

A mini review on Immunity boosters used in COVID-19

Dr. Mrinalini Damle^{1*}, Akshay Chandan², Dnyaneshwar Rathod³, Omkar Shinde⁴

^{1*}Head of Department, Quality Assurance, AISSMS College of Pharmacy, Pune.

^{2, 3, 4}Department of Quality Assurance, AISSMS College of Pharmacy, Pune.

AISSMS College of Pharmacy, Kennedy Road, Near R.T.O, Pune, Maharashtra 411001, India.

Abstract

This review emphasizes on use of herbs, minerals, plant-based food which can be helpful for enhancing the immunity in all age groups against COVID-19 infection. Balanced healthy diet can help in maintaining or boosting immunity. It is important for prevention and management of viral infections. Plant based foods increased the intestinal good consider as beneficial bacteria like Probiotics, Bifidobacteria which can helpful to improve gut health and immunity. Vitamins A, D, C are important to boost immune response. Some minerals like Zinc, selenium show potential benefits in viral respiratory infections. Different Nutraceuticals, probiotics, medicinal plants may also have some role in enhancing immune functions. In this review, we have summarized the benefits of Vitamins, Nutraceuticals, medicinal plants, and probiotics in viral infections. These can be helpful to enhance the immunity of the people in COVID-19.

Keywords- Coronavirus infection (COVID-19), immunity boosters, vitamins, minerals, plant-based foods.

Introduction-

COVID-19 attacks the people having low immune power in all age groups. The immune system is built on beneficial good bacteria that are present in the gut which protect human body from viral infections and diseases. When immune power is weak or low, it's an open invitation for infectious disease by Corona virus, pneumonia and other diseases like Heart diseases, diabetes. Our immune system is made up of complex collection of cell structure, different processes, chemicals that protect the body from foreign pathogens, viruses, bacteria and toxins. So, "Keeping our immune system healthy" is important key to prevent infections and disease.

Plant-based foods increase intestinal good bacteria which helps to boost our immune systems. According to Centre for Disease control and prevention, hydration plays vital role in monitoring body temperature. So, drinking of plenty of water is essential for a lot of reason. Staying hydrated enables minerals to circulate to all the parts of the body thus helps to maintain all body functions and ultimately it leads to decreased body infection to some extent. Making healthy lifestyle by consuming healthy nutritious food with enough sleep and exercise are the important ways to boost immune system. In addition, research shows that consumption of certain Vitamins, Minerals, Herbs, Nutraceuticals and other substances can improve immune power and ultimately protect against infection and illness¹.

Supplementing immunity-

A good strategy is to increase nutrients that may be lacking in diet. For normal levels, a daily supplement of vitamin D up to 600 to 800 IU is suggested. The absorption of vitamin D can increase if taken with fatty foods. Addition of some healthy sprinkle herbs (dried herbs) like ginger, garlic, turmeric, rosemary, will also introduce anti-inflammatory compounds that can be sprinkle (spread) and helpful to defend respiratory viruses².

Improved Diet-

The food plays an important role in overall health and immunity. Food should include carbohydrate diet, regular consumption of vegetables and fruits that are rich in beta carotene, ascorbic acid and other essential vitamins that can build up the immunity against pathogenic infections. Diet containing omega 3 and 6 fatty acids are also essential, several herbs like basil leaves, black cumin, certain seeds and nuts are good source of protein and vitamin E.

Probiotics like yogurt, fermented foods increase the good gut bacteria which increases nutrient absorption and it leads to increased immunity power².

Zinc and Magnesium-

Zinc has many important roles in our body. It is responsible for the activity of more than 300 different enzymes in our body. It has vital role in immune system functioning and cell mediated immunity such as neutrophils and killer cells. It can often be used to help battle with common cold. Sources of zinc include meat, eggs, whole grains, legumes, shellfish, tofu, oysters, hemp seeds, oatmeal, low-fat yoghurt, beef, shiitake mushroom (an edible mushroom) etc. Taking zinc for long time is safe for healthy adults. Daily dose is up to 40mg of elemental zinc.

An important mineral for our immune system is Magnesium. Magnesium keeps the immune system strong, helps to strengthen muscles and bones, and support many body functions (cardiac functions to brain functions). It helps hemoglobin in our blood which is responsible for delivering oxygen from lungs to entire body. Maintenance of blood oxygen level is important critical parameter in COVID-19 because it attacks on respiratory system. Sources of magnesium include Green leafy vegetables such as spinach, legumes, nuts, seeds and whole grains, avocado, dark chocolate, quinoa, oat meal etc¹.

Selenium-

Selenium plays an important role in the health of our immune system. This antioxidant helps lower oxidative stress in our body, which reduces inflammation and enhances immunity. Studies have demonstrated that increased blood levels of selenium are associated with enhanced immune response. It appears that adequate levels of selenium help to protect the host against viral infection. Sources of selenium include Brazil nuts, seafood's, organ meats, cereals, lettuce etc^{3,4}.

Copper-

Copper act antiviral agent and help to develop and differentiate immune cell. Experimental studies have proven that the long term intake of copper increases the ceruloplasmic activity. Benzylamine oxidase, oxidative damage and level of superoxide dismutase is higher when intake of copper is 7.8mg/day instead 1.6mg/day and has improved antioxidant activity. Low level of copper alter functioning of neutrophils and monophils that is the reason of low immune system and susceptibility toward sickness and infection⁵. Sources of copper are legumes, mushrooms, chocolate, liver, nuts and seeds etc^{6,7}.

Iron-

Iron is essential for strengthening and vigor and also plays role in synthesis of DNA and enzymes. Deficiency of Iron causes decrease in T-lymphocytes which is generally responsible for direct killing of infected host cell⁵. Sources of iron are dried beans, dried fruits, eggs (especially egg yolks), iron-fortified cereals, and liver. Others are lean red meat (especially beef), oysters, poultry, dark red meat, salmon, tuna, whole grains, etc⁸.

Vitamin D-

Vitamin D plays an important role in health and functioning of immune system. It is a fat-soluble nutrient. It can modulate the innate and adaptive immune responses. It is involved in production of protein that selectively kills infectious agent, viruses. Vitamin D has numerous effects on cells within immune system. It inhibits B cell (B lymphocytes- white blood cells) proliferation and blocks B cell differentiation and immunoglobulin secretion. Vitamin D additionally suppresses T cell proliferation and results in shift from a type of cytokine Th1 to a Th2 phenotype. Furthermore, it affects T cell maturation with a skewing away from the inflammatory Th17 phenotype and facilitates the induction of T regulatory cells. These effects result in increased production of anti-inflammatory cytokines such as IL-10 and gives anti-inflammatory action. Vitamin D also has effects on monocytes and dendritic cells (DCs). It inhibits monocyte production of inflammatory cytokines such as IL-1, IL-6, IL-8, IL-12 and TNF- α . It also inhibits dendritic cells differentiation and maturation. It is important for autoimmunity and promotes immune response. Vitamin D alters the action of T2 killer lymphocytes which can be helpful in reducing spread of bacteria and viruses.

Most of the peoples have deficiency of vitamin D which affects their immune function. Low levels of Vitamin D can lead to increased risk of respiratory infections, such as allergic asthma. Some research suggest that Vitamin D supplement can reduce the risk of respiratory infections and increase immune response. Vitamin D also increases production of anti-oxidation related genes (glutathione reductase) & increase in production of glutathione may leads to improve immune response.

The main source of Vitamin D for the body is sunlight. Body synthesizes vitamin D from direct sunlight on the skin when outdoors. Other food sources include oily fish- such as salmon, sardines, herring and mackerel, red meat, liver, egg yolks, fortified foods- such as some fat spreads and breakfast cereals, raw milk, mushrooms. Babies up to the age of 1 year need 8.5 to 10 micrograms of Vitamin D a day, Children from age of 1 year and adults need 10 micrograms of vitamin D a day⁷.

Vitamin C and E-

Vitamin C is important for improving immunity in children, adults, and elderly people. Vitamin C has beneficial effects on cellular functions of both innate and adaptive immune system. Vitamin C is a potent antioxidant that protects the body against endogenous and exogenous oxidative challenges, its action as cofactor for many biosynthetic and gene-regulatory enzymes plays key role in immune-modulating effects. Vitamin C stimulates neutrophil migration to site of infection, enhances phagocytosis and oxidant generation, and microbial killing. At the same time, it protects host tissue from excessive damage by enhancing neutrophil apoptosis and clearance by macrophages and decrease neutrophil necrosis. Thus, Vitamin C is necessary for the immune systems.

Vitamin C appears to be able to both prevent and treat respiratory and systemic infections by enhancing various immune cell functions. It can be treated by taking vitamin C supplements. (We can consume 200 mg) either from food or tablet. The upper limit for Vitamin C is 2000mg, and daily dose range is 250-1000mg¹. From Animal study it observed that Vitamin C also plays an important role in reduction of common cold. It reduces common cold 48% when dose given is 1000-8000mg/day⁹. Sources of vitamin C are citrus fruit, kiwi, mango, and vegetables such as broccoli, tomatoes, and peppers¹⁰.

Vitamin E is a fat-soluble antioxidant that can protect the polyunsaturated fatty acids (PUFAs) in the membrane from oxidation, it regulates production of reactive oxygen species (ROS) and reactive nitrogen species (RNS) and modulate signal transduction. And it results in immunomodulatory effects of Vitamin E. It considered as first line defense against lipid peroxidation and it is important for normal function of immune cells. Vitamin E modulates T cell function through directly impacting T cell membrane integrity, signal transduction, and cell division and also indirectly by affecting inflammatory mediators generated from other immune cells. The main constituents in Vitamin E is tocopherol which ultimately leads to improved immune systems¹.

Sources of vitamin E are Wheat germ oil, Sunflower seeds, Almonds, Sunflower oil, Safflower oil, Hazelnuts, Peanut butter, Peanuts, Corn oil, Spinach, Broccoli, Soybean oil, Kiwifruit, Mango, Tomato etc^{11,12}.

Vitamin B complex-

B vitamins including vitamin B6- pyridoxine has direct impact on immune function and gene transcription and expression, vitamin B6 helps the body to make new red blood cells which carry oxygen throughout the body. It also helps keep immune system strong. And Vitamin B12- cobalamin also has a role in immune system².

Sources for Thiamine (B1) are Cereals, brown rice, green vegetables, potatoes, pasta, liver, pork, eggs. For Riboflavin (B2) sources are Dairy products, leafy vegetables, legumes, liver, kidneys, yeast, and mushrooms. Niacin (B3) is available in meat, fish, wholegrain cereal, legumes, mushrooms, nuts. Pantothenic acid (B4) is obtained from meat, whole grain cereals, and broccoli. Pyridoxol (B6) can be from meat, fish, legumes, nuts, bananas, potatoes. Biotin (B7) is available in eggs, liver, pork, leafy vegetables. Folic Acid (B8) can be sourced from Leafy vegetables, legumes, citrus fruits and Cobalamin (B12) from meat, fish and other animal products etc¹³.

Vitamin A-

The human body converts beta carotene into Vitamin A (retinol); beta carotene is a precursor of Vitamin A. Vitamin A is micronutrient that is crucial for maintaining vision, promoting growth and development, and protecting epithelium and mucus integrity in the body. Vit A is also known as anti-inflammation vitamin because of its critical role in enhancing immune function. Vit A is involved in the development of the immune system and plays regulatory role in cellular immune response and humoral immune-macromolecules mediated (found in extra cellular fluid) responses. Vitamin A use in the treatment of several infectious disease¹⁴.

Sources of vitamin A include Liver (beef, pork, chicken, turkey, fish), cod liver oil, Broccoli leaf, Sweet potato, Butter Kale, Spinach, Pumpkin, Collard greens, Cheddar cheese, Egg, Apricot, Papaya, Mango, Pea, Broccoli, Milk etc¹⁵.

Medicinal plants-**Ginseng-**

Ginseng is the dried root of species panax ginseng having the synonym ninjin, panax, pannag. It belongs to family Araliaceae. Main chemical constituents present in ginseng are terpene glycosides, or saponins, commonly known as ginsenosides. They possess the immune-modulating activity by acting on hypothalamic-pituitary-adrenal (HPA) axis. Experimental study reveal that when exposed to ginsenoside the enhancement of natural killer cell activity and enhance cell phagocytosis¹⁶.

Ashwagandha-

Ashwagandha is the root and stem of species of withania somnifera having synonym Ashwagandha, winter cherry. Withania belongs to family solanaceae. Main chemical constituents present in ashwagandha are alkaloids and steroidal lactones. Ashwagandha improves body's defense by improving cell mediated immunity. It also has antioxidant properties¹⁶.

Amla-

Amla is the fruit of the species of Emblica Officinalis having synonym amla. Indian gooseberry belong to family phyllanthaceae. Main chemical constituents of amla includes polyphenols like gallic acid, ellagic acid, different tannins, minerals, vitamins, amino acids, fixed oils, and flavonoids like rutin and quercetin etc. Amla has the higher concentration of the Vitamin C and the polyphenols which act against the developing cancer cell. Amla detoxify the entire organ and improves the immunity¹⁷.

Giloy-

Giloy is the herb of the species Tinospora cordifolia having synonym Guduchi belong to family Menispermaceae. Fresh juice of giloy enhances the immunity. It helps to recover from cold, cough, tonsils it also have immunomodulation, anticancer, hepatoprotective, and hypoglycemic activity¹⁷.

Neem-

Neem is the medicinal plant from the species Azadiracta Indica having synonym Ravipriya, Vembaka, Nimba, Arishta and belong to family Meliaceae. Chemical constituents present in Neem are Nimbidin, Sodium nimbidate, Nimbin, Nimbolite, Gedunin, Azadiractin, Gallic acid¹⁸. Neem has the properties like anti-bacterial, anti-fungal, blood purifying agent and immunity booster¹⁷.

Mushrooms-

Medicinal mushrooms have been shown to have immune-modulating effects, they help to keep immune system in balance. Species includes Lion's mane, Shiitake, Yellow morel, Lingzhi, Turkey tail, Caterpillar fungus, Maitake, Rishi etc. some medicinal mushrooms have been found to have antitumor and immune-stimulant activity. And some are good sources of Vitamin B, fiber and antioxidant in the diet².

Garlic-

Garlic (allium sativum) appears to enhance the functioning of the immune systems by stimulating certain cell types such as macrophages, lymphocytes, natural killer (NK) cells, dendritic cells, and eosinophils, by mechanism including modulation of cytokine secretion, macrophage activation^{2,19}.

Turmeric-

Curcumin is main active compound in Turmeric (Curcuma longa). Curcumin helps in boosting up the immunity and helps to fight against viral replication. Curcumin is a potent immunomodulatory agent & also reduces inflammation. It acts as inhibitor of viruses, including dengue virus, hepatitis B, and Zika virus. Other biological action includes antitumor, anti-inflammatory, and antibacterial activities^{9,16}. Golden Milk- Half tea spoon Haldi (turmeric) powder in 150 ml hot milk - once or twice a day as per Ministry of AYUSH²².

Liquorice-

It is commonly known as Mulethi, Laung (Clove), the enzymes present in the herb are known to boost immunity naturally. It also have anti-inflammatory properties that may help to reduce the effects of free radicals causing pain and inflammation in body. The constituents present in the liquorice inhibit growth and cytopathology of numerous RNA and DNA viruses^{2,15}.

Echinacea-

Echinacea is genus, or group, of herbaceous flowering plant in the daisy family. Genus echinacea has ten species, which are commonly called coneflowers. Extracts of echinacea do seem to have an effect of the immune system. Research shows that it increases number of white blood cells, which fight against infection.

Elderberry-

Elderberries are a low-calorie food packed with Vitamin C, dietary fiber and antioxidants in the form phenolic acids, flavonoids and anthocyanins. The flowers are particularly rich in flavonoids. The berries and flowers also contain vitamins that may boost our immune systems. They could help tame inflammation, lessen stress, and help to protect heart. It can also be useful to prevent & ease cold and flu symptoms^{2,20}.

Lifestyle-

Yoga and exercise are useful for improving immune system. Exercise can help to raise the levels of white blood cells and antioxidants that can fight back against infections. Yoga is a way to strengthen vital organs and ultimately improves immunity. Pranayama includes different types of yoga which are related to respiration such as Bhastrika (forceful fast breathing), Anuloma- viloma (sequential breathing alternate closing of each nostrils), Ujjayi (ocean breath), Sitali (cooling breath) all these Pranayama are helpful in cleaning excessive mucus accumulated in bronchial alveoli (it means it is tool that increase total lung capacity). So, it can improve immune system²¹.

Antioxidants-

Glutathione is a powerful antioxidant. Glutathione protects host immune cells through its antioxidant mechanism and it provides optimal functioning of lymphocytes and other cells of the immune system ultimately enhances immunity. Source of glutathione include alliums, avocado, citrus fruits, asparagus, cruciferous veggies, spinach, Brazil nuts, cucumber, sulfur reach foods etc. Glutathione can take orally in dose of 500mg or by IV.

Quercetin is one of the important bioflavonoids present more than twenty plants. It can act as both “immune booster” and an “immune modulator”. It can calm down overactive parts of immune system. It can help to reduce detrimental aspects of the NLRP3 inflammasome, possibly preventing the risk of cytokine storm. It may inhibit viral entry into cells, possibly supporting prevention. It can also facilitate entry of zinc into cells promoting anti-viral activity.

Source of quercetin include onions, broccoli, berries, cherries, citrus fruits, radish leaves, dill, radicchio, capers, black and green tea etc¹.

Ayurvedic Immunity Promoting Measures (as per Ministry of AYUSH)-

1. Take Chyavanprash 10gm (1tsf) in the morning. Diabetics should take sugar free Chyavanprash. 2. Drink herbal tea / decoction (Kadha) made from Tulsi (Basil), Dalchini (Cinnamon), Kalimirch (Black pepper), Shunthi (Dry Ginger) and Munakka (Raisin) - once or twice a day. Add jaggery (natural sugar) and / or fresh lemon juice to your taste, if needed²².

Conclusion-

People those who have low immunity power are more prone to get COVID19 infection. Many supplements and plant-based foods and vegetables have important role in boosting immune response. Vitamins like C, D, A, B complex helps to improve immunity. Fruits like Oranges, Kiwi, papaya, etc. that are rich in Vitamin C have an important role in boosting immune systems. While vegetables like beetroots, spinach, broccoli, cauliflower are rich in Vitamin C that are good for immunity. Medicinal herbs like medicinal mushrooms, elderberry is also important for enhancing immune system. Along with these Yoga, Physical exercise, maintaining healthy lifestyle with balanced diet are the most important ways to keep our immune system healthy and it reduces chances infection and disease. All these supplements can be helpful for improving immunity and not for the treatment for COVID19.

References-

- [1]. Arshad MS, Khan U, Sadiq A, et al., (2020). Coronavirus disease (COVID-19) and immunity booster green foods: A mini review. *Food Sci Nutr.*, pp. 1-6.
- [2]. Dr. Chindarkar PV (2020). Immunity Booster Supplements to Fight against Viral Infection with Prominence on COVID-19: A Review. *Inter. J. Pharma O2*, vol. 2, no.3, pp. 0195-0205.
- [3]. Beck MA. Chapter 19 (2001). Selenium as an antiviral agent. D. L. Hatfield (Ed.). Selenium Kluwer Academic Publishers, pp. 235-246.
- [4]. Kubala J (2019), 7 Science-Based Health Benefits of Selenium. *healthline*, pp. 1-20.
- [5]. Dr. Chiplunkar. SV (2013). PERSPECTIVES Nutrition and Immune Health. Hindustan Unilever Limited, vol. 4, no.1, pp. 6-11.
- [6]. Collins JF, Klevay LM (2011). Copper^{1, 2}. *Adv Nutr*, vol. 2, no. 6, pp. 520-522.
- [7]. Jayawardena R, Sooriyaarachchi P, Chourdakis M, et al., (2020). Enhancing immunity in viral infections, with special emphasis on COVID-19: A review. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*, vol. 14, pp. 367-384.
- [8]. Seriki SA, Adebayo OF, Odetola AO (2017). Iron: From Dietary Sources to Utilization in the Body. *Glob J Nanomed*, vol. 3, no. 3, pp. 85-92.
- [9]. ROSE J (1999). Herbal and Nutritional Support for the Immune System. *CLINICAL NUTRITION INSIGHTS*, vol. 6, no. 2, pp. 4.
- [10]. Lykkesfeldt J, Michels AJ, Frei B (2014). Vitamin C¹. *Adv Nutr*, vol. 5, no. 1, pp. 16–18.
- [11]. Rizvi S, Raza ST, Ahmed F, et al., (2014). The role of vitamin e in human health and some diseases. *Sultan Qaboos Univ Med J*, vol. 14, no. 2, pp. 157-166.
- [12]. Carr AC, Maggini S (2017). Vitamin C and Immune Function. *Nutrients*, vol. 9, no. 11, pp. 1211-1235.
- [13]. Kennedy DO (2016). B Vitamins and the Brain: Mechanisms, Dose and Efficacy—A Review. *Nutrients*, vol. 8, no. 2, pp. 68-97.
- [14]. Huang Z, Liu Y, Guangying Qi, et al., (2018). Role of Vitamin A in the Immune System. *J. Clin. Med*, vol. 7, pp. 258-274.
- [15]. Oruch R, Pryme IF (2012). The biological significance of vitamin A in humans: A review of nutritional aspects and clinical considerations. *ScienceJet*, vol. 1, no. 19, pp. 13.
- [16]. Das S, Bordoloi R, Newar N (2014). A Review on Immune Modulatory Effect of Some Traditional Medicinal Herbs. *Journal of Pharmaceutical, Chemical and Biological Sciences*, vol. 2, no. 1, pp. 33-42.
- [17]. Patil A, Kakde MS (2020). Medicinal plant as a natural immunity booster for COVID19- A review. *Indian J of Integr Med*, vol. 2, no. 2, pp. 24-27.
- [18]. Dubey S and Kashyap P (2014). *Azadirachta indica*: A Plant with Versatile Potential. *RGUHS J Pharm Sci*, vol. 4, no. 2, pp. 39-46.
- [19]. Arreola R, Quintero-Fabián S, López-Roa RI, et al., (2015). Immunomodulation and Anti- Inflammatory Effects of Garlic Compounds. *Journal of Immunology Research*, pp. 13.
- [20]. Mirzaie A, Halaji M, Dehkordi FS, et al., (2020). A narrative literature review on traditional medicine options for treatment of corona virus disease 2019 (COVID-19). *Complementary Therapies in Clinical Practice*, vol. 40, pp. 101214-101222.
- [21]. Rajput DS (2020). Evolution, Ayurveda, immunity, and preventive aspects for emerging infectious diseases such as COVID-19. *Int. J. Res. Pharm. Sci*, vol. 11(SPL), no. 1, pp. 86-94.
- [22]. Krishnakumar PR et al., (2020). Ayurveda's immunity boosting measures for self care during COVID 19 crisis, Ministry of AYUSH, pp. 1-4.