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Review Article

Immune boosting role of vitamins in prevention of COVID-19 infection

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Abstract

In current pandemic of COVID-19, no effective preventive and curative medicine is available till date. Wearing masks, maintaining social distance and washing the hands etc are advised around the globe as a preventive measure. A healthy immune system is one of the most important weapons to fight against COVID-19. To maintain it, the body needs sufficient vitamins and other nutrients. It is vital to ensure adequate intake of vitamins and micronutrients to boost overall immune functions and prevent such life-threatening infections. Vitamins C, D and E are the essential vitamins with immunomodulatory properties to fight against COVID-19. In this review, the importance of supplementation with such vitamins is reviewed.

Keywords: COVID-19; Vitamin C; Vitamin D; Vitamin E; Immunity; Nutrition

1 Introduction

Currently, there are no approved treatments for COVID-19. However, various prevention strategies such as public hygiene, social distancing, public awareness and wearing facial masks and gloves are the recommended approaches to reduce COVID-19 infection. Recent evidence has highlighted that nutritional supplementation could play a supportive role in COVID-19 patients and boost the immune power [1].

Vitamin D is a fat-soluble nutrient essential to the health and functioning of immune system. This vitamin enhances the pathogen-fighting effects of monocytes and macrophages - white blood cells that are important parts of your immune defense - and decreases inflammation, which helps promote immune response [2, 3]. Vitamin C is perhaps the most popular supplement taken to protect against infection due to its important role in immune health. This vitamin supports the function of various immune cells and enhances their ability to protect against infection [4]. Vitamin C also functions as a powerful antioxidant, protecting against damage induced by oxidative stress, which occurs with the accumulation of reactive molecules known as free radicals. Vitamin E is vital for maintaining the overall health of elderly people, including their immunity. Vitamin E is a powerful antioxidant that can protect you from various infections, bacteria, and viruses. Vitamin E functions primarily as an un-specific, chain-breaking antioxidant that bans the spread of lipid peroxidation. Vitamin E performs a significant part in preserving immune responses, with such a small deficiency effecting immunity, or supplements with rates higher than prescribed, improving elderly people's humoral and cell-mediated immunity [5].

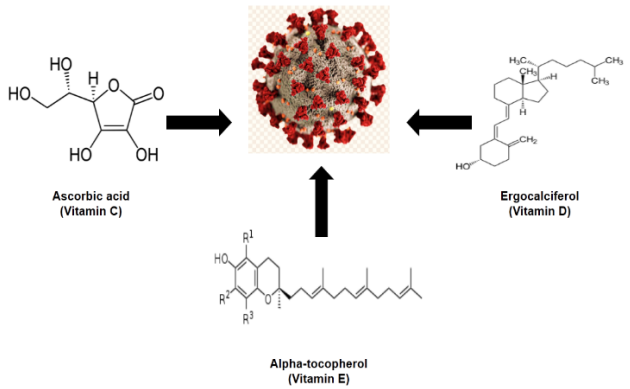

Figure 1. Vitamin C, D and E fight against COVID19

Dietary supplements containing vitamins likes C, D and E are a safe, low-cost, and effective way of helping the immune system fight off COVID-19 and other acute respiratory tract diseases (ARTD) according to published sources. Nutrients are well-known for their antioxidant properties and immune-modulatory effects. Deficiencies in these nutrients can result in immune dysfunction, and increase susceptibility to pathological infection. In fact, dietary insufficiency of vitamins and minerals has been observed in high-risk groups of COVID-19 patients, such as the elderly, increasing the morbidity and risk of mortality [6]. In this review the role of vitamins C, D and E in immunity to fight COVID19 infection are discussed.

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2 Nutritional deficiencies and diseases

Undoubtedly, nutritional deficiency can impair immune functions, which are meant to protect against disease or potentially damaging foreign bodies. Accordingly, maintaining a healthy immune system is critical at all times specially during the COVID-19 outbreak. Multiple factors weaken immunity, particularly poor diet and malnutrition, stress, lack of sleep, excess alcohol consumption, smoking and similar bad habits [7]. Nonetheless, vitamins can play a key role in optimising immune functions by boosting the body's defence mechanism and resistance to infection.

Table 1. Requirement of Vitamin C, D and E

Sl. No.	Vitamin	Male	Female	Average Daily Intake
1.	Vitamin C	90-100 mg	80-85 mg	75-100 mg
2.	Vitamin D	15 mcg (600 IU)	15 mcg (600 IU)	10–20 mcg (400–800 IU)
3.	Vitamin E	12-15 mg	10-12 mg	10-15 mg

3 The role of nutritional supplementation in COVID-19

Adequate levels of vitamins C, D and E are crucial during COVID-19 to reduce symptom burden and lessen the duration of respiratory infection. To support immune function during COVID-19 disease higher dietary intakes of vitamins D, C and E could be beneficial [5]. Research also supports a role for minerals such as zinc as they have antiviral effects and may improve immune responses and suppress viral replication. Therefore, the consumption of adequate amounts of vitamins through diet is essential to ensure the proper functioning of the immune system [8]. Fruits, vegetables, meat, fish, poultry and dairy products are good source of these vitamins.

Figure 2. Immune booster vitamins

4 Boosting the immune system with vitamin supplements

Vitamins are essential dietary constituents, which the body requires to function normally. Our bodies do not produce most vitamins, except vitamin D, which are required in small amounts to maintain good health. Therefore, these must be obtained via the food we eat. Together, vitamins and minerals are termed micronutrients because their requirement is minuscule unlike those of carbohydrates, proteins and fats, which are referred to as macronutrients [9].

Vitamin C, vitamin D, zinc, and an omega-3 fatty acid found in fish, docosahexaenoic acid, also known as DHA, are critical for immune function. The roles that vitamins C and D play in immunity are particularly well known. Vitamin C has roles in several aspects of immunity, including the growth and function of immune cells and antibody production. Vitamin D receptors on immune cells also affect their function. This means that vitamin D profoundly influences your response to infections.

Its deficiency is a major problem in populations subsisting on cereals with limited intake of green leafy vegetables and fruits. Vitamin A deficiency is widespread in India. Its supplementation in preschool children decreases mortality and morbidity from some forms of diarrhoea, measles and malaria by improving immunity [10, 11].

5 Vitamin C

Vitamin C, which plays multiple roles – synthesizing collagen, absorbing iron, scavenging free radicals and defending against infections and inflammation [12, 13]. Fruits (especially citrus), cabbage-type and green leafy vegetables, lettuce, tomatoes, potatoes, and liver of poultry birds comprise rich sources. Its deficiency can cause scurvy with symptoms such as bleeding gums, bruised skin, fatigue, appetite and weight loss as well as lower resistance to infections [14, 15]. A potent antioxidant, it contributes to immune defence by supporting various cellular functions of both the innate and adaptive immune system.

Table 2. List of foods high in vitamin C

Sl No.	Food Sources	Vitamin C mg/100g
1.	Rice hips	1000
2.	Guava	200
3.	Black currant	155-215
4.	Broccoli	90-150
5.	Kiwifruit	98
6.	Redcurrant	58-81
7.	Spinach	50-90
8.	Lychee	72
9.	Papaya	62
10.	Strawberry	57
11.	Orange	53
12.	Cabbage	30-60

6 Vitamin D

Vitamin D, synthesized by the body with the help of sunlight while some foods are its natural sources. These include oily fish, egg yolk, veal and mushrooms. Its deficiency is universal. Even in tropical countries such as India with ample sunshine, it remains deficient [16]. Epidemiological studies show vitamin D deficiency is present in most parts of India and across age, gender and socio-economic groups. The best-known function is in calcium absorption and bone

health while its role in supporting immunity is complex. Nonetheless, it improves innate and adaptive immunity while enhancing the pathogen-fighting ability of white blood cells [17].

Table 3. Vitamin D enriched food

Sl. No.	Food Sources	Vitamin D IU/100g
1.	Shiitake dried	1660
2.	Herring	680
3.	Swordfish	660
4.	Salmon	521
5.	Tuna fish	180
6.	Pork Sausage	52
7.	Beef liver	49
8.	Sardines	46
9.	Swiss Cheese	44
10.	Milk	40
11.	Egg	37
12.	Parmesan	28
13.	Mushrooms	18
14.	Cheddar cheese	12

7 Clinical Study

New study found 80% of COVID-19 patients were vitamin D deficient. Study upon 216 people with COVID-19 found that 80 percent didn't have adequate levels of vitamin D in their blood. The study also found that people who had both COVID-19 and lower vitamin D levels also had a higher number of inflammatory markers such as ferritin and D-dimer, which have been linked to poor COVID-19 outcomes. A different study found that COVID-19 patients who had adequate vitamin D levels had a 51.5 percent lower risk of dying from the disease and a significant reduced risk for complications. Medical experts theorize that maintaining adequate vitamin D levels may help lower risk or aid recovery from severe COVID-19 for some people, though more testing is needed. Vitamin D treatment should be recommended in COVID-19 patients with low levels of vitamin D circulating in the blood since this approach might have beneficial effects in both the musculoskeletal and the immune system [18].

8 Vitamin E

Vitamin E, naturally available as a group of eight fat-soluble compounds. The liver converts these into alpha-tocopherol – the chemical nomenclature for vitamin E. Nuts, seeds, and vegetable oils are among the best sources of alpha-tocopherol. Green leafy vegetables are also rich in vitamin E. It is a potent antioxidant and can modulate immune functions. Although its deficiency is rare, supplementation significantly enhances immune functions, especially in the elderly [19].

Table 4. Vitamin E enriched food

Sl. No.	Food Sources	Vitamin E mg/100g
1.	Sunflower Oil	42.3
2.	Safflower Oil	34.1
3.	Almond	26.2
4.	Wheat germ	16.2
5.	Olive oil	15.8
6.	Corn oil	14.3
7.	Brazil nut	5.7
8.	Dandelion greens	3.4
9.	Coriander leaves	2.5
10.	Quinoa	2.4
11.	Butte	2.4
12.	Collards	2.3
13.	Radicchio	2.3
14.	Avocado	2.1
15.	Spinach	2.0

9 Immunomodulatory role of vitamin C

Vitamin C acts as an antioxidant that can scavenge reactive oxygen species (ROS), thereby, protecting biomolecules such as proteins, lipids and nucleotides from oxidative damage and dysfunction. Vitamin C accumulates in leukocytes, in concentrations of 50-100 fold higher than in the plasma. During infection, vitamin C that is present in leukocytes is rapidly utilized. Disturbance of the balance between antioxidant defenses and oxidant generation can alter multiple signaling pathways involving proinflammatory transcription factors, such as nuclear factor κB (NF-κB). Increasing levels of oxidants lead to activation of NF-κB, triggering a signalling cascade, with the end result of further production of oxidative species and inflammatory mediators. NF-κB is involved in inflammatory responses, the pathogenesis of certain diseases and viral infection. Inhibition of NF-κB can be a therapeutic mode against viral infections [20]. Vitamin C acts as an antioxidant that can scavenge reactive oxygen species (ROS), thereby, protecting biomolecules such as proteins, lipids and nucleotides from oxidative damage and dysfunction. Vitamin C accumulates in leukocytes, in concentrations of 50-100 fold higher than in the plasma. During infection, vitamin C that is present in leukocytes is rapidly utilized. Disturbance of the balance between antioxidant defenses and oxidant generation can alter multiple signalling pathways involving proinflammatory transcription factors, such as nuclear factor κB (NF-κB). Increasing levels of oxidants lead to activation of NF-κB, triggering a signalling cascade, with the end result of further production of oxidative species and inflammatory mediators. NF-κB is involved in inflammatory responses, the pathogenesis of certain diseases and viral infection. Inhibition of NF-κB can be a therapeutic mode against viral infections [21].

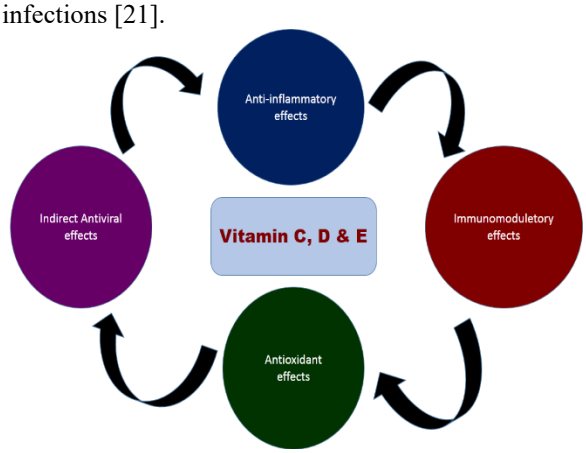

Figure 3. Various effects of Vitamin C, D and E

10 Immunomodulatory role of vitamin D

Vitamin D is a fat-soluble steroid hormone precursor that arises from ultraviolet B (UVB) radiation exposure of 7-dehydrocholesterol (7-DHC) in the epidermis of the skin, where it is transformed into the circulating precursor cholecalciferol. In the liver, cholecalciferol is hydroxylated to form 25-hydroxyvitamin D, which is transformed into the active hormone 1,25-hydroxyvitamin D (1,25(OH)2D) in the kidneys. Vitamin D has roles in a wide range of body systems, including in both innate and adaptive immune responses. Vitamin D enhances innate cellular immunity through stimulation of expression of antimicrobial peptides, such as cathelicidin and defensins. Defensins maintain tight and gap junctions, adherens and enhance the expression of anti-oxidative genes. Viruses such as influenza are known to significantly damage the integrity of epithelial tight junctions increasing the risk of infection and pulmonary oedema. Vitamin D is known to maintain the integrity of these junctions [22, 23]; with low levels of vitamin D receptor expression leading to increased expression of claudin-2 and inflammation.

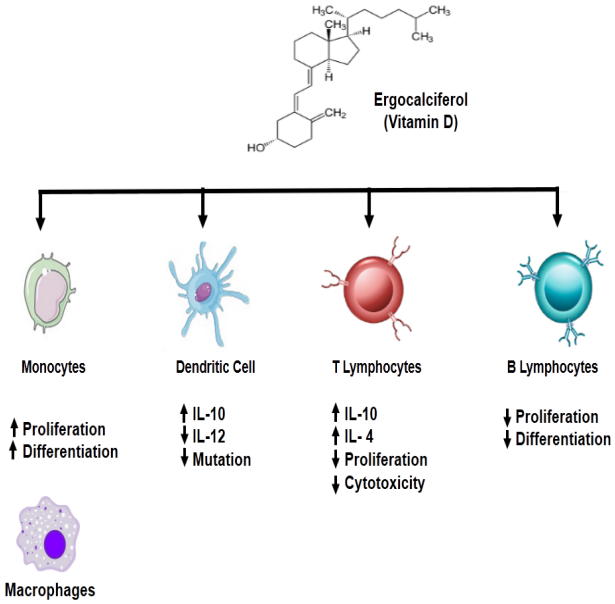

Figure 4. Immunomodulatory role of vitamin D

11 Immunomodulatory role of vitamin E

Vitamin E is a fat-soluble antioxidant that can protect the polyunsaturated fatty acids (PUFAs) in the membrane from oxidation, regulate the production of reactive oxygen species (ROS) and reactive nitrogen species (RNS), and modulate signal transduction. Immunomodulatory effects of vitamin E have been observed in animal and human models under normal and disease conditions. With advances in understanding of the development, function, and regulation of dendritic cells (DCs), macrophages, natural killer (NK) cells, T cells, and B cells, recent studies have focused on vitamin E's effects on specific immune cells. Previous studies summarized the immunological changes observed with vitamin E intervention in animals and humans, and the cell-specific effects of vitamin E with the mechanisms of immunomodulation and effects of vitamin E for immunological diseases along with its role in various other diseases [24, 25].

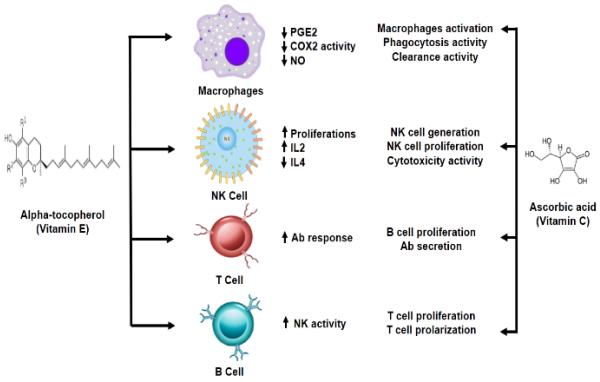

Figure 5. Immunomodulatory role of vitamin E & C

12 Conclusion

Plant-based foods and nutrients play vital role in modulation of immune responses in the human body. Various vitamins like C, D, and E have been reported to provide important effects on improving immunity. Consumption of vegetables and fruits rich in vitamin C and vitamin E in a regular diet is recommended to achieve adequate recommended daily intake of such nutrients. This is particularly useful in improving immunity against COVID-19 pandemic.

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Conflict of interest

The authors have no conflict of interest to declare.

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