhavisterol, kaempferol, Liriodendrin, quercetin and transcaftaric acid. The mentioned molecules were docked with the main protease of SARS-CoV-2 to discover novel SARS-CoV-2 inhibitors from *B. diffusa* which could be potential drugs to cure COVID-19.³¹

| Sr.no | Name | Dose | Price |
|-------|--------------------------------------|-----------------------------|--------|
| 1 | Zandu Punarnava capsule | 1 to 2 cap twice a day | 199.00 |
| 2 | Healthvit punarnava capsule | 1 to 2 cap twice a day | 129.00 |
| 3 | Baidyanath Punaenava Varishtha syrup | 1 to 2 teaspoon twice a day | 131.00 |

Chirata (*Swertia chirata*)

Swertia chirata Buch Ham (Gentianaceae) is a perennial herb. Significant decrease in delayed type hypersensitivity shown with use of methanolic extract of Chirata and also beneficially prohibit the production of lymphocytes (CD3) intracellular cytokines (IL-2 and IFN- γ). So, further research require to explore Chirata to develop an immunosuppressive agent which will be effective and

having no or minor side effect. Phytochemical screening shows the presence of phenolic compound like flavonoids, alkaloids and tannins which may have role in the immunomodulatory activity. Chirata shows proven therapeutic potentials like antiviral, immunomodulatory and antiinflammatory activities and it will be beneficial to acquire immunity against Covid-19 attack.⁴

| Sr. no. | Name | Dose | Price |
|---------|------------------------------|--|--------|
| 1 | Vedic herbal tablet | 1 tab/day | 660.00 |
| 2 | Shrihari herbal chirata tab | 1 tab twice a day | 980.00 |
| 3 | Sage herbal capsule | 1 cap twice a day | 229.00 |
| 4 | Dawn lee immune herbs powder | 1 teaspoon with boil water twice a day | 300.00 |

Black Pepper (*Piper nigrum*)

Black pepper is a flowering vine in the family Piperaceae, cultivated for its fruit, known as a peppercorn, which is usually dried and used as a spice and seasoning. One tablespoon (6 grams) of ground black pepper contains moderate amounts of vitamin K (13% of the daily value or DV), iron (10% DV), and manganese (18% DV), with trace amounts of other essential nutrients, protein, and dietary fibre.³² Black pepper (marich) contains principal

monoterpene compounds in the pericarp were α -pinene (9.2%), 2- β -pinene (14.3%), δ -3-carene (21.5%) and DL-limonene (18.8%), and the primary sesquiterpenes were α -copaene (5.1%) and caryophyllene (17.2%). Drug shows immune-modulatory, analgesic, antiplatelets, antioxidant, antihypertensive, anti-asthmatic, antipyretic, anticancer, antiinflammatory, antidiarrheal, anxiolytic, antidepressants, antispasmodic, antifungal, antiulcer, antimetastatic, antiapoptic,

antibacterial and anti-amoebic properties. The concentrate of drug and its phytochemicals like piperine, control the balance of the cytokines generation of Th1, Th2, Th17, and Treg cells, downturn the aggregation of inflammatory cells, blocks the expressions of GATA3, IL-4 and 6, IL1b, IL-17A and TNF α , increase INF-gamma and IL10 secretions in Broncho-alveolar lavage fluid and upsurge macrophage activation and B and T cell propagation.⁴ Various chemical constituents obtained from black pepper include piperine, piperamide, piperic acid, piperolein-B, piperlonguminine,

pellitorine, piperitine, eugenol and kusunokinin in addition to some volatile oils. Piperine shows a strong antiinflammatory activity and thus can be repurposed for suppression of hyper inflammation induced during COVID-19³³. Also, piperine is a potent antioxidant and protect against oxidative damage by neutralizing free radicals, ROS, and hydroxyl radicals⁷¹. Due to these properties, piperine can be used as a therapeutic compound to protect from the oxidative stress and hyper inflammation due to COVID-19.³³

| Sr.no. | Name | Dose | Price |
|--------|------------------------------|----------------|--------|
| 1 | A to Z immune tablet | 1 tab/day | 215.00 |
| 2 | Charak Kofal immunity tablet | 1 to 2 tab/day | 360.00 |

Harsinger (Night flowering jasmine)

The harsingar plant is found in the Oleaceae family and is well known in India. The leaves of this plant have shown to have strong immunomodulatory activity. The leaves contain tertiary and quaternary alkaloids which increase immune-bioactivities. The following constituents are found primarily in the leaves: nicotiflorin, oleanolic acid, nyctanthic acid, friedeline, lupeol, mannitol, glucose, fructose, and iridoid glycosides. The flowers contain nyctanthin, Dmannitol, carotenoid, β -monogentiobioside ester of α -crocetin, among others. The leaf extract enhances circulating antibodies and increases total white blood cell counts, which further boosts immunity. Another

study showed the immunomodulatory activities of an aqueous extract of its flowers with splenocytes proliferation and the induction of cytokines. The harsingar plant is also used as an antiviral agent against COVID-19 due to its antiviral potentiality. An *in vitro* study established it as an antiviral agent when an ethanolic crude extract of the plant and two isolated compounds from the extracts were tested separately against encephalomyocarditis Semliki forest viruses. In another research study, the antiviral activity of water, ethanol, and acetone extracts of *Nyctanthes arbor-tristis* was tested on *enterovirus* and reported as potent antiviral agent.⁵

| Sr.no. | Name | Dose | Price |
|--------|--|-------------------------------------|--------|
| 1 | Harsinger capsule | 1 to 2 cap twice a day | 410.00 |
| 2 | Ayush harsinger powder | 1 to 2 spoon twice a day with water | 299.00 |
| 3 | Organic India immunity booster capsule | 1 to 2 capsule twice a day | 215.00 |

Amalki (Amrutaphalam)

Amalaki belongs to the family- Phyllanthaceae and its fruits are one of the most important fruits to be used as immunomodulators for repeated respiratory infections in humans. The fruit is rich in vitamin C and other active constituents with its main flavonoids being kaempferol, ellagic acid, and gallic acid. The extract acts as an adaptogen and improves immunity. It enhances IL-2, NK (natural killer) cell activity, Antibody-Dependent Cellular Cytotoxicity (ADCC), and gamma-IFN production and inhibits apoptosis. Currently, the fruit is essentially utilized to improve immunity against COVID-19 due to it being a rich

source of vitamin-C. Phyllaemblicin B, the phytoconstituent extracted from the roots showed inhibitory potential for the Cocksackie virus while its phenolic content revealed effectiveness against herpes simplex viruses (HSV) 1 and 2. The phytochemical 1, 2, 4, 6-tetra-O-galloyl β -D-glucose from *P. emblica* showed antiviral activity for HSV *in vitro*. Pentagalloylglucose inhibited influenza A virus replication through the prevention of adsorption of the virus and the suppression of the release of the virus. *P. emblica* plant extracts also showed anti-HIV properties by inhibiting reverse transcriptase enzyme of the virus.⁵ Amalaki is a rich source of vitamin C

(Ascorbic acid). Acharya Charaka has described that Amalaki is the best rejuvenating herb and useful in relieving cough and skin diseases. Amalaki improves both cell mediated and humoral immuneresponse. It enhances IL-2, gamma –IFN and naturalkiller (NK) cell activity. Amalaki is a well-known drug for its anti-oxidant, detoxification and antiaging activity. *P. emblica* has an antibacterial effect on Gramnegative and Gram-positive organisms due to the presence of

flavonoids component. Antimicrobial activity of flavonoids is probably due to the ability to form complex with extracellular and soluble proteins, or with bacterial cell walls which disrupts the microbial membranes. Pulmonary antioxidant defences are widely distributed in lungs and include both enzymatic and non-enzymatic systems. The primary non-enzymatic antioxidants are membrane-bound vitamin C and vitamin E. Amalaki is the richest source of vitamin C.²⁵

| Sr.no. | Name | Dose | Price |
|--------|--|----------------------------|--------|
| 1 | Amalki Rasayan tab vitamin C | 1 tab twice a day | 351.00 |
| 2 | Himalaya Amalki immunity wellness tablet | 1 tab twice a day | 174.00 |
| 3 | Zandu Amalki capsule | 1 to 2 capsule twice a day | 500.00 |

Kutki (Katuka Rohini)

Kutki is part of the Scrophulariaceae family and it is an effective immunomodulator and effective against liver and respiratory disorders. The plant extract contains the phytoconstituents kutkin, picroside, vanillic acid, D-mannitol androcin and apocynin. The picroside boosts the immune system by increasing phagocytosis and, cell-mediated and humoral immunity. Its immunomodulatory activity was evaluated in Complete Freund's Adjuvant-induced stimulation of a peritoneal macrophage model and lipopolysaccharide stimulated RAW 264.7 murine macrophages which resulted in significant immunomodulatory activity. Apart from this activity,

the plant is also useful against viral infection. Recently, four new bis-iridoid glycosides, saungmaygaosides A–D, and six known iridoid glycosides were isolated from the n-butanol extract of the stems of *Picrorhiza kurroa* and evaluated for viral protein R inhibition activity.⁵ Aqueous and ethanolic extracts of *Picrorhiza kurroa* have been reported for stimulating humoral responses by various immune mechanisms which includes mediators releasing in hypersensitivity as well as tissue responses at the target site organ of these mediators Sharma, et al. One of the Biopolymeric fraction from this plant RLJ-NE-205 also showed cell-mediated immune response by stimulating CD4+ and CD8+ T cells.³²

| Sr.no. | Name | Dose | Price |
|--------|------------------------|---------------------------|--------|
| 1 | Kutki Yakritas capsule | 1 to 2 cap twice a day | 899.00 |
| 2 | Dawn free immune herb | Half teaspoon twice a day | 219.00 |
| 3 | Herbal Daily Kutki | 1 to 2 cap twice a day | 240.00 |

Drumstick plant (*Moringa Oleifera*)

The drumstick plant is found in the family-Moringaceae and is distributed throughout India. Its leaves, flowers, and fruits have significant immunomodulatory activity. The leaves contain mainly niaziminin A, and niaziminin B, niaziminin, and the flower contains mainly flavonoids such as quercetin, isoquercetin, kaempferol, kaempferitin. Its fruits contain isothiocyanate, nitrites, thiocarbamates, beta sitosterol. Glucosamine specific lectin from the leaves show an immunomodulatory effect via NK cell activity and Antibody-Dependent Cellular Cytotoxicity (ADCC). The antiviral activity of the chloroformic leaf extract of *Moringa oleifera* was studied against the Foot and Mouth disease virus

and showed potent antiviral activity using the MTT assay (3-(4, 5-Dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide). A recent article revealed *Moringa oleifera* contains high levels of potassium (K) which decreases the infection in patients with COVID-19 caused by the SARS-CoV-2 virus.⁵ *Moringa* leaves and seeds are enriched in vitamin C, vitamin A, calcium, and potassium content. The traditional, industrial, nutritional, and medicinal values used in folk medicine are diversified in *Moringa oleifera* for numerous health reasons, especially for the symptoms (e.g., fever, muscle pain, or asthma) of COVID-19 patients. *Moringa peregrina* has several pharmacological properties, including anti-microbial, antidiabetic,

antioxidant, anti-inflammatory, anti-spasmodic, anticancer, reduction of lipid activity, and cognitive problems. Black cumin, a component of this plant, is well-known in obstructive respiratory conditions for its robust immune regulation, anti-inflammation, and

antioxidant advantages that have been used for decades for medicinal purposes. Thymoquinone, Nigellidine, and α -hederine from *N. sativa* can impact the immune responses against COVID-19 on molecular grounds.⁸

| Sr.no | Name | Dose | Price |
|-------|------------------------|------------------------|--------|
| 1 | Himalaya shigru tablet | 1 to 2 tab twice a day | 138.00 |
| 2 | Aduna Moringa capsule | 1 to 2 cap twice a day | 400.00 |
| 3 | Indus moringa capsule | 1 to 2 cap twice a day | 343.00 |

Almond (Sweet Almond)

Almond (Family: Rosaceae) is commonly known as badam and available in India and many other countries. The almond seed is very effective in chronic cough and pneumonia and has an effective soothing effect on the throat. It is a rich source of vitamin-E which boosts immunity. The seed contains mainly various amino acids, vitamin E, and also oil. From oil, diolein and triolein are isolated. Thereafter, it revealed that almonds contains high levels of cytokine i.e., interferon- α (INF- α), interleukins (IL-

12), INF-gamma and tumour necrosis factor (TNF- α) that improved the immune surveillance of the peripheral blood mono nuclear cells towards viral infections and also significantly decreases in the Herpes simplex virus (HSV-2) replication. The extract produces high levels of cytokine i.e., interferon- α (INF- α), interleukins (IL-12), INF-gamma, and tumour necrosis factor (TNF- α) that boosts an immunity in blood mononuclear cells towards viral infections.⁵

| Sr.no | Name | Dose | Price |
|-------|---------------------------------|------------------------|--------|
| 1 | Neuherbs tripple immunes tablet | 1 to 2 tab twice a day | 199.00 |
| 2 | Oziva daily multi tablet | 1 tab /day | 424.00 |

Broccoli (Brassica Oleracea italika)

Broccoli is in the Brassicaceae family and the flower provides many health-promoting properties, and is cultivated in many countries. The flower contains a high content of flavonoids, glucosinolates, indole-3-carbinol, isothiocyanates, vitamins (especially vitamin E, C, K), mineral nutrients, essential oils, phenolics (such as kaempferol, and quercetin) and polypeptides. Sulforaphane, an isothiocyanate

isolated from the flower acts as an immune booster through the enhancement of phagocytic activity of the peritoneal macrophages and the reduction of elevated levels of TNF-alpha production by lipopolysaccharide (LPS) stimulated macrophages. The immunomodulatory activity of pectins extracted from broccoli stalks (*Brassica oleracea* var. *italica*) were studied *in vivo* and *in vitro* by the activation of macrophages.⁵

| Sr.no. | Name | Dose | Price |
|--------|-----------------------|----------------------|---------|
| 1 | Brocoli powder | 1 to 2 teaspoon /day | 1400.00 |
| 2 | Glucoraphanin capsule | 1cap/day | 120.00 |

Brief description of herbal plants mentioned above: ^{4,5,8,21,25,32,}

| Name | Biological source | Phyto-constituents | Uses |
|-----------|--|---|---|
| Aloe vera | Aloe is dried juice from the bases of th leaves collected by incision, like Aloe perryi, or Aloe barbadensis, from family Liliaceae. | Anthraquinone glycoside derivatives, derivatives, flavonoid phytosterols, naphthalene analogs, lipids, and vitamins | Wound healing, antiinflammatory, anticancer, antidiabetic, antiulcer, antihyperlipidemic activity, antioxidant, immunomodulatory action |

| | | | |
|-----------------|--|--|--|
| Giloy | Herbaceous vine of the <i>Tinospora cordifolia</i> , belongs to family Menispermaceae | Alkaloids, diterpenoid lactones, glycosides, steroids, sesquiterpenoid, phenolics, aliphatic compounds. | Immunomodulatory activity, antioxidant, antidiabetic, Jaundice, rheumatism, urinary disorder, skin diseases, diabetes, inflammation, radioprotective properties, |
| Shatavari | Shatavari is derived from dried roots and tuberous roots of <i>Asparagus racemosus</i> , from family Liliaceae | Steroidal saponins, isoflavones, asparagine, racemosol, polysaccharides | Immunomodulatory, antidiabetic, antioxidant, anticancer, hepatic, and neuroprotective effect, antimicrobial, antiurolithiatic, etc |
| Liquorice | Liquorice consists of subterranean and unpeeled stolons, roots and glabra, belonging to Family Leguminosae. | Glycyrrhizine, liquiritic acid, glycyrrhetol, liquiritin, isoliquiritin, asparagin, traces of tannin | Antibacterial, antiinflammatory, antioxidant, antiviral, hepatoprotective, and immunomodulatory activities |
| Chirata | Consist of entire herb of chirata, <i>Swertia chirata</i> , belonging to family Gentianaceae. | Sawertiamarine, xanthones, mangiferin, amarogenitine, balanophenin, oleanolic acid, | Use for fever, constipation, immunomodulatory agent, upset stomach, loss of appetite, intestinal worms, skin diseases, and cancer |
| Black Pepper | Fruits of <i>Piper nigrum</i> , also known as black pepper the Piperaceae family. | Piperidine, N-transferuloytyramine, Methylene dioxy cinnamic, Piperettine, Ascorbic acid, Trichostachine, Citronellol, Serine, etc | Immunomodulatory, antioxidant, antiplatelets, antihypertensive, antiasthmatic, antipyretic, analgesic, anticancer, antiinflammatory, antidiarrheal, antispasmodic, etc |
| Harsingar | <i>Nyctanthes arbor-tristis</i> , also known as the Night-flowering jasmine or family Oleaceae | Palmitic, oleic and myristic acids. leaves of the plant contain benzoic acid, fructose, glucose, amorphous resin, ascorbic acid, methyl flavanol glycosides. | The leaves of the Harsingar plant have been used to treat a different kind of fevers, cough, arthritis, worm infestation, |
| Amalki | <i>Phyllanthus Emblica</i> , also known as emblica tree, or amla is a deciduous tree of the family phyllanthaceae. | Amalaki bark contains Leucodelphinidin, Procynidine, tannin, 3-O gallated procynidine, ellagic acid. | Improve immunity, antibacterial, antioxidant, antimicrobial, the drug used as ingredient in various compounds |
| Kutki | It consists of dried rhizome of <i>Picrorhiza kurroa</i> exbenth. Family - Scrophulariaceae | It contains kutkin, bitter glycosides which contain two C9 iridoid glycosides, picrosides, kutkosides | Used to treat disorder of liver and upper respiratory tract, reduce fever and to treat dyspepsia. |
| Drumstick plant | <i>Moringa oleifera</i> is a drought resistant tree of the family-moringaceae | It contains Alkaloid, saponins, tannins, steroids, phenolic acid, flavonoids | Immunity booster, anti-inflammatory, antimicrobial, antioxidant, antitumor, antidiabetic |
| Almond | Almonds are edible nuts of <i>Prunus dulcis</i> family Rosaceae | Contain lipids around 50% proteins 25% and carbohydrate 20% it is bioactive compound | Boost immunity, reduce inflammation, heart disease, reduce blood pressure |

| | | | |
|------------|---|--|--|
| Punarnava | Boerhavia diffusa is a species of flowering plant in the four O clock family. | Punarnavin alkaloid, phytasterols, ligands, Punarnavaside, Alanine, Boerhavic acid. | Immunomodulatory, Adptogenic, Chemopreventive, antiviral activity, bronchial asthma. |
| Coneflower | Echinacea is a genus of herbaceous flowering plant in the daisy family. | It contains alkamide, ketoalkene, caffeic acid, polysaccharides, glycoproteins. | Antioxidant, common cold, cough, bronchitis, upper respiratory tract infection, inflammatory condition. |
| Broccoli | Broccoli is an edible green plant in the cabbage family | Glucosinolates, dithiones, indoles, glucoraphanin, S-methycysteine, sulfoxide, indole carbinol | Boost immunity, Antioxidant, reduce inflammation, protect against cancer, support Healthy immune system. |

CONCLUSION:

The herbs which are mentioned in this review are used as immunomodulators and help to fight against the virus. Many herbal medicinal plants show immunomodulatory, antiviral, anti-inflammatory and antioxidant properties, it may be considered for the treatment of COVID-19. Additionally, these herbs possess anti-inflammatory, antiviral, antioxidant, antimicrobial, anticarcinogenic, antiulcer and antinephrotoxicity activities in different studies. This herbal medicinal therapy can be used as primary and adjuvant therapy for the prevention and cure from the deadly coronavirus. Due to COVID-19 immunomodulatory herbs use for immunity boosting as well as build up the patient immunity.

ABBREVIATIONS

ACE-2 Angiotensin converting enzyme 2
ADCC- Antibody Dependent Cellular Cytotoxicity
COV-2 Corona virus 2
COVID-19- Corona Virus Disease 19
CCL2- Monocyte chemoattractant protein 1
CD8- Cluster of differentiation 8
CD4- Cluster of differentiation
DNA- Deoxyribonucleic acid
DPT- Diphtheria pertussis tetanus vaccine
HCoV- Human corona virus
IgG - Immuno globulin G
INF- Intermediate range nuclear forces
IL - Interleukin
LPS- Lipopolysaccharides
MMI- Macrophage migration index
PAMS- Pathogen associated molecular patterns
SARS- Severe acute respiratory syndrome
TNF- Tumor necrosis factor
WBC- White blood cell

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