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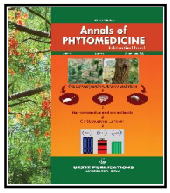

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Foods for protection against COVID-19: An overview

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Abstract

Pandemics have at all times been devastating due to their severity and rate of spread. December 2019, also witnessed a wide spreading havoc around the world whose emergence and outbreak was first reported in China's Wuhan area. Major role in the pandemic was played by a spherical virus with spike protein which was named as corona. Coronavirus disease is a viral respiratory infectious disease caused due to novel strain of SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus-2) which is accompanied by symptoms similar to common cold, Middle East respiratory syndrome and severe acute respiratory syndrome, *etc*. The elderly persons and people suffering from lifestyle diseases are more prone to severe COVID-19 and its respiratory complications. Immune system played a major role particularly in this disease as people having good immunity could tackle the virus more easily that too with high recovery rate. Essential macro and micronutrients like carbohydrates, proteins, minerals, vitamins, bioactive compounds and polyphenols are found important to combat with COVID-19. These nutrients and phytochemicals are found in various foods like vegetables, fruits, dairy products, herbs, spices, *etc*. Different fruits (citrus, papaya, berries, *etc*.) and vegetables (broccoli, tomatoes, spinach, *etc*.) are rich in micronutrients like minerals, vitamin C, vitamin D and flavonoids. Herbs and spices (clove, cinnamon, tulsi, *etc*.) have been widely used for medicinal purpose from ancient time as they contain a diverse amount of bioactive compounds. Similarly, dairy products are potential carriers of phytochemicals and have an important role in regulating homeostasis related to the immune system. All mentioned sources possess positive effect on the human body by alleviating many chronic ailments like cardiovascular disease (CVD), diabetes, cancer, *etc*., and strengthen the immune system. All these compounds work in such a way that they modify the metabolism or mechanism of the pathogens, thus restricting the replication and production process of the virus. This review particularly focuses on the food spectrum that has been used for prevention and protection against COVID-19 disease.

1. Introduction

Ever since the emergence and outbreak of the coronavirus (COVID-19) in Wuhan, province of China, in December 2019, the virus has been wreaking havoc across the globe (Huang *et al*., 2020). The term "coronavirus" has been derived from the Latin word "corona", which means "crown" and it belongs to the family of viruses known as *Coronviridae*. It is further classified into the subfamily *Corona-virinae* and has three genera *Alpha coronavirus*, *Beta coronavirus* and *Gamma coronavirus*. Genetic material of SARS-COV is single stranded RNA with 29003 nucleotides in an open frame. It is basically coiling of phosphate and capsid protein to form nucleocapsid phosphoprotein, covered by envelop which is associated with 4 structural proteins-membrane P, spike P, hemaglutin dimer and envelop P. This virus is zoonotic (Amin and Jha, 2020) which means it gets transmitted between humans and animals. It spreads from person-to-person through respiratory droplets during exhaling, coughing or sneezing by an infected person which turn into pandemic within no time (Indumathi and Sharma, 2022). It causes infection in upper throat, nose, throat windpipe, lungs or sinuses (Almaghaslah *et al*., 2020), however, symptoms vary according to various places, strains, age of person and their eating habit. Besides, lockdown has created a feeling of anxiety and fear which causes unhealthy lifestyles and poor dietary patterns. Among all parameters it was found that healthy diet, nutritional status and interaction of various food components with immunity is responsible for powerful immune system and can directly or indirectly prevent COVID-19 (Thakur *et al*., 2019; Indumathi and Sharma, 2022). Sedantary and modern lifestyle has made us victim of smoking, alcoholism, lifestyle diseases, and fast food. This unhealthy eating habit is main reason of obesity, diabetes, cardiovascular diseases, hypertension due to high amount of salts and sugars. Macro and micronutrients which are abundantly present in fruits and vegetables like vitamins C and D, zinc, selenium, phytochemicals like flavonoids, terpenoids, carotenoids, tannins, alkaloids are found to have antioxidant, antiviral, anticarcinogenic, and anti-inflammatory activity as well as they are known to reduce

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respiratory infections thus, reducing the impact of COVID-19 (Hamid *et al*., 2021). Proteins, fatty acids and oils, are found to have antiviral, antifungal, and antibacterial properties (Mani *et al*., 2020). Present review will focus on different macro and micronutrients, bioactive compounds present in different fruits, vegetables, dairy products, herbs and spices, their health impacts in human body in relation especially with the recent pandemic of COVID-19.

2. Role of diet in immune system

Maintaining a healthy diet is very important to make natural body defence system strong by enhancing the level of immunity, thus helping in combating various diseases like COVID and promote viral clearance. Strength of immune system plays pivotal role in fighting against infection and viral diseases (Indulekha *et al*., 2021).

2.1 Impact of unbalanced diet on immune system

Many factors are responsible for making immune system incapacitate. Out of which, drinking, smoking, age factor, autoimmune diseases and malnutrition are the common ones which are associated with the severity of COVID-19. These factors make host's epithelial cells susceptible for inducing angiotensin I, angiotensin II which furthers binds to angiotensin receptor I and leads to progression in viral infection. This will lead to the production of weakened natural-killer cells, cytokine storm and interlukin- 6,8,10 which results in hyper inflammation and reduction in secretion of antibodies. These above effects possess negative impact on human's respiratory system and ultimately leading to respiratory distress syndrome and multiple-organ failure as shown in Figure 1 (Chaari *et al*., 2020).

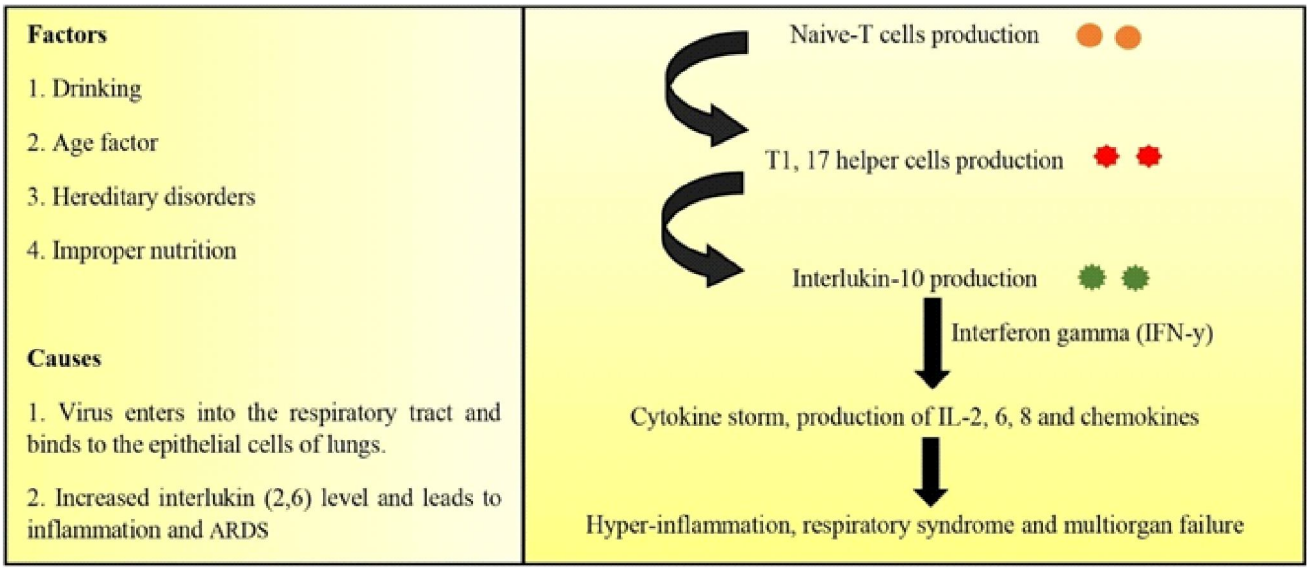

Figure 1: Impact of unbalanced diet on immune system.

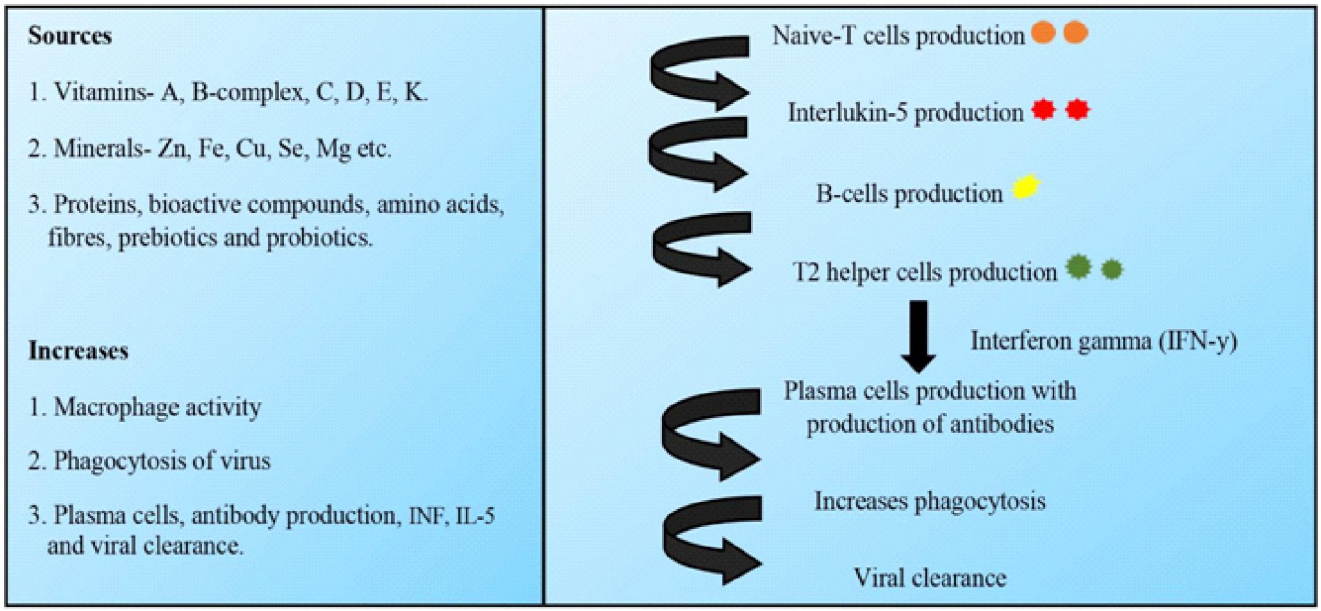

Figure 2: Impact of balanced diet on immune system.

2.2 Impact of balanced diet on immune system

A good immune system has the potential to impede the adverse effect of the disease. Different type of vitamins (vitamin A, B, C, D, E, K), minerals (Zinc, Selenium, Iron, *etc.*), carbohydrates, fibre and other essential macro and micronutrients (Pro and prebiotics, polyphenols) contribute to good diet. These nutrients play immunomodulatory functions along with strong antioxidant properties which are important to combat disease like COVID-19. Diet comprises of good load will increase the production of T and B lymphocytes, natural-killer cells and antibodies. This will help in clearing viral infection and producing cytokine in required amount and making body aware of the foreign invaders (pathogens, viruses, *etc.*) and fight against them as shown in Figure 2 (Chaari *et al.*, 2020).

3. Nutritional interventions for treatment of COVID-19

Evidences have shown a significant relationship between diet, immunity and vulnerability towards diseases (Figure 3). Deficiency of macro and micronutrients dysregulate the immune system and interferes with the phagocytosis of viruses. A healthy diet contains-healthy portions of vitamins, minerals, bioactive compounds, pre and probiotics (influence immune responses through their effects on gut microbiota composition), proteins, carbohydrates, *etc.* Among different nutrients, specific nutrients exert positive effect on host's immune system through modulating cell mediation, differentiation and production of signaling molecules and counteracting the effects of coronavirus in human body (Valdes-Ramos *et al.*, 2010; Wypych *et al.*, 2017; Gombart *et al.*, 2020 and Junaid *et al.*, 2020).

Since we all are aware of the harmful effect of disease related to malnutrition and their prevention by promoting nutritional supplementation (Norman *et al.*, 2008; Schuetz *et al.*, 2019). Different fruits, vegetables, poultry, meat products containing polyphenols and other bioactive compounds have been claimed to have potentially antiviral and immunomodulating properties. Polyphenols have been reported very capacitating in regulating T cells production, pro-inflammatory cytokines production and repressing the production of cytokine storm which cause ARDS (Acquired Respiratory Distress Syndrome) (Yahfoufi *et al.*, 2018; Yang *et al.*, 2020).

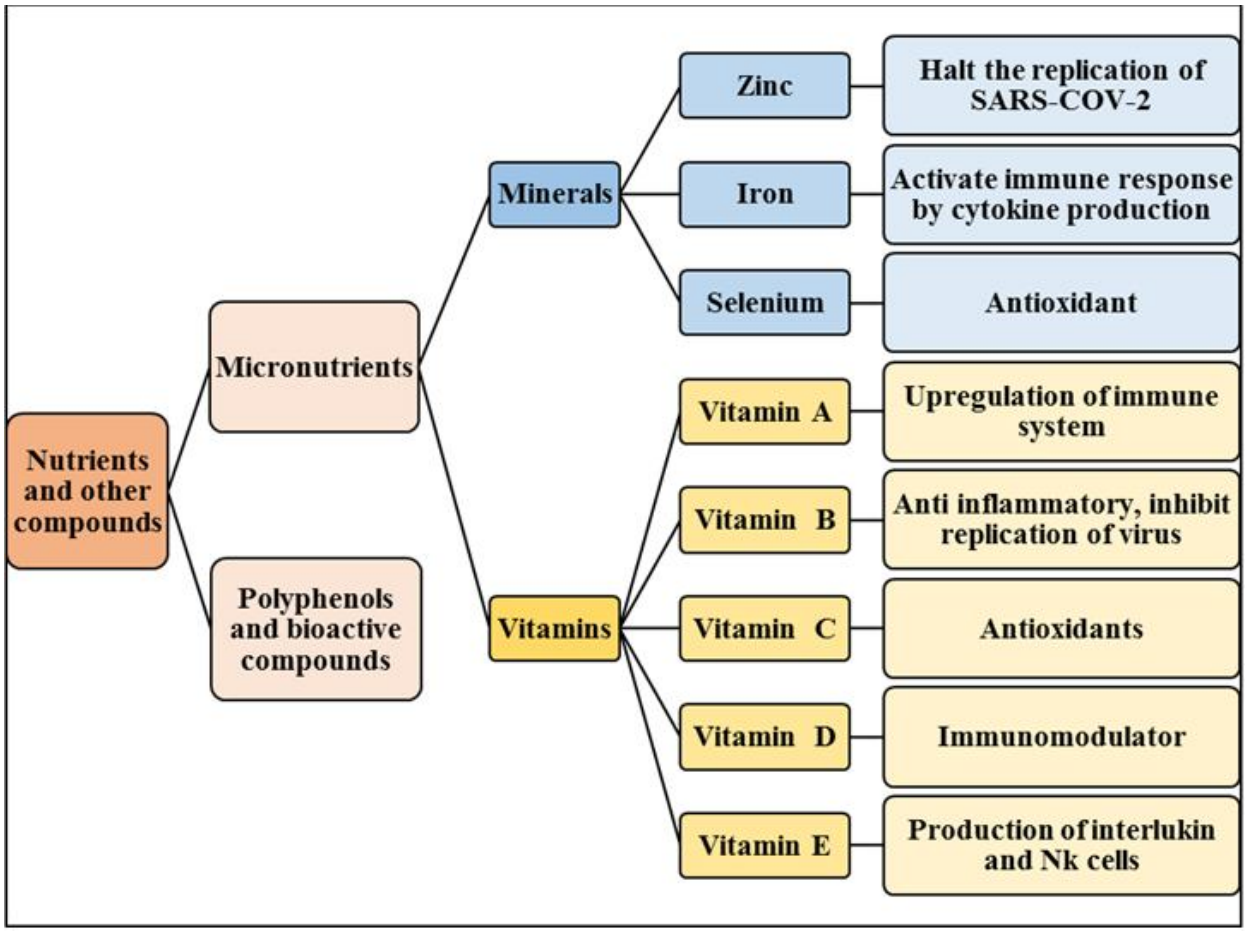

Figure 3: Role of various nutrients in combating COVID-19.

Varietal uptake of vitamins, minerals and micronutrients have been reported in enhancing the responses of adaptive (acquired) and innate (natural) immune system (Gombart *et al.*, 2020). Micronutrients deficiency leads to inhibition of antibody production by impairing the production of T and B cells. For example, zinc helps in halting the replication of SARS-COV virus and vitamin-D has been shown to decrease risk of respiratory infections/severity of respiratory infections. Deficiency of zinc and vitamin D has shown impaired adaptive and innate response and an increased risk of systemic infections (Martineau *et al.*, 2017; Junaid *et al.*, 2020).

3.1 Vitamins

Vitamins are the organic components/dietary components which possesses antioxidant and immune-regulating properties (Gorji and Ghadiri, 2020). Vitamin A regulates the interferon gene expression in host's cells, act as T-cell effectors and further support the maturation and differentiation of immunity cells (Gombart *et al*., 2020). Vitamin B is naturally occurring component in the host's gut which is of utmost importance for production of red blood cells (RBC). Vitamin B complex comprised of 8 vitamins and all of them play significant role in regulation of colonic immunity and effective barrier against intestinal diseases. Vitamin C is well known for its antioxidants, antiviral properties, reducing inflammation and collects neutrophils that perform phagocytosis and ultimately halts the multiplication of virus. In SARS-COV 2 immune cells work in such way, it leads to production of interlukin-6 and 8 which further causes cytokine storm. Uptake of vitamin C works against the cycle by producing pro-inflammatory cytokines along with interlukin-10 and inhibit the hyper-inflammation caused during COVID (Shakoor *et al*., 2021).

Vitamin D is a fat soluble secosteroid which helps to maintain calcium-phosphate metabolism. Vitamin D comprises of two major groups ergocalciferol (D_2) and cholecalciferol (D_3) which play vital role in activating macrophages and inhibits renin accumulation, which is associated with the production of angiotensin converting enzyme and causes-ARDS, cardiac injury and multiple organ failure in COVID patients (Sajadi *et al*., 2020). Vitamin E is another vitamin of utmost importance and also known as tocopherol or tocotrienols. Out of 4 tocopherols, α-tocopherol has maximum bioactivity which is a potent inhibitor of protein kinase C, monocytes and prevent platelet aggregation (Hemila, 2016; Meydani *et al*., 2018). Vitamin K on the other hand is another fat soluble vitamin which further regulate the macrophage activity which leads to proteolysis and helps in clearance of virus. During the COVID infection, tumour necrosis factor increases along with IL-6,8 and causes thromboembolic in arteries which further triggers blood clotting. Introduction of vitamin K counteracts these factors by activating anticoagulating factors, and act as antithrombotic component in host cells (Klok *et al*., 2020). Different vitamins, their sources, role in COVID-19 have been listed in Table 1.

Table 1: Sources of vitamins and their role in COVID-19 management

Vitamin	Sources	Role in COVID-19	References
Vitamin A (Retinol)	Carrots, sweet potato, liver, spinach, cantaloupe, leafy greens	• Facilitates adaptive and innate immune system • Anti-inflammatory and antioxidant properties	Gudas, 2012; Zabetakis *et al*., 2020; Jovic *et al*., 2020; Ferreria *et al*.,2020; Shakoor *et al*., 2021
Vitamin B complex Thiamine (B_1) Riboflavin (B_2) Niacin (B_3) Pantothenic acid (B_5) Pyridoxine (B_6) Biotin (B_7) Folate (B_9)	Egg, salmon, milk, avocado, yeast, chicken, spinach, legume, brown rice, whole grains, leafy greens, oysters	• Essential component for production of red blood cells (RBC) • Improve immune response by reducing pro-inflammatory cytokines, supporting endothelial cells	Parra *et al*., 2018; Mehmel *et al*., 2020; Dos-Santos, 2020; Shakoor *et al*., 2021
Vitamin C (Ascorbic acid)	Aonla, kiwi, strawberries, oranges, tomatoes, mango, leafy greens, lemon, grapefruit	• Exhibit antioxidant and antiviral properties • Counteracts with production of IL-6, 8 by producing IL-10	Carr and Maggini, 2017; Sajadi *et al*., 2020; Cheng *et al*., 2020; Hiedra *et al*., 2020
Vitamin D (Calciferol)	Egg, salmon, liver, cheese, canned fish, oysters, cereals	• Exhibit antiviral properties by increasing the production of cathelicidin and defensins. • Inhibit renin production which causes ARDS	Martineau *et al*., 2017; Hashemifesharaki and Gharibzahedi, 2020; Klok *et al*., 2020; Bilezikian *et al*., 2020
Vitamin E (Tocopherol)	Wheat germ oil, vegetable oil, spinach, nut oils, leafy greens	Immunomodulatory properties-activates cellular and humoral immune cells	Hemila, 2016; Meydani *et al*., 2018; Ferreria *et al*., 2020; Shakoor *et al*., 2021
Vitamin K Phylloquinone (Vitamin K_1) Menaquinone (Vitamin K_2) Menadione (Vitamin K_3)	Green leafy vegetables, salad dressings with soyabean and canola oil	• Involved in synthesis of protein and physiological functions. • Anti-thrombotic agent	Mccann and Ames, 2009; Klok *et al*., 2020; Anastasi *et al*., 2020; Janssen *et al*., 2020

3.1.1 Severity of COVID infection associated with vitamin-D deficiency

Vitamin D is a steroid hormone, which resembles the structure of sterols and function like a hormone. Vitamin D is a fat soluble vitamin and involved in calcium and phosphorus absorption. Biologically active form of vitamin D_3 is 1,25-dihydroxycholecalciferol which is converted enzymatically in kidneys and liver (Nelson *et al*., 2008). Vitamin D deficiency is positively related to the severity of ARDS, MERS, tuberculosis, respiratory ailments and COVID as it plays important role in the regulation of adaptive and innate immune response (Jayawardena *et al*., 2020). Vitamin D binds with VDR (vitamin D receptors) in nucleus and makes genes. These genes produce mRNA which further produces proteins and antimicrobial peptides: cathelicidins and defensins (Pizzini *et al*., 2020). These peptides make perforations in the outer membrane of virus structure and leads to destruction of the virus. Deficiency of vitamin D leads to reduction in macrophage activity, proteolysis, phagocytosis of virus, T helper cells, B cells, interleukin-6, 10 and human body is more susceptible towards SARS-COV virus (Casanova *et al*., 2020). During, viral infection liver produces angiotensin and further converted to angiotensin I by enzymatic (renin) transformation. Further lungs converts angiotensin I to angiotensin II which causes cytokine storm, fibriosis, hyperinflammation in the epithelial cells and leads to ARDS, MERS and multiorgan failure as shown in Figure 4 (Bilezikian *et al*., 2020).

Vitamin D	**Vitamin D and SARS-COV-2**
• Fat soluble vitamin involved in calcium absorption mechanism. • Regulate the innate and adaptive immune system	• Uptake of vitamin-D has been shown to decrease severity of respiratory infections • Vitamin D deficiency is associated with increased susceptibility to infections like ARDS, MERS-COV-2
Vitamin D and antimicrobial peptides	
Cathelicidins	**Defensins (α and β defensins)**
• Stimulating action on macrophages and further leads to phagocytosis of virus	• Make holes in the outer membrane of virus and destroys them
Poor vitamin D status leads to contact with SARS-COVID-2	
↓ • Reduction in production of macrophages • Reduction in proteolysis • Reduction in phagocytosis of virus • Reduction in T helper cells production • Reduction in B cells, plasma cells • Reduction in production of IL-10, 6, 8	↓ Liver produces Angiotensin (Precursor) ↓ Renin Angiotensin-I (Produced in kidney) ↓ ACE I Angiotensin-II (Produced in lungs) ↓ Increases inflammation and fibrosis ↓ ARDS, MERS, multi-organ failure

Figure 4: Role of vitamin D and its deficiency in COVID progression and severity.

3.2 Minerals

It is well established that nutritional deficiency can impair and adversely affect one's immune system by infections. In the absence of effective treatment, strong immune system is of utmost importance to fight against diseases. A mineral is a chemical element required as an essential nutrient by the organism to perform functions necessary for life. Minerals are of two types: macro and microminerals which

play vital role in human body to prevent cardiovascular and cerebrovascular diseases (Zabetakis *et al*., 2020). Ivanov *et al*. (2020) have reported the role of minerals in regulating angiotensin converting enzyme in human body during COVID. Sodium regulates ACE2 gene expression and maintains electrolyte balance in body during the viral infection SARS-COV-2. A study conducted by Lippi *et al*. (2020) revealed that deficiency of sodium increases the severity of COVID. Among different minerals, potassium, phosphorus, chloride, sodium are needed to maintain proper fluid balance, nerve transmission and muscle contraction. Low amount of sodium and potassium in host body, leads to hypokalaemia which triggers respiratory problem and ultimately causes ARDS and acute cardiac injury. Considering the outcome of COVID-19, deficiency of phosphorus (hypophosphatemia) in host body weakens the immune system thus, making body incapacitate to recover which leads to disease progression (Ni *et al*., 2020). Among microminerals, zinc plays very important role in enhancing the potential of immune system. Being involved in anti-inflammatory pathways, zinc lower down the production of ACE-2 ultimately inhibiting inflammation (Zhang *et al*., 2020a, b). Interlukin-2 and 10 are crucial to fight against the inflammation caused during COVID, iron being a potent chelator is involved in chelating the inflammation and increases the production of TNF (Tumor Necrosis Factor alpha) and IFN (Interferons alpha and gamma) factor. Furthermore, copper among all microminerals is considered as essential nutrient as it is directly involved in the innate and adaptive immune system. It also possesses the potential to neutralize infection viruses such as poliovirus, HIV-1 and COVID and boost immunity (Raha *et al*., 2020). Injectable doses of selenoproteins like GPX1 inhibit or counterbalance the oxidation and inflammation in the cells caused during SARS-COV-2 (Seale *et al*., 2020). These observation suggests the crucial role of minerals (macro and micro) in combating against SARS-COV-2, hence it can be concluded that high intake of minerals has a significant impact on SARS-COV-2 infection. Sources of minerals, RDA and their role in COVID listed in Table 2.

Table 2: Sources of minerals, estimated average requirements (EAR) and their role in COVID management

Minerals	Sources	EAR	Role in COVID	References
Sodium	Chicken, breads, soups, cheese, eggs, cured meats	2000 mg/day for men and women	• Regulate electrolytic balance in body • Role in gene expression of ACE2	Lippi *et al*., 2020; Habib *et al*., 2020
Potassium	Bananas, avocado, potatoes, spinach, dried apricots	4700 mg/day for men and women	• Maintains nerve transmission and muscle contraction • Lowers down the effect of inflammation and hypokalemia	Alwaqfi and Ibrahim, 2020; Lippi *et al*., 2020
Phosphorus	Fish, yogurt, tofu, broccoli, milk, salmon, eggs	700 mg/day for men and women	• Repairs damaged cells and tissue • Hypophosphatemia causes infection in epithelial cells. Adequate quantity is required	Ni *et al*., 2020; Xue *et al*., 2020
Zinc	Shellfish, meat, grains, seeds, cereals or wholegrain breads	17 mg/day for men and 13 mg/day for women	• Halts the replication of viruses • Significant role in regulating adaptive and innate immunity	Bonaventura *et al*., 2015; Zhang *et al*., 2020a,b
Selenium	Fish, shellfish, eggs, red and organ meat, nuts like brazil nuts.	40 µg/day for men and women	• Potent antioxidant and anti-inflammatory • Seleno proteins lowers down the severity of COV2 infection	Zhang and Liu, 2020; Seale *et al*., 2020
Iron	Tofu, spinach, lentils, broccoli, beef, liver, oysters	19 mg/day for men and 29 mg/day for women	• Regulate production of red blood cells • Chelation property leads to inhibition of inflammation and production of TNF and IFN factor	Budi *et al*., 2015; Wu *et al*., 2018

3.3 Polyphenols and bioactive compounds

The great possibilities of bioactive from fruits and their by-products to maintain or improve health, is increasing the interest in finding new products with positive pharmacological effects (Hamid *et al*., 2020b). Polyphenols are the micronutrients/secondary metabolites which occur naturally in the plants. They are included in many supplements though they are easy to get in the diet from food like-fruits, vegetables, spices, honey, grains, wine, *etc*. Polyphenols are characterized as reducing agents, and together with other dietary reducing agents, vitamin C, E and carotenoids they are referred as potent antioxidants and protects body against oxidative stress and associated diseases such as cancer, coronary heart disease and hyper-

inflammation (Kashyap *et al*., 2017; Thakur *et al*., 2020; Hamid *et al*., 2022). The structure of SARS-COV virus contains 4 types of membrane proteins, out of which S-glycoprotein membrane is the one which enters into host's epithelial cells and further replicates. Among different polyphenols, lutein and quercetin interfere with the mechanism of replication of virus by binding with S protein and making it incapacitate to multiply. Other than S protein, ACE2 have gained popularity during COVID for being a major enzyme. RAAS (Renin Angiotensin Aldosterone System) controls blood pressure level, with and during infection angiotensin I is converted to angiotensin-2 which causes vessels to narrow, resulting in high blood pressure and inflammation in cells. Resveratrol and eriodyctiol were reported to bind with the ACE2 receptors and inhibit the down regulation of ACE II and the multiplication mechanism (Rathinavel *et al*., 2020). Other bioactive compounds/nutraceuticals also improve individual's immune response and act primarily as immuno-modulators, and assist our defence system. Managing the infection caused by the pathogens/viruses, prevent aberrant immune response caused by autoimmune diseases leading to weakening of innate immune system, regulate the working of immune stimulators by inhibiting the binding and replication mechanism of virus. The majority of nutraceuticals/ bioactive compounds function as both immuno-stimulatory and inhibitors of viral infection into the host genome (Mehrotrov and Jadhav, 2021). Among different nutraceuticals-polyunsaturated fatty acids from different origin possesses antiviral, anticoagulant, antithrombotic properties and ability to perform biosynthesis of SPM (Special Resolving Meditators) which are essential during SARS-COV-2 to lowers down the inflammation and infection severity (Sandhaus and Swick, 2020; Ratha *et al*., 2021). With the increasing infection, the viral load in the mucosal layers of gut also increases which ultimately hinders the growth of gut microbiota (Hashimoto *et al*., 2012). In order to improve the survival of living microbes in the gut, adequate amount of prebiotics should be taken along with probiotics which leads to positive symbiotic effect on digestive system and gut microbiota (Swanson *et al*., 2020). Probiotics strains (*Bifidobacterium lactis, Lactobacillus brevis, Lactobacillus acidophilus*) improve the production of natural killer cells, T cells along with interferons and antibodies production in the host's cells (Baud *et al*., 2020). Sources and mechanism of action of bioactive compounds have been listed in Table 3.

Table 3: Sources and mechanism of action of bioactive compounds

Bioactive compounds	Sources	Mechanism of action	References
Polyphenols	Vegetables, green tea, blue and strawberries, spinach, plums, grape, onion, tomato, jamun	• Exhibit great binding affinity towards S-protein of SARS-COV-2 virus and further hinders its replication • Exhibit anti-inflammatory and antiviral properties	Zhang *et al*., 2008; Godfrey *et al*., 2012; Hamid *et al*., 2017; Lin *et al*., 2017; Kaihatsu *et al*., 2018; Thakur *et al*., 2018; Hamid *et al*., 2020a; Levy *et al*., 2020; Wahedi *et al*., 2020; Tahmasebi *et al*., 2020; Walls *et al*., 2020; Derosa *et al*., 2021; Djuricic and Calder, 2021; Thakur *et al*., 2021
Lutein	Kale, spinach, corn, broccoli, green peas, carrots, egg, pumpkin, parsley, leafy greens	• Inhibit the productions of mast cells, which leads to inflammation • Binds with spike protein of SARS-COV-2 and inhibit the virus multiplication	
Quercetin	Apple, tomatoes, cherries, black tea, grape, red wine, kale, broccoli, onion, buckwheat	• Exhibit both anti-inflammatory and antithrombotic properties • Quercetin regulates the inhibition of virus replication by interfering in the mechanism of binding	
Resveratrol	Grapes, wine, peanuts, cocoa, blueberries, cranberries, raspberries, mulberries	• Exhibit antiviral properties against Middle Respiratory Syndrome (MERS-COV-2) • Inhibit virus multiplication and spontaneous death of cells (apoptosis)	
Curcumin	Turmeric, mango ginger, curry powder	• Reduces the production of cytokines, IL-6 and 8, thus prevent inflammation • Inhibits the binding of S-glycoprotein to ACE receptors	
Polyunsaturated fatty acid	Walnuts, fish, soyabean oil, safflower oil, flax seeds or flax oil	• EHA and DPA exhibits anti-inflammatory properties by directly acting on inflammation cells *via* membranes • Uptake of omega-3 fatty acid leads to production of specialized pro-resolving mediators (SPMs)	
Prebiotics	Bananas, garlic, onions, asparagus, chicory, oats, leek, barley, inulin, chickpea, cocoa	• Prebiotics increases the production of beneficial microbes in the gut and improves immunity • Inhibits infection progression by inhibiting virus multiplication mechanism	
Probiotics	Yogurt, kefir, sauerkraut, pickles, miso, tempeh, kimchi, sourdough bread, cheese	• *Lactobacillus acidophilus* increases the production of IgA and IgA antibody-secreting cell responses • Regulate innate and adaptive immune system and protect intestinal walls	

4. Foods for boosting immune system against COVID-19

4.1 Fruits and vegetables

For maintaining good immune system, one needs to maintain balanced diet. Fruits and vegetables play an important role in human nutrition and health as it contains good amount of vitamins, minerals and other compounds which help in improving immune system (Sharma *et al*., 2019). Progression in viral infection occurs with the increasing inflammation and cytokine production in the epithelial cells of body. Different fruits and vegetables like citrus fruits, aonla, jamun, papaya, berries, pomegranate, broccoli, cauliflower, onion, and ginger are known for quenching respiratory diseases, anti-inflammatory properties, regulation of various functions in body and other medicinal properties (Bhatt *et al*., 2021). Consumption of fruits and vegetables will not only help us to tackle coronavirus but also strengthen the immune system to combat with other diseases that could be equally dangerous (Baidya and Sethy, 2020).

4.1.1 Role of fruits

Citrus fruits (lemon, orange, grapefruits, mandarins, *etc*.) contain wide amount of phytochemicals (flavonoids) like hesperidin which binds to the key protein of COVID and inhibit its multiplication (Bellavite and Donzelli, 2020). Citrus fruits contain other flavonoids and phenolic compounds which have antioxidant and antithrombotic properties. Amla being the richest source of vitamin C helps in boosting immune system. It contains different phytochemicals-ellagic acid, phyllemblic acid, gallic acid which improve the digestion and help in treating different diseases like-diabetes, asthma, cold and cough. Watermelon contains good amount of lycopene, vitamin B_6, C which are capable of lowering down the inflammation and respiratory problems. Jamun consists of phytochemicals which have many medicinal properties such as anti-inflammatory, antidiabetic, antimicrobial and antiallergic, *etc*. (Srivastava and Chandra, 2013). Papaya contains variety of vitamins like A, B, C which are very important to boost immunity. It contains a major compound-carpaine and folic acid which helps in reducing the blood pressure by converting homocysteine into amino acids, which otherwise causes heart stroke (Aravind *et al*., 2013). Pomegranate contains good amount of vitamins C and E which helps in enhancing the defence system of body and protects body from oxidative damage (Kumar, 2020). Being a potent source of antioxidants, vitamin C, A, potassium and manganese, berries were considered most important fruit during COVID pandemic. They contain high amount of polyphenols which reduce the damage caused to the cells due to free radicals and ultimately serves to good immune system. Figure 5 shows some examples of fruits and their nutrients for combating COVID-19.

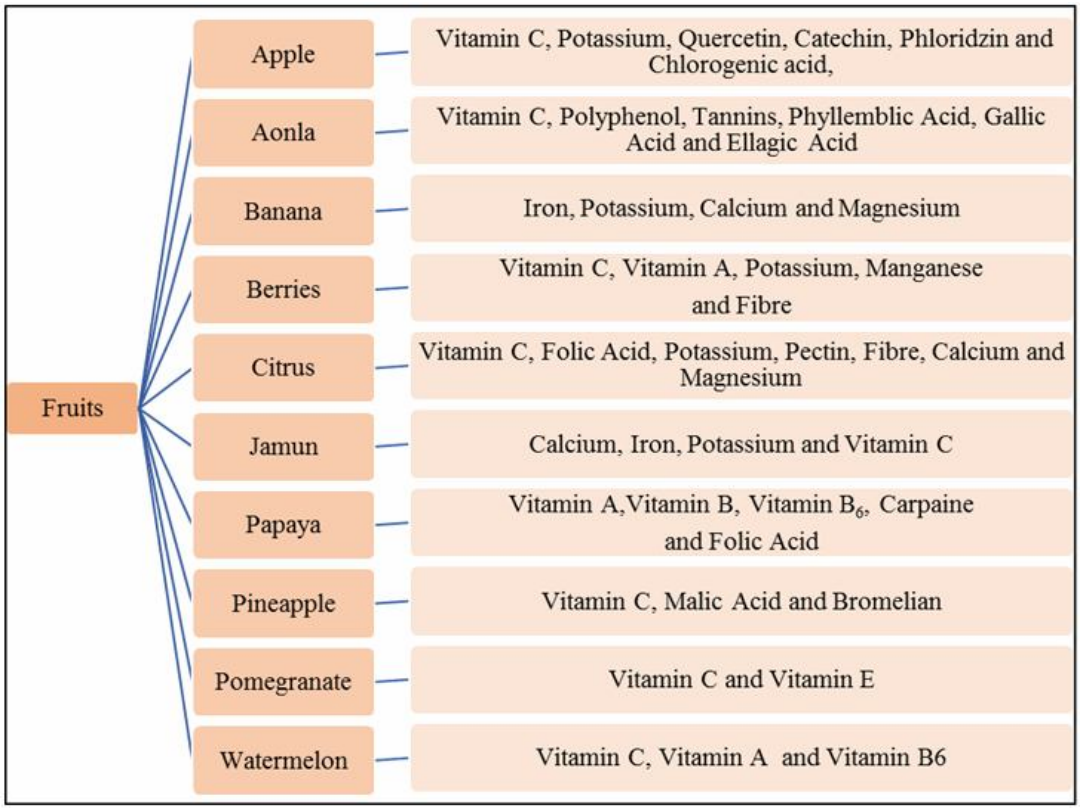

Figure 5: Fruits and their nutrients for combating COVID-19 pandemic (Adapted from Baidya and Sethy, 2020).

4.1.2 Role of vegetables

Vegetables are important source of many nutrients, including dietary fibre, folate vitamin A, C, potassium, magnesium, zinc, *etc*. Among different vegetables green leafy vegetables, are well known for their antioxidant and phenolic activities, which helps in lowering the risk of cardiovascular and cancer like diseases. Broccoli contains very high amount of calcium, magnesium and potassium which maintains healthy immune system and regulates blood pressure. Other than macro it also contains micro, minerals-zinc and selenium which regulates adaptive and innate immune system (Shubha *et al*., 2020). Choline and glutathione play very important role in maintaining the

cell's structure, adaptive and innate immune response which are present in cauliflower. Cauliflower also contains antioxidant compounds such as-vitamin K, vitamin C and manganese which lowers the risk of oxidative stress caused during the viral infection (Morris *et al*., 2013). Brussel sprouts contains large amount of vitamin C and antioxidant compounds like α-lipoic-acid which helps in boosting immunity by fighting against the oxidative stress caused during infection (Salehi *et al*., 2019). Spinach is the most nutritious vegetable among green leafy vegetables. It contains-wide amount of vitamins, flavonoids and phenolics compounds. Being a very good source of vitamin K_1 spinach also has antithrombotic properties. Beetroot is a rich source of iron and antioxidants which helps in regulating the production of red and white blood cells and act as an excellent detoxifying agent in human body. Carrots are rich source of α-carotene and phytonutrients which increases the production of T-cells, macrophages which improves immune system. Carrots are rich source of dietary, soluble fiber that helps in maintaining blood sugar level and lowers the risk of inflammation. Ginger and onion has been used since ages for their medicinal and therapeutic properties. Moreover, ginger helps in regulating good blood flow throughout the body and reduces the inflammation caused due to viral/pathogenic infection. Blood sugar can be significantly lowered down by the uptake of onion. Onion contains organic compounds such as-flavonoids, fructans, organosulfur compounds and possesses antimicrobial and antiviral properties (Sagar *et al*., 2020). Figure 6 shows some examples of vegetables and their nutrients for combating COVID-19.

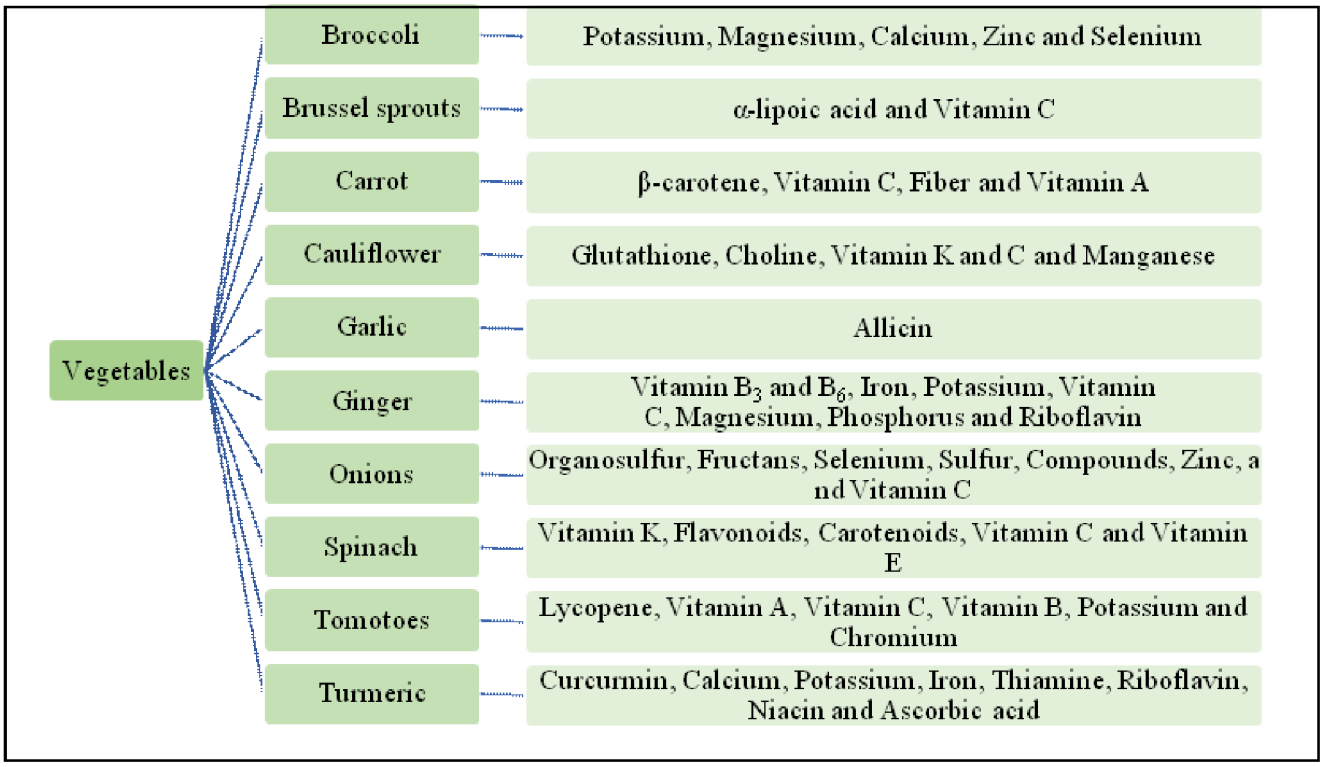

Figure 6: Vegetables and their nutrients for combating COVID-19 pandemic (Adapted from Baidya and Sethy, 2020).

4.2 Dairy products

Dairy products have been reported as an important part of healthy diet that helps in strengthening body immune system and prevent viral or other infections (Mahdavifar *et al*., 2021). Dairy products contain different bioactive compounds like-conjugated linolic acid, one of the most important fatty acid which reduces the inflammation and severity of COVID (Reynolds and Roche, 2010 and Cobre *et al*., 2021). Among different dairy products, milk contains some biologically active proteins-casein and whey proteins which have both anti-inflammatory and antioxidant characteristics. Milk also contains other compounds like B-casomorphin, lactoferrin which controls granulopoiesis and controls the function of natural killer cells. A study was also conducted by Gouda *et al*. (2021) and he reported that yogurt consumption during COVID reduced the infection and hospitality period, being a potent probiotic food with bioactive peptides. Developing the awareness among the people about healthy diet has become so important to fight against diseases. Various products like probiotics, prebiotics, bioactive peptides, functional food and nutraceuticals have gained the importance in a balanced and nutritious diet. Dairy products have gained great attention due to their immunomodulatory and health promoting properties as a base material for many functional foods (Nagpal *et al*., 2012). Different herbs and spices like tulsi juice, turmeric powder, coriander and ginger juice are used for fortifying, enriching the dairy products to make them functional because of their antimicrobial, antiviral, antimutagenic, immunomodulatory and many other health promoting properties. Turmeric is widely used for its medicinal and therapeutic properties and contains curcumin which have great binding affinity towards the S protein of virus and inhibits its replication. The bioactive compounds present in *Ocimum sanctum*, *Cymbopogon citratus*, *Ilex paraguariensis*, *Foeniculum vulgare* Mill increases the antioxidant activity, restrained the amino acid synthesis and retards the activity of the protease enzyme required for its multiplication (Hasneen *et al*., 2020; Mohammadi and Shaghaghi, 2020). Few examples for herbal based dairy products have been listed in Figure 7.

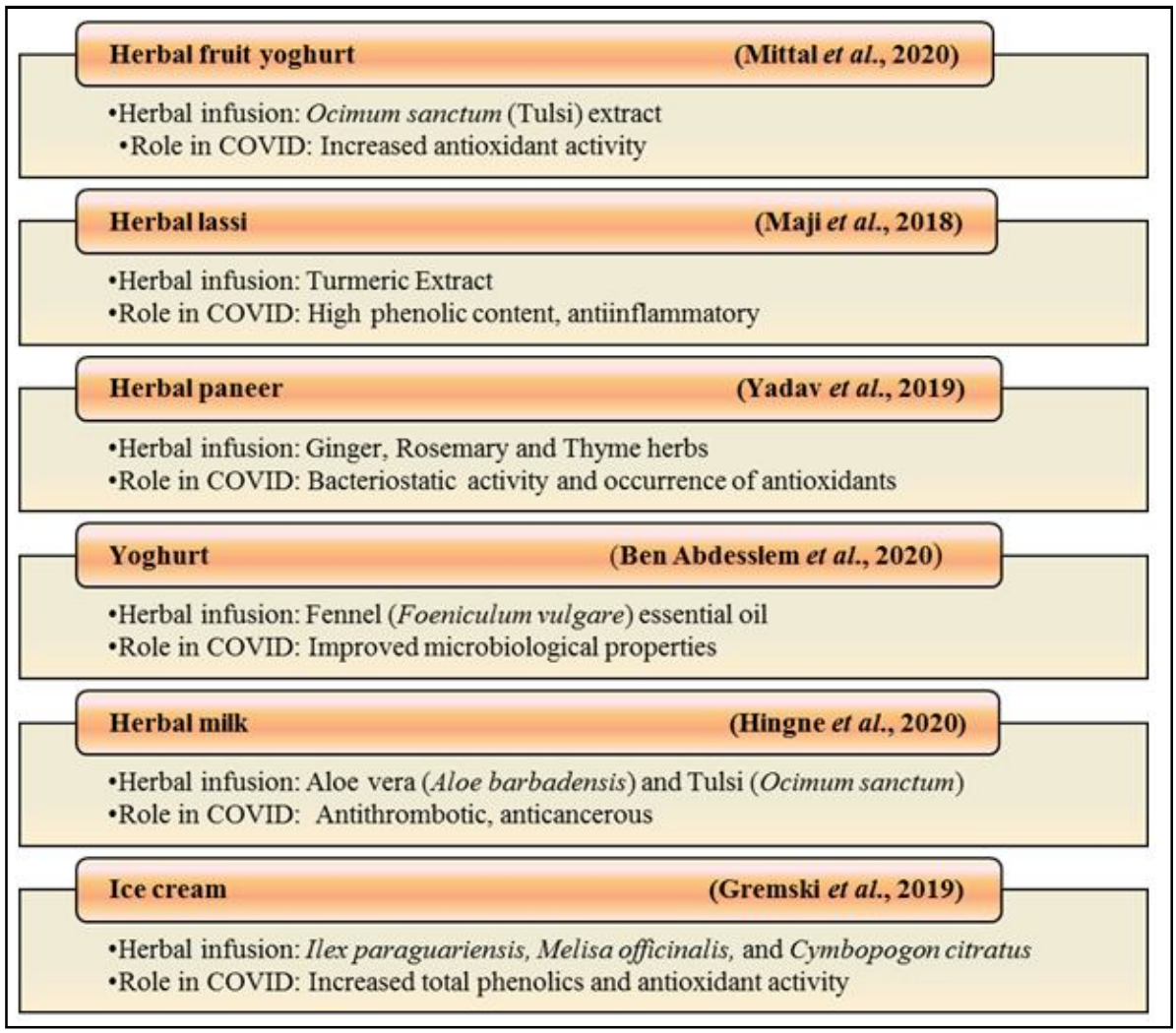

Figure 7: Herbal dairy products against different target organism.

4.3 Spices and herbs a healing way towards COVID-19

Spices and herbs have been in use since ages due to their antioxidant and antimicrobial properties (Table 4) and explored continuously to lessen the effect of diseases like COVID (Islam *et al*., 2020). Spices and herbs contain variety of compounds-flavonoids, phenols, tannins, bioactive compounds, *etc*. which possesses not only medicinal but therapeutic properties also. Leaves of plants which are consumed as such are termed as "herbs", whereas the dried part of the plant are consumed as "spices" (Bhattacharjee and Sengupta, 2008; Yashin *et al*., 2017). Among different medicinal plants and spices-garlic, heart-leaved moonseed, holy basil, clove, cinnamon, black pepper are some known for their antiviral and immunity boosting properties (Singh *et al*., 2016). In folk medicine, clove is the familiar culinary spice. Clove is used in three forms namely dried bud, oil and oleoresin and known for its antithrombotic, antiviral, antibacterial and immunomodulatory properties (Aisha *et al*., 2011). Its therapeutic use claims that it helps in treating various respiratory ailments, various viruses and preventing progression in COVID infection (Bahramsoltani and Rahimi, 2020). Black pepper, which is also known as 'king of spices' or 'black gold' is widely used as one of the most important drug in Indian medicines. Piperine is the main alkaloid which is present in it and responsible for its pungent taste and possesses different pharmacological properties such as antidepressant, antiviral, antihypertensive, germicide (Yoo *et al*., 2019). Among various medicinal plants, giloy is the most important one to combat the viral diseases like COVID. Giloy (*Tinospora cordifolia*) also known as 'heavenly elixir' as it boosts the immunity (Kumar, 2020). Its aqueous and ethanolic extracts had anti-inflammatory and germicidic activities and ameliorate viral diseases like COVID (Balkrishna *et al*., 2021). Ginger (*Zingiber officinale*) also known as sunthi in the Unani system of medicine (Bashir and Afrin, 2019). It is a rich source of bioactive compounds and contains alkaloid zingiberol, zingerone and paradol which have analgesic, antiarthritic and antimetic properties (Sulochna *et al*., 2020). Nimbin, nimbidin, nimbolide, limnoids are different terpenoids obtained from the bark of neem, and researchers have reported them to possess antidiabetic, antiviral, antimicrobial and immunomodulatory properties (Alzohairy, 2016). Bioactive compound obtained from neem leaves 'hyperoside' widely used as a potent drug against influenza virus (Ahmad *et al*., 2016).

Table 4: Role of herbs and spices in combating COVID-19

Spice/herb	Bioactive compounds	Effects
Turmeric	Curcumin, demethoxycurcumin	Exhibits antiinflammatory, antimicrobial, immunomodulatory properties
Ginger	Gingerols, shogaols	Exhibits antihypertension, germicidic and immunity boosting properties
Clove	Eugenol, gallic acid	Treat cold, cough, respiratory ailments and boost adaptive and innate immunity response
Black pepper	Piperine, eugenol	Exhibits antidepressant, antiplatelet, antihypertensive and antioxidant properties
Giloy	Octacosanol,heptacosanol	Prevent production of pro inflammatory pathway, antiviral ,boosts cellular and humoral immunity

5. Conclusion

It is evident from above that "We are what we eat". Communities with low immunity have suffered a setback during recent pandemic, making it crystal clear fact that right eating and drinking has immense impact on body's ability to prevent, fight and recover from infections. It is also a known fact that different organs of body regenerate their cells after a specific time. Thus, eating right and plant based food is beneficial for the healthy functioning of body. Fruits, vegetables, dairy products, herbs, spices all can be categorised as natural immune boosters. Not only this, their extracted phytochemicals and bioactives can be used to fortify the food products which originally lack them or face loss during processing. Flavonoids, carotenoids, terpenoids etc are known to possess antioxidant, anti-ageing, antiviral, anti-diabetic, anti-inflammatory, antibacterial activity which directly or indirectly can play a vital role in the prevention of COVID-19. In future, more research is needed co-relating the aspects of functional food, healthy eating, body exercises, boosting immune system and prevention of diseases. We need to be ready to fight the mutations of corona virus by incorporating healthy foods in diet.

Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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