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Significance of nuts in strengthening immune system during COVID-19

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Abstract

Viral infections are contagious and deadly. Many viral attacks in the past decades including COVID-19 have turned into pandemics and cost millions of lives. Treatment to virus is difficult as they transform themselves into many variants. Thus, an intelligent way of keeping oneself out of the trouble is through better nutrition that enhance immune responses. Foods that provide high quantities of nutrients are vegetables, fruits and nuts. They are rich in fibres, fats, protein, vitamins, minerals and plant bioactive compounds like phytosterols, polyphenolics, flavonoids, *etc*. Many studies and randomised control trials have proven their therapeutic effects and health promoting capacities. These compounds interfere with the pathways of metabolic mechanisms in the human body and work by either providing a protective scope or by destroying any harmful incomings into the body; that would disrupt the homeostasis. In this article, nuts and their nutritive components that administer healthy benefits are discussed. Almonds, cashew nuts, pistachios, peanuts, chestnuts and Brazil nuts are examined and reviewed here. The nutritional composition of these nuts and their mechanism to offer medicinal properties are explained in detail. Apart from nutritional values, these nuts are rich source of antioxidants that confer anti-inflammatory and immunomodulatory features. These activities enhance the immune responses by activating the defense mechanisms. Apart from the intake of highly nutritious diet, practising social distancing, isolation and better sanitation procedures are highly beneficial to avoid the severity of the viral attacks.

1. Introduction

1.1 Coronavirus

Coronavirus (COVID-19), a worldwide pandemic has costed many lives. It is caused by the novel coronavirus SARS-CoV-2, which belong to the Coronaviridae virus family. The first case of this virus was found in Wuhan, China in 2019; among the patients with pneumonia symptoms (Shakoor *et al*., 2021). Similar kinds of virus from same family have caused diseases like SARS (Severe Acute Respiratory Syndrome) and MERS (Middle East Acute Respiratory Syndrome) in 2002 and 2011, respectively. Paules *et al*. (2020) stated that virus transmitted from animal to human in the first place, making it a zoonotic transmission; which then got transferred from humans-to-humans through physical contact and other physical activities like coughing and sneezing, *etc*. The general symptoms of this disease are fever, cough, headache, respiratory disorders, pneumonia, *etc*. It keeps evolving as the virus variant evolves. About 80% of the affected patients suffer from moderate symptoms, while around 14% and 6% patients suffer from severe and critical symptoms, respectively (Alagawany *et al*., 2021). The pathogenesis of the COVID-19 virus was explained by Mason (2020) in three steps. The first step is usually asymptomatic. Initially, the point of entry of the virus is through nasal cavity where it attaches to the epithelial cells and replicates. The second step is to enter the site of action, lungs through the respiratory tract which brings the onset of moderate symptoms. During the third step, the virus replicates manifold and transmits to the target organs, thereby completing the development of the disease by showing severe symptoms. It is reported that 80% of the people affected by coronavirus suffer from very moderate symptoms that does not need hospital care (Leung *et al*., 2003). But, old age and poor immune system contribute to worsening conditions along with severe to critical symptoms. Studies also show that patients with medical history of cardiovascular diseases, diabetes, pulmonary and respiratory disorders and obesity are more vulnerable to the virus. The virus affects lungs, liver, kidney causing fatal conditions (mortality rate-49%-China CDC-Centres for Disease Control and Prevention) (Wang *et al*., 2020).

1.2 Development of immune system through nutrition

A good immune system has the ability to counteract the harmful effects of the disease. Immune system is the most important functioning to fight infection and viral diseases like coronavirus as it gets activated when a foreign particle enters the human body and starts its action against it (Indhuleka *et al*., 2020). Research evidence suggests that nutritional interventions plays an important role in COVID-19 management and treatment. WHO (World Health Organisation) reports that a balanced diet contribute to an efficient working of the immune system. This diet comprises a good load of vitamins, minerals, carbohydrates, polysaccharides, lipids, fibres, other essential macro and micronutrients (Chowdhury *et al*., 2020).

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Nutrients that perform immunemodulatory functions along with powerful antioxidant properties are necessary to combat this disease. Protein rich foods provide antiviral activities. Vitamin B protects the body from infection while vitamin C provides protection against flu-like symptoms (Wessling-Resnick, 2018). Vitamins A, D and E are equally important in protection against COVID-19. Minerals like zinc, copper, selenium improves the functioning of immune system. Foods like fruits, vegetables, legumes, nuts, whole grains offer these nutrient in abundance. Apart from these nutrients, many phytochemicals and functional foods have shown to be important in improving the immune functions. The beneficial impact of these nutrients decreases the threat of serious illness and death.

2. Immunomodulatory functions of nutrients

2.1 Polysaccharides

Polysaccharides are essential macromolecules formed with many monosaccharaides linked together through gylocosidic bonds. They possess many health giving properties like immunomodulatory activities and antioxidative properties which makes it an important constituent to boost the immune system (Chang *et al*., 2015). Chen and Huang (2018) reported that these polysaccharides with phenolics and protein show antiviral activities against influenza, herpes simplex virus, human immunodeficiency hepatitis virus, *etc*. β-glucan is one such dietary polysaccharide that has the ability to destroy the viral substances by producing cytokines and activating the immune cells (T lymphocytes, natural killer cells and dendritic cells) of the host; showing its antiviral capabilities (Urbancikova *et al*., 2020). Several studies suggest that β-glucan acts as an immunomodulatory agent in various diseases like HIV infection, influenza, cancer, *etc*. (Thirumdas *et al*., 2021). Fructans are another group of polysaccharides that show beneficial activity according to the chain of the fructose groups. Toll-like receptors (TLR) in these fructans work on initiating innate-immunity as an armour against both viral and bacterial diseases. Research conducted by Kumar *et al*. (2015) on rats showed antiviral and immunomodulatory functions in the fructans by producing nitric oxide which in turn stimulated the interleukins, interferon-gamma and tumour necrosis factors. Sulphated polysaccharides are another group of polysaccharides that shows therapeutic attributes against many viruses including HIV, rotavirus, *etc*. These sulphated polysaccharides provide a protection like cover against the virus, thereby preventing the adsorption of the viral matter into the host (He *et al*., 2020). This action produces the immune cells (macrophages, lymphocytes, *etc*.), immune-stimulatory particles, nitric oxide. These actions on-course destroy the virus and improves the immunity to the host.

2.2 Proteins

Lectin and lactoferrin are a group of proteins that has antiviral capacity. Lectins are glycan-binding proteins that acts on innate immunity, thereby improving immune responses during bacterial and viral infections. Lectin interacts with the viral surface with sugar and shows their antiviral activity (Singh *et al*., 2020). Another mode of action is by immunomodulatory functions through IL-1β, TNFα and INFγ (Sabater-Molina *et al*., 2009). Lectins have proven to be effective against HIV, influenza and coronaviruses (Hwang *et al*., 2020). Lactoferrins are group of proteins that bind to iron. This molecule enhances the innate immunity. They produce cytokines, T-helper cells. The mode of action of lactoferrin is by interfering with the adsorption process of the virus on the host and also activating the T helper cells, natural killer cells (Wakabayashi *et al*., 2014). Also lactoferrins possess iron that act as antioxidants.

2.3 Lipids

Some fatty acid increases the immunity in the host by inactivating the microbes. Studies by Das (2018) suggest that PUFA lyse the microbe's membranes which constrain the viral replication. Omega-3-fatty acids have metabolites that improves immune functions on this basis. Lipoxin is bioactive form of arachidonic acid that enhances the defense activities of the host, thereby improving the immune reactions. Medium chain fatty acids like palmitic, palmitoleic and lauric acids offer antiviral activity (Park and Gallagher, 2017). Lipids also contribute to anti-inflammatory actions and act as antimicrobial agents.

2.4 Minerals

2.4.1 Zinc

Zinc is one of the most important minerals to improve the immunity in human body. It especially controls the innate immunity by producing antibodies, as well as interfering in the signalling pathways of both specific and non-specific immunity (Wessels *et al*., 2017). Zinc acts as immunomodulatory agent, antioxidant, antiviral agent and anti-inflammatory agent (Alroy *et al*., 1995). Immune activities including the production of monocytes, natural killer cells and interferons are enhanced in the presence of zinc (Gombart *et al*., 2020). Functioning of immune cells like neutrophils, T cells, B cells, macrophages, *etc*., are supervised by zinc. Zinc also acts as a cofactor for antioxidants like superoxide dismutase and establishes its anti-oxidant activities in reactions involving stabilisation of sulphydryls against oxidation and reducing the oxidative injuries. It also increases the NF-κB activation improving the immune functions (Jarosz *et al*., 2017). Zinc induces the production of a sulphydryl rich protein called metallothionein that reduces free radical damages of the cell. This protein also acts as an intracellular sensor detecting oxidative stress, thereby regulating immune functions (Gupta *et al*., 2019). Zinc is said to provide protection against respiratory diseases like pneumonia, influenza, common cold, *etc*., also against viral infections like HIV, Hepatitis C, Herpes, SARS, *etc*. (Thirumdas *et al*., 2021). Depletion of zinc in the patient's body makes them exposed to infectious diseases due to bacteria, virus, fungus, *etc*. (Karacabey and Ozdemir, 2020). Zinc deficiency has proven to cause disturbance in the homeostasis of immune responses that leads to abnormal lymphopoieses, affects the intercellular cytokine signalling which ultimately depress the immune response (Maares and Haase, 2016). It also affects the lung tissues by increasing the pro-inflammatory cytokines. Zinc supplementation enhances the expressions of IL-2 and IL-2R-α mRNA. It also increases the concentration of natural killer cells, T-cells, *etc*. Randomised control trials conducted to study the effect of zinc supplementation shows imcreased cytokine responses, CD4+T cells (Jayawardena *et al*., 2020). Research conducted by (Barnett *et al*., 2016) shows that supplementation of zinc 30 mg/day for 3 months increased the concentration of T-cells in serum. In the context of COVID-19; zinc ions interact with zinc ionophorepyrithione and curb the viral replication. Chloroquine has antiviral activity that possess zinc. Studies suggest increasing the concentration of zinc in the same increases its antiviral activity (Skalny *et al*., 2020). Other ways of destructing the COVID-19 virus is by targeting the zinc ions of the virus with the zinc ions of the antiviral drug disulphiram making it inactive (Lin *et al*., 2018). Zinc supplementation for COVID-19 patients have recorded lesser damage due to respiratory infections.

2.4.2 Iron

Iron is involved with innate immune responses of the human body. It acts by interacting with other life-substances forming metal-enzymes and protein like iron catalases and lactoferrin (an iron chelated protein that acts as first line of defense), respectively that enhances the immunity (Fatima *et al*., 2020). Iron is required in the working of DNA synthesis, DNA repair, regulation of gene expression, cell proliferation and respiration and other important activities like maturation of lymphocytes to regulate immune functions. T cells differentiation and production of cytokines are looked after by iron (Gombart *et al*., 2020). Iron deficiency causes respiratory disorders. But, iron is also an important source of viral replication. Thus, overdose of iron have shown to cause viral infection (Luo *et al*., 2020). High levels of iron in serum contribute to hepatitis B virus, HIV, *etc*. This can be overcome by using iron-chelating to interact with free iron and making them unavailable for viral replication (Luo *et al*., 2020).

2.4.3 Copper

Copper plays a vital role in maintaining the immune system of our body. Copper possess antiviral and antibacterial properties (Jayawardena *et al*., 2020). Increasing copper intake to 7.8 mg/day improved the antioxidation status, and thus immune function. Copper also chelates with thujaplicin that restricts the viral replication of influenza. Copper in its ionic form involves in redox reaction that creates holes in the viral membrane leading to the destruction of its genetic material (Thirumdas *et al*., 2021). Copper ions perform virucidal actions against virus like herpes that damages the virus by causing oxidative damages (Vincent *et al*., 2018). Copper also acts as an antioxidant by reacting with superoxide dismutase. It also produces T cells, natural killer cells, neutrophils, macrophages, *etc*., which enhances the immune functioning. Copper acts as anti-inflammatory agent too.

2.4.4 Selenium

Selenium is a trace element that possesses anti-inflammatory activity and antioxidant attributes. The antioxidant property of selenium is attributed to the selenoprotein enzymes (Kieliszek, 2019). These proteins also ensures the production of interferon. Selenium when supplemented with 50-100 µg/day elevated the plasma levels which improved the immune functioning by increasing the immune responses through increased levels of IFN-γ, IL-8 and IL-10, T-cells, NK cells. When supplemented with 200 µg/day, selenoproteins show virucidal actions (Gombart *et al*., 2020). The mechanism of selenium against virus is by reducing the oxidative damage and increasing the production of CD8+T cells which induces proliferation of T cells and IL-2 (Turnlund *et al*., 2004). In the context of COVID-19, selenium is an inhibitor of NF-kB which is an important pathway for the progression of coronavirus in the host body. This decreases the effect on endothelial cells and prevents the aggregation of blood cells. Studies also show that supplementation of selenium has proven effective against COVID-19. Selenium when used along with saponins of ginseng stem enhances the immune responses (Ma *et al*., 2019). Selenium protects the body by radical scavenging, protection against oxidative stress and also by maintaining the antibodies levels.

2.5 Vitamins

Vitamins are a group of biocompounds that is highly essential for maintaining a hale immune system. Most of these vitamins cannot be produced by the body itself, hence must be supplemented through food (Thirumdas *et al*., 2021).

2.5.1 Vitamin A

Vitamin A is a fat soluble vitamin that exist in many active forms like retinol, retinal and retinoic acid. β-carotene, a precursor of vitamin A acts as antioxidants. Retinoic acid is the most active form which is responsible for immunity through anti-inflammatory actions and also the production of antibodies like IgA (Mullin, 2011). Retinol proliferates the immune cells such as lymphocytes and T-cells at the site of infection. Vitamin A enhances the production of interleukins that rejuvenate pulmonary functions (Yang *et al*., 2015). Deficiency of vitamin A decreases the immune responses and also increases the oxidative damage and inflammation. Reduction in the retinoic acid inhibits the type 1 interferon pathway that disrupts the normal immune functioning. This is a pattern seen in COVID-19. Supplementing vitamin A increases the activity of B and T cells. In children, supplementation of vitamin shows improved antibody response after administering vaccines (Huang *et al*., 2018).

2.5.2 Vitamin C

Vitamin C is a water soluble compound that supports normal growth and development of the body. It acts as a good enzymatic co-factor in collagen production and hormone synthesis (Kim *et al*., 2013). Vitamin C is the most effective antioxidant that scavenges free-radicals and also has immunestimulant impact on phagocytic conditions (Fatima *et al*., 2020). Studies suggest that vitamin C supplementation increased protection against viral and bacterial infections. 12 g/day of ascorbic acid enhanced the immunity of patients with respiratory tract infection. Similarly, 15 g/day of ascorbic acid reduced the mortality rate of COVID-19 (Carr, 2020). Vitamin C increased the production of interferon α/β, a vital antiviral factor that boosts immunity. It also increases the immune responses against common cold and flu (Kim *et al*., 2011). Vitamin C improves the innate and adaptive immunity. It overlooks various cellular functions, thereby improving the immune responses. The epithelial barrier against virus and skin scavenging ability is done by ascorbic acid (Alagawany *et al*., 2021). It collects and complies neutrophils that perform chemotaxis phagocytosis that kills the microbes. Vitamin C is also required for neutrophil clearance and apoptosis that inhibits tissue damage and necrosis (Carr and Maggini, 2017). Vitamin C accrue 100 times more in leukocytes than in plasma. During the onsite of an infection, this vitamin C is utilised faster from leukocytes than from plasma. During the COVID-19 infection, the release of pro-inflammatory cytokines increase along with IL-1β and TNF-α which further stimulates the production of IL-6 and IL-8. Introduction of vitamin C counteracts this by production of anti-inflammatory cytokines like IL-10 which works against IL-6 and controls inflammation against the virus attack (Shakoor *et al*., 2021).

2.5.3 Vitamin D

Vitamin D is a fat soluble vitamin that has two groups D2 and D3. D3 is the group that is involved in the immune system functioning (Fatima *et al*., 2020). It is responsible for both innate and adaptive immunity and also ACP (antigen-presenting cells) (Aranow, 2011). Vitamin D plays a vital role in the mechanisms of immunemodulatory functions. 1,25-dihydroxy cholecalciferol (1,25 (OH)2D), a vitamin D metabolite is important in expressing immune responses by activating macrophages and other cell differentiation and proliferation

(Fatima *et al*., 2020). This metabolite also advocate chemotaxis and phagocytosis of macrophages. Discovery of vitamin D receptor (VDR) increased the scope of vitamin D beyond its calcium homeostasis and involvement in the mineral and bone health (Wu *et al*., 2019). VDR along with vitamin D activating enzymes are elevated by T cells and B cells activation. Vitamin D also induces T-cell proliferation; where Th0 is differentiated into Th1, Th2, Th17, *etc*., that in turn produces cytokines; stimulating innate immune responses against pathogens. Th1 and Th17 are responsible for intracellular pathogenic immunity; while Th2 is responsible for extracellular immunity through humoral immunity. Dendritic cells which are responsible for adaptive immunity is also affected by vitamin D. Vitamin D provides protection against various diseases like hepatitis C, HIV, respiratory infections, inflammatory bowel disorder, multiple sclerosis, rheumatoid arthritis, type 1 diabetes, immune disorders, *etc*. (Colotta *et al*., 2017). Clinical trials by Jolliffe *et al*. (2013) reported the connection between vitamin D deficiency and the risk of upper respiratory tract infections. Similarly, another RCT reported that vitamin D supplementation with very high dosage like 1,00,000 IU/month decreased the respiratory tract infections in aged patients. Vitamin D induces the production of cathelicidin and defensins, antimicrobial peptides that have the potential of an antiviral agent (Shakoor *et al*., 2021). They show chemotactic activity against viral replication (Klotman and Chang, 2006). Vitamin D supplements along with antiviral drugs has been proven to be effective against HIV, hepatitis, *etc*. Daily intake of 250 µg of vitamin D shows beneficial effects against common cold, respiratory infections by enhancing the physical barrier and boosting the immunity (Grant *et al*., 2020). COVID-19 is more prevalent among elderly age groups. This can be attributed to the fact of less exposure to sunlight and, hence lesser production of 7-DHC (7-dehydrocholesterol) in the skin (Shakoor *et al*., 2021).

2.5.4 Vitamin E

Vitamin E is another fat soluble vitamin important in regulating immune functions. It is also known as tocopherols (α, β) or tocotrienols. It activates cellular and humoral immunity. Vitamin E increases the T-lymphocyte proliferation and T-cells through cell division. It also acts as antioxidant by scavenging free-radicals. Vitamin E possess chromanol ring in its molecular structure that has the ability to abort PUFA oxidation (Lee and Han, 2018). Vitamin E acts as a chain-breaker of PUFA that absorbs lipid peroxyl radicals which prevents oxidation reactions. Trolox (6-hydroxy-2,5,7,8-tetramethylchroman 2-carboxylic acid), an analogue of vitamin E has also shown to reduce the oxidative stress. Vitamin E has more radical scavenging capacity than vitamin C (Boulebd, 2020). Vitamin E enhances the T-cell production and also supresses the T-cell reducing factors like PGE_2. Vitamin E supplementation on mice was conducted in many studies. BouGhanem *et al*. (2015) suggested that 500 mg/kg of vitamin E in the diet decreased viral titers affected by influenza and also decreased pulmonary bacterial infection and lung inflammation due to *Streptococcus pneumoniae*. Han *et al*. (2000) said that this was due to enhanced Th1 responses through IFN-γ and IL-2. Human studies on vitamin E supplementation by Meydani *et al*. (1990) showed that adults who were administered with 200 mg/day for 365 days were less susceptible to respiratory infections when compared to the counterparts who were administered with placebo. The mechanism of vitamin E in immune system was studied by Wu *et al*. (2016). Vitamin E influences the T-cell division and membrane integrity that acts against respiratory disorders. This produces IL-2 in excess and enhances the immune responses. It also maintains the Th1/Th2 balance. Also, vitamin E possess antiviral capabilities against hepatitis B and other virus (Reboul, 2017). The following studies suggest negative impact of excess vitamin E on human health. Hemilä and Kaprio (2008) reported vitamin E supplementation increased risk of pneumonia among adult smokers. A similar result was observed among adult patients of respiratory infections. They were supplemented with 200 IU/day of vitamin E. No prominent changes were observed due to the intake of vitamin E (Meydani *et al*., 2004). A study called Alpha-Tocopherol Beta- Carotene Cancer Prevention (ATBC) showed positive, neutral and negative effects of vitamin E supplementation on pneumonia and common cold. The difference in the results were attributed to smoking history, residence, age and many other factors (Hemila and Kaprio, 2011). These disparities should be cleared with consistently characterised population for research.

3. Health outcomes of nuts

Nuts are usually included more in Mediterranean diets and cuisines. Recently, the health outcomes of nuts are vastly read and experimented and are being recommended as an important inclusion in regular diets or as a supplement for nutrient deficiency. These nuts are usually known for its lipid content, especially MUFA (Monounsaturated Fatty Acid) and PUFA (Polyunsaturated Fatty Acid). Other health promoting macro and micronutrients present in nuts are fibres, proteins, vitamins (E, B), and minerals (Mg, Cu, Ca, P, Zn, Se) and also bioactive compounds (Souza *et al*., 2015). Tree nuts like cashew nuts, almonds, Brazil nuts, walnuts, pistachio nut and legume seed like peanuts are examined and reviewed here. Almonds and cashews have high fraction of MUFA/SFA's while Brazil nuts have lower fractions of the same. Walnuts consist of elevated levels of PUFA's (linolenic acid). Among tree nuts, almond possess highest fibre content (12.5 g/100 g of nuts), while in legume seeds, peanuts are a rich source of both fibre and proteins. The bioactives rich in these nuts are α-tocopherol in almonds, phenolics in walnuts, phytosterols in peanuts, selenium in Brazil nuts, *etc*. (Souza *et al*., 2017).

These nuts have many favourable consequences on diseases like CVD (Cardiovascular disease), diabetes, obesity, hyperlipidaemia, metabolic disorders, cancers and improve the insulin resistance, lipid profile, and inflammation status and reduces the oxidative stress. Consumption of 10 g of almonds everyday increased the HDL, while consumption of 60 g of almonds every day decreased the LDL concentrations (Li *et al*., 2011). Similarly, including 75 g of walnuts regularly in the diet decreases the risk of CVD and improves the endothelial functions (Ma *et al*., 2010). 40 g of pistachios reduced the glucose concentration by improving glucose metabolism and also reduced LDL and increased HDL concentrations, thereby improving the lipid profile for better cardiovascular function. Approximately, 50 g of peanuts provides a feeling of satiety and maintains the glucose level. It also enhances the fat oxidation rate, thereby keeping a check on weight gain (Alves *et al*., 2014). In the aspect of immune responses, antioxidation and anti-inflammatory status of a nut is the most vital factor. Dietary factors such as omega-3 fatty acids, arginine, fibre, vitamin E, magnesium, zinc and selenium are the major determinants in anti-inflammatory mechanisms. A good microbiota is also essential to maintain a healthy immune system. Skins of almonds are rich source of prebiotics. They have polymerised polyphenols, ellagitannins and fibres that are non-bioaccessible that

renders it unreactive into the colon. This further enhance the concentration of good bacteria *(Bifidobacterium* spp. *and Lactobacillus* spp.) in the gut and increases the immunity. Similarly, pistachios and walnuts also possess the prebiotic nature in them (Gervasi *et al*., 2021).

Most of the nuts have an allergic potential. Consumption of certain nuts elevates serum levels of immunoglobulin and makes the body sensitive to it. This can be reduced through processing steps like roasting that neutralises the allergic reactions and also improves the health-promoting attributes (Downs *et al*., 2016).

Table 1: Nuts and their related health outcomes

Sl. No	Nut	Scientific name	Active ingredients	Health benefits
1	Almond	*Prunus dulcis*	Unsaturated fatty acids, vitamin E, vitamin B, Mg, P, K	Controls LDL, antioxidant, improves gut microbiota.
2	Peanut	*Arachis hypogaea*	Arginine, soluble fibres, vitamin B	Cardiovascular protection, improves lipid profile
3	Cashew nut	*Anacardium occidentale*	MUFA, Zn, Cu, Ca, Mg	Hypertension, cancer, anti-inflammatory
4	Pistachio	*Pistacia vera*	Vit B6, Cu, Mn, carotenoid	Diabetes, Obesity, CVD
5	Walnut	*Juglans regia*	Omega-3 fatty acids, vitamin B6, Cu, Mg, Zn, Ca	Obesity, CHD, CVD, metabolic syndrome
6	Chestnut	*Castanea dentate*	Starch, P, Ca, Mg, GABA	Brain functions, digestive disorders, antioxidant, anti-inflammatory, anti-carcinogenic properties
7	Brazil nut	*Bertholletia excels*	Se, Zn, Cu, omega-3	Cardioprotective, immunomodulatory function

Source: USDA

Table 2: The effect of nut consumption on cardiovascular risk factors summary of scientific evidence

S.No	Variables	Effect	Level of evidence
	Epidemiologic studies		
1.	Coronary heart disease	Decrease	++
2.	Sudden cardiac death	Decrease	+
3.	Ischemic stroke	No change	+
4.	Heart failure	No change	+
5.	Hypertension	Decrease	+/-
6.	Diabetes	No change/decrease	+/-
7.	Cancer	No change/decrease	+/-
8.	Gallstone disease	Decrease	+
9.	Complications of diverticular disease	Decrease	+
10.	Inflammatory markers	Decrease	+
11.	Body weight	No change/decrease	++
	Clinical studies		
1.	Blood cholesterol	Decrease	++
2.	Insulin sensitivity	No change/decrease	+/-
3.	Blood pressure	Decrease	+
4.	Oxidation	No change/decrease	+/-
5.	Inflammation	No change/decrease	+/-
6.	Vascular reactivity	Increase	+
7.	Body weight	No change	++
8.	Visceral adiposity	Decrease	+

+/- equivocal evidence; + limited evidence from few studies; ++ consisting evidence in several studies (Ros, 2010).

4. Immunomodulatory functions of nuts

4.1 Almond: *Prunus dulcis* (Mill.) D.A.W.B.B

Almonds are classified as dry fruits. They are small sized nuts but loaded with nutrients. Almonds are filled with vitamins (E, A, B) and minerals (Mn, Ca, Mg, P, K). They are also a good source of proteins, fat and fibres (Chen *et al*., 2006). Catechin, epicatechin, kaempferol, *etc*., are some flavanoids that regulate the inflammatory process in the body. Flavanones (naringenin) and anthocyanins (cyanidin and delphinidin) along with phenolic acids (caffeic acid, ferulic acid, vanillic acid, p-coumaric acid) possess radical scavenging properties. These nutrients and fibres produce antioxidant and immune-modulatory activities (Burns *et al*., 2016). The almond skin is rich in fibres that acts as substrate for good microbiota. Studies show an increase in the count of *Bifidobacterium* and *Lactobacillus* sp. when 10 g/d of almond skin was consumed for a period of 6 weeks (Liu *et al*., 2014). *Lactobacillus* work in good digestion, helps lactose intolerant patients by reducing diarrhoea and constipation. It also prevents other pathogenic infections including IBS (Irritable Bowel Syndrome). *Bifidobacterium* enhances the production of vitamin B and stimulates the functioning of immune system. It also decreases the blood cholesterol and ammonia levels. Both these bacteria produce the compound β-galactosidases that maintains the gut health (Brigidi *et al*., 2001). Apart from maintaining good microbiota, consumption of almonds also decreases the risk of harmful microbes like *C. perfringens* that cause gastrointestinal disorders (Liu *et al*., 2014). Other similar studies suggest, almonds reduced the production of inflammatory cytokines. Prebiotics and probiotics have the potential to improve the immune system. Parkar *et al*. (2008) studied that the abundant polyphenols present in the almonds also ensures a healthy gut, and thereby a good immune system.

Almonds also advocate heart health by inversely affecting the cardio vascular disorders. The phytosterols and fibres in almonds promote hypocholesterolemic effects; while the fat content in almonds promote vascular health. Copper and α-tocopherol looks after the antioxidant properties (Chen *et al*., 2006). He also reported that almond consumption of 100 g/day decreased total cholesterol and low-density lipoprotein by 9% and 12%, respectively. Fraser *et al*. (2002) studied the effect of almonds on weight gain/loss. Inclusion of 56 g/day for 6 months resulted in non-significant mean weight gain (400 grams). No difference in waist/hip ratio was observed. Almonds have satiety property that makes the person consume lesser quantities of other foods. Also, the almond fats are not completely absorbable by human cell; thus increase in weight cannot be attributed due to almonds. Another study by Wien *et al*. (2003) introduced almonds in their low-calorific diet for obese patients. 84 g/day of almond was included in their diet. The results showed decrease in weight, BMI, waist/hip ratio and fat content. This study also showed increase in insulin concentration. Almonds have low glycaemic index. Vitamin E in the form of α-tocopherol is a very important component in almonds; which is also an important component that possess variety of health benefits. It has high antioxidant capabilities. It also maintains the lipid concentrations which helps maintains cholesterol levels (Jambazian *et al*., 2005). Studies show that consumptions of nuts also protects cancer.

Consumption of almonds by people who put their body to extreme physical activities is recommended. Physical exercise tends to produce more reactive oxygen species (ROS). This puts extra pressure on the antioxidant defense system which affects the normal functioning of immune system (Yi *et al*., 2014). This can be balanced by almonds since it has unsaturated fatty acids and large quantities of antioxidants that boosts the antioxidant defense system. Also, the presence of quercetin and arginine in almonds helps maintain the mitochondrial production that compensates for the extra workouts by producing oxygen in excess (Campbell *et al*., 2004). It also regulated the CHO and glycogen pathways that maintains the energy levels of the athletes. Overall health benefits of almonds include protections against CVD, diabetes, obesity, cholesterol, *etc*., due to its cardioprotective properties and hypolipidemic effects.

Table 3: Nutritional composition of almond

S.No	Nutrient (Unit)	Per 100 g
1	Energy (Kcal)	579
2	Carbohydrate (g)	21.55
3	Protein (g)	21.26
4	Fat (g)	49.93
5	Dietary fibre (g)	11.80
6	Vitamin E (α-tocopherol) (mg)	25.87
7	Vitamin A (IU)	5.00
8	Niacin (mg)	3.93
9	Riboflavin (mg)	0.81
10	Manganese (mg)	2.54
11	Calcium (mg)	248
12	Magnesium (mg)	275
13	Phosphorus (mg)	474
14	Potassium (mg)	728

Source: USDA

Almonds are considered as dry fruits that are consumed during cold to prevent any infections. The antioxidants present in almonds scavenges the free radicals and prevents any kinds of infections with its anti-inflammatory and antihepatotoxic properties (De, 2020). The vitamins and minerals found in almonds strengthens the bone

and muscle functioning. Antiviral activities of the almond skin was observed due to the presence of polyphenols and fibre. These polyphenols are bioaccessible for digestion in the gastrointestinal tract. These aid in the release of cytokines that act against virus. Activation of immune cells occur with the components in the almond skins. Interleukins, interferons, *etc*., are proliferated due to the presence of nutrients in almonds. The almond skin is rich in fibre that influence the inflammation of protein kinase C (PKC) and nuclear factor kappa B (NK-kappa B). Along with antiviral properties and anti-inflammatory properties, they also possess immunomodulatory functions (Arena *et al*., 2010). Due to its protective nature against so many disorders and the presence of antiviral properties and other health benefits, almond can act as a prospective immune booster food for COVID-19 or any other ailments.

4.2 Peanut: *Arachis hypogaea* L.

Peanuts are also known as groundnut, which is also seen as an edible portion of the legume family (Fabaceae). China is the largest producer of peanuts with 45% of overall production while India is in the second place with 16% share (USDA, 2015). They are used to extract oil in large quantities. They are also used for the manufacturing of peanut butter in large scale and also other eatables involving peanuts. Peanuts are consumed to combat malnutrition in under-developed countries as they are rich source of protein, fat and fibre. The most popularly cultivated peanut varieties are Spanish (in candy, salted peanuts and peanut butter), Runner (in peanut butter), Virginia and Valencia. The latter two varieties are preferred for its large size and shells, oil content, flavour, *etc*. (Arya *et al*., 2016).

The wide ranged nutritional composition of peanuts confer wide aspect of health benefits. Protein, fat and fibre content contributes to its major nutrients. The proximate composition of peanuts were estimated as 20.7%-25.3% of protein, 31%-46% of crude fat, 1.2%-2.3% of ash, 1.4%-3.9% of crude fibre, 21%-37% of carbohydrate and 4.9%-6.8% of moisture (Alhasaan *et al*., 2017). Proteins are usually found more in animal products. For vegetarians and vegans, peanuts are the perfect source of protein. This is estimated through its amino acid contents and its digestibility. The amino acid composition varies from different varieties of peanuts. But, an average peanut contains all 20 essential amino acids. The highest quantity of amino acid present is arginine; while the least quantity of amino acid present is sulphur-amino acids (methionine and cysteine) (King *et al*., 2008). This aminoacid profile makes it a suitable nut for protein fortification. The digestibility quotient for peanuts is 81% according to PDCAAS (Protein Digestibility Corrected Amino Acid Score). For raw peanuts, the digestibility score is 92.65%. These score make peanut protein's more bioavailable than soybean who's PDDCAAS is 72% even though, it possess more protein content. These PDCAAS scores are very similar to eggs and other meat sources (FAO, 2002). Nuts in general have higher lipid content. Peanuts are rich in unsaturated fatty acids, especially MUFA, monounsaturated fatty acids. The health benefits of these unsaturated fatty acids are providing protective actions against CVD, atherosclerosis, *etc*. They advocate artery-clearing and maintains good blood flow. RCT studies by Alves *et al*. (2014) showed consumption of high-oleic peanut along with calorie-deficient diet led to fat loss along with insulin secretion. Study by Bonku and Yu (2020) on the effects of MUFA and PUFA on body health reported that they are beneficial against cancer, cognitive reduction and obesity, CVD. Also, HDL was maintained to provide the benefits of good cholesterol. Peanuts are a good source for healthy calories (Arya *et al*., 2016). The dietary fibre present in peanuts helps in reducing the risks of osteoarthritis, heart diseases, and metabolic disorders like diabetes, cancer, gastrointestinal disorders and other immune disorders. It also lowers the cholesterol levels and has low glycemic index. The soluble fibres react in the gut with the good microbiota and confer health benefits. The insoluble fibres have the ability to interact with carcinogens and other toxic substances, which later can be eliminated through faeces (Wong *et al*., 2006). 100 grams of peanuts provide 75 % RDA of niacin, 60 % RDA of folate, 53 % RDA of thiamine, 10 % RDA of riboflavin, 35 % RDA of pantothenic acid, 27 % RDA of pyridoxine, 55.5 % RDA of vitamin E. It is a great source of vitamins B and E which are important in boosting immunity.

Thiamine is needed for metabolism of energy and nerve functioning. Riboflavin is needed in metabolism of other components like fats, carbohydrates and proteins. This vitamin is also involved in ATP synthesis. Niacin is vital for good digestive and nervous system functioning. Folates, pantothenic acid and choline are collectively required for normal functioning of the body (Bonku and Yu, 2020). Vitamin E acts as antioxidant and maintains the functioning of cell membranes. Vitamin E reduces the risk of coronary heart diseases, cancer and other diseases. Vitamins B and E are sensitive to heat. Thus, consumption of raw peanuts is highly beneficial rather than roasted and other processed peanuts (Chukwumah *et al*., 2007). The mineral content of peanuts are also huge. 100 grams of peanuts contain 127 % copper, 84 % manganese, 57 % iron, 54 % phosphorus, 42 % magnesium of RDA levels. They are also rich in antioxidant minerals like selenium, manganese and cooper. These minerals aid in decreasing the inflammation reactions due to infections and also protect the body from pathogenic attacks (Song *et al*., 2005).

Arginine is an amino acid present in excess in peanuts. It is an important component in the functioning of immune system. It enhances the production of T-cells and activates the immune system. Studies have proven that arginine can be used in treatment of disorders related to depressed immune system like HIVS, cancer, *etc*. (Arya *et al*., 2016). Resveratrol is stilbenes phenolic compounds that are produced when affected by microbes or even due to stress or injury (Jeandet *et al*., 2012). This antioxidant rich peanut has the potential to fight against cancer, heart diseases, autoimmune disorders like Alzheimer's and even inflammations caused by infections (Gagliano *et al*., 2010). An array of phytosterols are present in peanut that offer protection against inflammatory disorders. These phytosterols decrease the blood cholesterol by interrupting its synthesis pathway and also by maximizing its output. Lopes *et al*. (2011) reported that the presence of phenolics acids and flavanoids in the peanuts increase their antioxidant concentration. Some research also report that when peanuts are consumed with their skin doubles the antioxidant levels.

Similarly, roasting and boiling of peanuts improves the antioxidant concentration. These antioxidants neutralize the harmful free-radical movement, thereby minimizing the damage made by oxidation reactions. This mechanism prevents the incoming of many metabolic and immune disorders (Ros, 2010).

Table 4: Nutritional composition of peanut

S.No	Nutrient (Unit)	Per 100 g
1	Energy (Kcal)	567
2	Carbohydrates (g)	16.13
3	Protein (g)	25.80
4	Fat (g)	49.24
5	Dietary fibre (g)	8.5
6	Vitamin E (mg)	8.33
7	Thiamine (mg)	0.640
8	Riboflavin (mg)	0.135
9	Niacin (mg)	12.066
10	Manganese (mg)	1.934
11	Copper (mg)	1.144
12	Zinc (mg)	3.27
13	Phosphorus (mg)	76
14	Magnesium (mg)	168

Source: USDA

4.3 Cashew nut: *Anacardium occidentale* L.

Cashews belong to Anacardiaceae family. Cashew nuts originated from Brazil and are one of the top commercial crops in India. It is also called as "Wonder nut" as it is the only nut found outside the fruits' pulp. The fruit, bark, leaves and shell of this plant has many benefits. Cashews are a very tasty nut that can be consumed raw and are used in many cuisines. Apart from savoury purpose, cashew nuts provide enormous health benefits. Cashew kernels possess 25% of carbohydrates, 46% of fats and 21% of proteins. Apart from these basic nutrients, cashews are also rich in a wide range of vitamins, minerals and other plant phenolics (Vyavahare *et al*., 2020).

The fats in cashew nuts are mostly unsaturated, both MUFA and PUFA (60% and 20% of total fat) which confer health benefits. They prevent CVD and other metabolic disorders like obesity, diabetes, *etc*. The MUFA related oleic acid is rich in cashews that work as cardioprotective agent, as unsaturated fats are good for heart. These unsaturated fat decrease the triglyceride content in the blood due to thermogenic effect, and thereby reduces the risk of heart blockage. Also, the good cholesterol HDL is more in cashews than the LDL, making it a good source of fat. Studies show copper deficiency increases the risk of hypercholesterolemia (Bes-Rastrollo *et al*., 2009). It was suggested that consumption of cashew nuts reduced the risk of CVD. These nuts due to the presence of MUFA are associated with glucose metabolism which enhances the insulin pathway along with AMPK activation and GLUT4 translocation. The anacardic acid along with polyphenols and fibres in cashews also enhance the insulin pathway, improving its antidiabetic activity and lipid profile (Jamshidi *et al*., 2021). Cashews are also rich in polyphenolics like proanthocyanidins that offer protection against cancer. They also possess high copper content that reduces the effect of toxic cells. Copper has free-radical scavenging capacity that acts in the antioxidant mechanism. Also, it catalyses superoxide dismutase reactions that provide antioxidant defences. Copper also synergistically works like lysyl oxidase enzyme that works in bone and muscle functioning. Collagen structure involves contribution of copper. Copper deficiency also cause anaemia, osteoporosis, cholesterol, *etc*. (Marquardt *et al*., 2012). Along copper, calcium and magnesium are important in bone health. Magnesium acts as calcium blockers in nerves. If, there is a magnesium deficiency, calcium tend to enter the nerve cells. Calcium in nerves causes delirious effects causing over contraction. Thus, required amount of both magnesium and calcium is required to maintain blood pressure, soreness, fatigue and general body health. Apart from these minerals, cashews are also rich in potassium, phosphorus and zinc that are required to maintain a healthy working immune system (Ijarotimi *et al*., 2012). Vitamin E contributes to approximately 6 mg/100 g of cashews, the highest among its counterparts. Vitamins A and B complex were also found in abundance in these nuts. Bioactive compound lignans and aglycones are present in cashews that contribute to antioxidant capacity and its anti-inflammatory properties and also provide protective effect against CVD, hormonal cancers and osteoporosis. Studies by Cordaro *et al*. (2020) showed that cashew nuts consumption increased analgesic, antioxidant and anti-inflammatory properties. Other studies also highlighted that these nuts reduced the damage caused by malfunctioning of intestinal barrier. This restricts the pathogen and their toxic materials, thereby preventing the inflammation of liver and kidney and its functioning.

In the aspect of boosting immune health, the presence of vitamin B, vitamin E and zinc boosts the functioning of immune system. Copper especially renews the blood vessels that helps maintain immune health. Pereira *et al*. (2018) conducted research and established the effects of cashew extracts combined with polyanhydride nanoparticle in the immune responses of mice. It stimulated humoral and cell mediated immune responses. Cytokine production was recorded that also proliferated IL-10, IL-12, and IFN-γ. This shows its immunomodulatory properties. The cashewnut tree gum exudate (CNTG) have many medical properties. They show anti-inflammatory activities against tumours and other infections caused by pathogens. The lipopolysaccharides in cashews produce destructive effects against microbes and toxic tumours through macrophage proliferation. This is done by stimulating phagocytic activities that in turn increases the cytokine concentration and TNF-α and IFN-α and IFN-β and interleukins (Leung *et al*., 2006).

Cashews are eaten in its raw form as kernels and also as roasted nuts. Due to its lower oil content, air dry roasting of cashews are preferred. High temperature treatments not only increases its palatability, but also its nutritional values. Total phenolic contents of cashew nuts increased from 20% to 344% when processed at different conditions. Flavonoids such as catechin, epicatechin, *etc*., and phenolic acids like gallic acid, p-coumaric acid, *etc*., have also risen in concentration due to heat treatment. Tests also show rise in antioxidant activities under such conditions (Chandrasekara and Shahidi, 2011). These processing techniques also reduce the allergenic effect of cashews. Roasting of cashews reduced the reactivity of the allergens (Ana o 3 and Ana o 1 presents in these nuts (Tufail *et al*., 2019).

Table 5: Nutritional composition of cashew nut

S.No	Nutrient (Unit)	Per 100 g
1	Energy (Kcal)	553
2	Carbohydrate (g)	30.19
3	Protein (g)	18.22
4	Fat (g)	43.85
5	Dietary fibre (g)	3.3
6	Vitamin E (mg)	5.31
7	Thiamine (mg)	0.56
8	Niacin (mg)	1.062
9	Riboflavin (mg)	0.058
10	Calcium (mg)	37
11	Potassium (mg)	660
12	Iron (mg)	6.68
13	Zinc (mg)	5.78
14	Copper (mg)	2.2
15	Magnesium (mg)	292
16	Phosphorus (mg)	593

Source: USDA

4.4 Pistachio nut: *Pistacia vera* L.

Pistachio nuts originated from Asian Minor countries. They belong to Pistacia family. These nuts have a desert like taste. Pistachio trees grow up to 12 m. Their leaves are oblong-ovoid shaped and dark green in colour. These trees are dioecious. Fruiting of these trees need up to five years; while it takes ten years for the crop to become economically viable. The whole pistachio nut is enclosed inside a shell called endocarp. The seed inside the shell is called kernel and is covered with thin seed coat. The nut itself varies from light green to greenish yellow as it matures. Pistachio nuts are consumed fresh as raw, dried, roasted, and sometimes salted. They are used in many eatables like pastries, desserts, *etc*. (Kashaninejad and Tabil, 2011).

Pistachios have high nutritive profile which is rich in carbohydrates, fats, proteins and vitamins and minerals. Pistachios contain 10% of fibres that give a satiety feeling when consumed. This property helps in treating obesity. Also, pistachios have low glycaemic index that reduces the postprandial glucose; thereby treating diabetes (Terzo *et al*., 2019). The fat content in pistachio is less about 45.4 g/ 100 g of which, 5.6 g is saturated fatty acids, 13.7 g is PUFA and 23.8 g is MUFA. The unsaturated fatty acids like oleic and linoleic acids possess cardioprotective properties. Also, palmitoleic acid in the form of MUFA in pistachios possess anti-inflammatory properties. When these nuts are grown in high temperatures of 25ºC and above, the presence of saturated fatty acids can be prevented (Satil *et al*., 2004). Pistachios constitute about 20% of protein by weight. Arginine (9.15 g/100 g) one of the most important amino acid in maintaining homeostasis is found in abundance in these nuts. It is known as a precursor of NO, which has many health benefits like modulating antioxidant activities. It also regulates vasodilation process in treating CVD and neurodegenerative disorders (Venkatachalam and Sathe, 2006). Vitamin B-complex is found in excess as many units exceed the RDA. Similarly, vitamins A, E and K are also present in pistachio that gives protective nature against CVD, T2DM, bone metabolism and other inflammatory disorders. Vitamin B6 promotes a good blood flow and maintains the lymphoid glands (lymph nodes, spleen and thymus). These glands are responsible for proper functioning of immune system by producing the immune cells for defense. Minerals like P, K, Mg, Mn, Zn, Se Cu and Ca are present in pistachio nuts. They are responsible for regulating cellular functioning and prevent against CVD and other metabolic disorders and also to maintain the blood pressure. Zinc and selenium in specific is responsible for working of immune system (Huang *et al*., 2006). Pistachios are also rich in plant phytochemicals. The phenolic compounds of pistachios like flavonoids, anthocyanin, phenolic acids, tannins, *etc*., shows chemopreventive, cardioprotective and vaso-protective abilities. They also show high antioxidant and anti-inflammatory activities which decreases the risk of cancer and CVD; and reduces the LDL. The harmful effects of lipid oxidation are reduced when these phenolic compounds interact with metal (Bulló, *et al*., 2015). Pistachios are the only nuts that has significant amount of α-and β-carotene, lutein and zeaxanthin, a form of carotenoid. They show strong antioxidant properties. They exhibit mechanisms to decrease the LDL synthesis and maintain a good lipid profile (Karppi *et al*., 2010).

Nuts in general are perceived as high fat content foods. But in reality, good cholesterol and good fat helps in reducing the body fat content and body weight. Studies show that when pistachios are consumed at regular intervals, there was a visible reduction in BMI. Thus, these nuts are employed in diets. The high fat, protein content and unsaturated fats give a satiated feeling and also produce thermogenic effects that reduce the risk of obesity. RCT conducted to evaluate the effect of pistachios on weight control. Low calorie diet along with pistachio supplementation was introduced to obese people (Gulati *et al*., 2014). The result showed significant reduction in the BMI along with waist: hip ratio. Pistachios also increase the insulin sensitivity that reduces the risk of T2DM. Proanthocyanidins in

pistachio nuts inhibit the inflammatory responses of epithelial cells by curbing the NF-κB mechanisms (Gentile *et al*., 2015). Adiponectin, an adipocyte-related hormone that possess anti-inflammatory activities have been found to increase in concentration due to pistachio inclusion in the diet. The polyphenols and other phytosterols in pistachios acts as free radical scavenger. Lipid oxidation due to reactive oxygen species are prevented by these nuts. The leaves and the hull of pistachios also possess antioxidant properties, and hence can be used as supplements in pharmaceutical industries (Grace *et al*., 2016).

Table 6: Nutritional composition of pistachio nut

S.No	Nutrient (Unit)	Per 100 g
1	Energy (Kcal)	560
2	Carbohydrate (g)	29
3	Protein (g)	26.16
4	Fat (g)	45.4
5	Dietary fibre (g)	10.6
6	Vitamin C (mg)	5.6
7	Vitamin E (mg)	2.86
8	Thiamine (mg)	0.87
9	Riboflavin (mg)	0.16
10	Niacin (mg)	1.3
11	Vitamin B6 (mg)	1.7
12	Calcium (mg)	105
13	Magnesium (mg)	121
14	Phosphorus (mg)	490
15	Zinc (mg)	2.2

Source: USDA

4.5 Walnut: *Juglans regia* L.

Walnut was originated in Central Asia and Eastern European countries. It belongs to Juglandaceae family. China is the top producer of walnuts while India is the seventh largest producer. It has been in use for many thousands of years. Walnuts are used in daily consumption due to its numerous health benefits. These nuts are brain shaped and also highly associated with brain's wellness. Walnuts possess huge amount of fats, protein, vitamins and minerals. It is also rich in anti-oxidant sources and other healthy plant polyphenols. These nuts provide protection to various body functions and effects many diseases and disorders like CVD, high cholesterol, cancer, neurological disorders, inflammatory disorders, immune functions, *etc*. Apart from consumption for its nutritional benefits, walnuts are used for dyeing and manufacturing of wool (Hayes *et al*., 2016).

The fat in walnuts is around 65% of its weight. These fat constitute to its energy through the calorie content. The fat in walnuts is mostly mono-unsaturated fatty acids; especially omega 3 and omega 6 fatty acid and arachidonic acid. These omega fats are highly beneficial in cardio health. These improve the lipid profile and reduces the cholesterol content. Many studies established a strong link between the fats present in walnuts and its protective nature for CHD, CVD and metabolic disorders like hyperlipidaemia (Micha and Mozaffarian, 2010). Omega 3 and omega 6 showed relationship between increased proinflammatory responses. Research conducted by Tapsell *et al*. (2004) produced results that inclusion of walnuts in the diet of T2DM improved the subjects HDL and improved their lipid profiles. This has an impact on the cardio health. Another aspect of the importance of omega fats were studied by many researchers. They deduced a connection between consumption of walnuts and the hormone levels in the serum. Two of the most important such hormones that has anti-inflammatory effects are adiponectin and apolipoprotein. The higher the ratio of omega 3: omega 6 fat, the higher the carcinogenesis occurs (Jiang *et al*., 2012). Linolenic acid present in walnuts as PUFA destructed the cancerous cells. Also, omege 3 fatty acids are used in the treatment of neurological disorders like Alzheimer's in ageing patients. Experiments on rat show the correlation between walnut consumption and enhanced cognitive abilities (Willis *et al*., 2009). The presence of tocopherols prevents lipid oxidation.

Fibre and protein content in walnuts attributes to many medical benefits. The amino acid, arginine is a precursor of NO, which acts an effective vasodilator. These nuts also constitute important minerals like copper, phosphorus, manganese, *etc*., they are vital in maintaining the immune system (Fatima *et al*., 2018). Walnuts are a rich source of vitamins E and B complex. Vitamin E is present in two forms (α-tocopherol and γ-tocopherol). Walnuts satisfy about 140% of the RDA of vitamin E. This fat soluble vitamin acts as a strong antioxidant that scavenges free radicals and keeps the body from inflammation or infections. Vitamin B as thiamine, niacin, riboflavin, folate, B6, pantothenic acid is present in walnuts. They also provide anti-inflammatory effects. This vitamin specifically controls the blood pressure and checks on heart health and also maintains the functioning of nervous system. Vitamin B is very important to regulate the immune system (Sen and Karadeniz, 2015).

Walnuts possess a complex variety of phytochemicals including tannins, phenolic acids, flavonoids, *etc*. The extract of walnut consisting of ellagic acid and other polyphenols like tannins has proven to inhibit plasma and LDL lipid oxidation. Studies also show regular consumption of walnuts reduced LDL due to the effects of these polyphenolic compounds along with α-tocopherol (Anderson *et al*., 2001). The phenolic acids (especially ellagic acid) proves to be an inhibitor of cancer cells. These acids also inhibit auto-oxidation of lipids. Stilbenes in walnuts assume the form transresveratrol (trans-3,4',-5-trihydroxystilebene). This compound exhibit antimicrobial activity. They also possess anti-inflammatory, antioxidant and anti-tumour properties (Smoliga *et al*., 2011). Ellagitannins is the polyphenol structure present in walnut that is hydrolysed with mineral acids from digestion to obtain ellagic acid. This ellagic acid is further metabolised as urolithins A and B which is absorbed in the human body. These ellagic acid also plays a protective role in nicotine-

induced toxicity in rat models. The blood lymphocytes filled with nicotine increased the oxidation process which destructed the DNA processing (Sudheer *et al*., 2007). Ellagitannins also show high anti-inflammatory properties by inhibiting the inflammatory process. Affecting the inflammatory molecules like NO, IL-1β, TNF-α, COX-2, *etc*. Walnuts are known for its immunomodulatory properties. The presence of oligopeptides in walnuts attribute to this bioactivity. This was tested on mice by Mao *et al*. (2020) to study the effect of walnuts oligopeptides and its immunomodulatory effects. The study proved the phagocytic capabilities of walnuts by increasing the innate and adaptive immunity. The concentrations of NK immune cells, T cells, spleen cells, cytokines, *etc*., increased exponentially. B-lymphocytes were activated producing antibodies. Immunoglobulins are produced during any external pathogenic attack. This shows the effect of walnuts on the immune system of the human body.

Table 7: Nutritional composition of walnut

S.No	Nutrient (Unit)	Per 100 g
1	Energy (Kcal)	654
2	Carbohydrate (g)	13.71
3	Protein (g)	15.23
45	Fat (g)	65.21
6	Dietary fibre (g)	6.7
7	Vitamin E (mg)	0.7
8	Vitamin K (µg)	2.7
9	Vitamin C (mg)	1.3
10	Thiamine (mg)	0.341
11	Riboflavin (mg)	0.15
12	Niacin (mg)	1.125
13	Vitamin B6 (mg)	0.537
14	Calcium (mg)	98
15	Iron (mg)	2.91
16	Magnesium (mg)	158
17	Phosphorus (mg)	346
18	Potassium (mg)	441
19	Zinc (mg)	3.09
20	Manganese (mg)	3.414

Source: USDA

4.6 Chestnut: *Castanea sativa* Mill.

Chestnuts are edible nut varieties that grow in temperate regions in northern hemispheres. They belong to Fagaceae family (Beech family). These nuts have been a staple food in European and Asian countries where cultivation of cereals was difficult. It was also called as 'bread-tree' due to this reason. Italy is the leading producer of chestnut. Due to its health benefits, the consumption of chestnut has doubled in the past few decades. They are rich in carbohydrate, fibre, and vitamin and mineral but low in fat content. Chestnuts are sold as raw nut, roasted, boiled, frozen and also crystallised. They are usually marketed after a few processing steps to improve their organoleptic properties and to make them more palatable; since they possess a bitter taste in its natural form due to the presence of tannins (Wani *et al*., 2017). These marketed nuts are used in many edible foods like cakes, bread, gluten-free beers, candied nuts, *etc*. Not just nuts, the whole plant of the chestnut has been proven beneficial. Flowers, nectar, pollens, bark, kernel, *etc*., all have good antioxidant property, antitumour activity and also protect against metabolic and cardiodisorders. The honey from the chestnuts' flowers is abundant in minerals like calcium, manganese and potassium which enhances it antibacterial properties; hence used for wound dressing. Similarly the flowers possess antimelanogenic property and can be used in food and pharmaceutical industries (Sapkota *et al*., 2010).

Chestnuts are rich in starch content, accounting for about 50% of its weight. Its starch content is more than that of potatoes, and hence are consumed for its health benefits. Amylose and amylopectin and the sugar content in the form of sucrose provide the energy source from chestnuts. These sugars also act for its palatability factor. The fibre content of these attribute to the protective nature for metabolic disorders, cardiovascular disorders, lipid profile, *etc*. In contempt of low fat content, these nuts possess good amount of unsaturated fatty acids like linoleic and linolenic acids that attribute to neuroprotective and cardioprotective properties, along with anti-tumour activities (Vasconcelos *et al*., 2010). The protein content in chestnut is ordinary that meets about 9.2% of RDA in females and 7.6% in males. Aspartic acid, glutamic acid, arginine, GABA are the prominent amino acids contributing to the medical benefits. GABA is known for its mechanism as neurotransmitter inhibitor which regulates the CNS functioning. This property protect the human body against neurological disorders like Alzheimer's and Parkinson's diseases (Gajcy *et al*., 2010). The chestnuts are rich in vitamins C and E which are the most essential vitamins to maintain immune system. They provide good protection against pathogens and also possess anti-inflammatory and antioxidant activities. Vitamin E provides protection against CVD and cancers. Vitamins A and B-complex are also seen in a considerable amount in these nuts. Thiamine, riboflavin, folates, pantothenic acid, *etc*., works to provide good brain and nervous system functioning (Barros *et al*., 2011). These nuts are also abundant in minerals like Ca, K, P, Zn, CU, *etc*., The bioactive compounds like phenolic acids, flavanoids, *etc*., are present in the whole plant rather than just the nuts. Some important polyphenols that provide health-promoting activities are ellagic acid and gallic acid. These compounds provide antiplasmodic and anticarcinogenic activities (Okuda, 2005).

There are numerous health benefits provided by chestnut consumption. Due to its less fat content, it can be confidently eaten by people who are conscious of weight gain. The essential fatty acids present in chestnuts maintain the serum lipid profile, insulin activity and also immune functions. The extracts of the nuts reduced the cholesterol level and also decreased the lipid oxidation, specifically

LDL that induces damages in cardiovascular pathways. Fibres in chestnut also participates in the mechanism that control fat in the body. Jesch and Carr (2017) elucidated a pathway to understand this process. The fibres in the nuts are fermented by the microbiota which lag the gastric emptying process and enhances the glucose uptake *via* glucose transporter type 4 expression. This will lead to less absorption of fat while the excretion of fat is more. Fibres also improve the gut flora (*Bifidobacterium* and *Lactobacillus*) that decreases the LDL and cholesterol levels. These dietary fibres also provide therapeutic effects against diabetes and many types of cancer. Cancer protection is associated to the bioactive compounds in the chestnut like omega-3 fatty acids, ellagic acid, gallic acid, vitamin C and vitamin E. These vitamins synergistically act as a strong antioxidant and reduce the risk of CVD and cancer. While vitamin B increases the iron metabolism and improves the hematologic condition (Powers, 2003). Chestnuts possess optimal amount of both macro-elements and micro-elements. Calcium deficiency results in osteoporosis, hyperlipidaemia and also increases the blood pressure. Magnesium deficiency results in metabolic disorder, cardiovascular disorders, *etc*. Potassium is important in CNS functioning. Zinc and copper are very important minerals in regulating the immunomodulatory functions (Martínez-Ballesta *et al*., 2010). The chestnut honey has innumerable health properties. It is used for treating cold and upper respiratory tract infections. It also possess strong antioxidant and anti-inflammatory activities. Güne *et al*. (2017) reported that the honey show antimicrobial activities against virus, bacteria and fungi due to its phenolic content. Propolis is a bee product that can be generated form chestnut flowers. This product has shown to improve the host defense mechanisms and provide antimicrobial properties. The propolis flavonoid enhances the cellular and humoral mediated immunity.

Table 8: Nutritional composition of chestnut

S.No	Nutrient (Unit)	Per 100 g
1	Energy (Kcal)	196
2	Carbohydrate (g)	44.2
3	Protein (g)	1.6
4	Fat (g)	1.3
5	Vitamin E (mg)	1.2
6	Vitamin C (mg)	40.2
7	Thiamine (mg)	0.23
8	Riboflavin (mg)	0.168
9	Niacin (mg)	1.1
10	Vitamin B6 (mg)	0.4
11	Calcium (mg)	27
12	Iron (mg)	0.9
13	Magnesium (mg)	30
14	Phosphorus (mg)	93
15	Copper (mg)	0.4
16	Zinc (mg)	0.52
17	Manganese (mg)	0.3

Source: USDA

4.7 Brazil nut: *Bertholletia excelsa* Humb. & BONPL.

Brazil nuts originated in the South America. They belong to Lecythidaceae family and grows in tropical regions. The Brazil nut trees are evergreen and grow very tall up to 150 ft in height. Its nuts are round in shape about 6 inches in diameter. These Brazil nuts bear fruits that are pear-shaped. These Brazil nut fruits individually consist of 12 to 24 nuts. These nuts are elongated in shape (Yang, 2009). This nut is known for its selenium content. It satisfies about 100 times the RDA of selenium. Selenium is an excellent source of anti-oxidant and plays a very important role in immunemodulatory functions. This element also reduce the risk of neurodegenerative disorders, cancers, *etc*. It also regulates thyroid functioning (Meplan and Hesketh, 2014).

The nutritional composition of Brazil nuts is 3.5% of water, 12.3% of carbohydrates, 14.3% of protein and 66.4% of fats. This high level of fats and protein usually gives a satiety feeling after consumption of this seed. They have low concentration of saturated fats (15%) and large quantities of unsaturated fatty acids (MUFA-25% and PUFA-21%). These unsaturated fatty acids in Brazil nuts are mainly oleic, linoleic, omega-3 (7%) and omega-6 fatty acids (Cardoso *et al*., 2017). The protein content in these are lower when compared to other nuts. Brazil nuts contain various trace elements that provide many healthy attributes. These elements are used as co-factor in many metabolic pathways in the body. Brazil nuts are rich in magnesium, calcium, zinc and selenium. Other minerals present in these nuts are copper, chromium, iron, *etc*. Selenium in Brazil nuts are the highest than any other nuts like cashew nuts, walnuts, peanuts, *etc*. The concentration of Se is dependent on the type of soil. Brazil nuts grown in central parts of Brazil, have more Se concentration than the same type of Brazil nuts grown in western Brazil (Dumont *et al*., 2006). The bioactive compounds in nuts include phenolic acids, flavanoids, phytosterols, *etc*. The main activities of these compounds are antioxidant and anti-inflammatory properties. In Brazil nuts, these bioactives are either in esterified or free form. Brazil nuts and almonds possess the highest concentration of polyphenols in comparison to its counterparts (Alasalvar and Bolling, 2015). Brazil nuts consist of considerable amounts of tocopherols, flavanols and sterols. Other important value addition providing compounds found in these nuts are ellagic acid, gallic acid, protocatechuic acid and catechin. These attribute to the nuts' antioxidant capabilities. The brown skin on the kernels contains more quantities of these phenolics than the kernel and other parts. Brazil nuts consist of higher concentration of squalene, which is a strong antioxidant.

The most unique feature of Brazil nut is the immense amount of selenium. Though, it does not primarily act as an antioxidant, it acts as an important antioxidant enzyme. This element along with zinc and copper provides a strong immune system. Functioning of thyroid glands is regulated by Se. This is highly necessary as thyroid and its hormones are one of the first line of defense. Se with vitamin E acts

against many cancers and provide anticancerous property. The mechanism behind this is by stopping the cell cycle of the tumour cells and promoting apoptosis (Jiang *et al*., 2001). Many RCT shows the connection of increased intake of selenium in diet and decrease in the risk of many cancers including prostate cancer, mammary cancer, gastric cancer, colon cancer (Yang, 2009). Consumption of these nuts (50 g) increased the IL-10 which promotes anti-inflammatory activities while decreased pro-inflammatory interleukins. Antioxidant inducing selenoproteins were increased in the serum due to inclusion of these nuts in the diet. Colpo *et al*. (2013) conducted studies suggesting that 20 g of Brazil nuts increased the HDL and decreased the concentration of LDL. Thus, these nuts can be used by obese patients to improve their lipid profile without increasing their cholesterol levels. Insulin levels were regulated during this period. All these evidences show the nuts' protective nature against CVD.

Table 9: Nutritional composition of Brazil nut

S.No	Nutrient (Unit)	Per 100 g
1	Energy (Kcal)	656
2	Carbohydrate (g)	11.47
3	Protein (g)	14.3
4	Fat (g)	66.4
5	Dietary fibre (g)	7.5
6	Vitamin E (mg)	7.87
7	Vitamin C (µg)	0.7
8	Thiamine (mg)	0.6
9	Riboflavin (mg	0.035
10	Niacin (mg)	0.3
11	Vitamin B6 (mg)	0.1
12	Calcium (mg)	160
13	Iron (mg)	2.4
14	Magnesium (mg)	376
15	Phosphorus (mg)	725
16	Copper (mg)	1.7
17	Zinc (mg)	4.1
18	Manganese (mg)	1.2
19	Selenium (mcg)	1917

Source: USDA

5. Conclusion

Proper nutrition is required to support the immune system to work against pathogenic attacks. Deficiency of these macro and micro nutrients take a toll on the bodys' health. In times of pandemic like COVID-19, intake of highly nutritious balanced diet provides many health-promoting activities. Foods like vegetables, fruits and nuts that boost the immune system should be strictly accommodated in the daily diet to counteract the pathogens. PUFA, omega-3 fats, vitamins E, C, B-complex and minerals like zinc, copper and selenium play a vital role in enhancing the immunomodulatory properties. The anti-inflammatory capability and antioxidant status of the body are very important to provide protection against diseases. Flavanoids, phytosterols, phenolic acids, *etc*., are bioactive compounds that promote healthy attributes. Nuts are energy dense food with many health effects that are backed up by profuse evidences from clinical trials and epidemiological studies. Inclusion of nuts in diet administer cardio-protective effects and also protects from metabolic disorders, obesity, diabetes, inflammation, *etc*. Apart from these properties, nuts also enhance the immunity in human body by offering protection from external pathogens. The nuts discussed here are almonds, cashew nuts, peanuts, walnuts, Brazil nuts and chestnuts which contain various beneficial components in abundance and consumption of these nuts in required quantities offer well-being.

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Conflict of interest

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

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