Vitamins & Minerals
ISSN: 2376-1318

Aslam et al., Vitam Miner 2017, 6:1
DOI: 10.4172/2376-1318.1000153

Review Article Open Access

Vitamins: Key Role Players in Boosting Up Immune Response-A Mini Review

Muhammad Farhan Aslam[1,3], **Saad Majeed**[1], **Sidra Aslam**[4] **and Jazib Ali Irfan**[2,3*]

[1]*Human Nutrition and Dietetics, Department of National Institute of Food Science and Technology (NIFSAT), University of Agriculture, Faisalabad, Pakistan*

[2]*Biotechnology, Centre of Agricultural Biochemistry and Biotechnology (CABB), University of Agriculture, Faisalabad, Pakistan*

[3]*National Institute for Biotechnology and Genetic Engineering (NIBGE), Faisalabad, Pakistan*

[4]*Bioinformatics, Beijing Normal University, Beijing, China*

[*]**Corresponding author:** Jazib Ali Irfan, Biotechnology, Centre of Agricultural Biochemistry and Biotechnology (CABB), University of Agriculture, Faisalabad, Pakistan, Tel: +923465449709; E-mail: jazibali10@yahoo.com

Received date: March 07, 2017; **Accepted date:** March 17, 2017; **Published date:** March 31, 2017

Abstract

Vitamins perform different functions in our body and to boost up immune response towards pathogens is one of them. Immunity provides protection to life by its three main such as skin, cellular response, and humoral immune response. Both vitamins quality and quantity within the body promote systematic immune processes by regulating T-lymphocytes, antibodies, and cytokines formation. In this review, we will summarize the role of water soluble and fat soluble vitamins to boost up immunity functions. Vitamins A, C, and E mainly aid in enhancing the skin epithelium barrier function. With the exception of vitamin C, all the vitamins are claimed to be essential for antibody production. Most of the vitamins are applied in our body to produce a cell-mediated response with the production of cytokines and T-lymphocytes. Supplementation of the diet with vitamins in specifically selected appropriate quantities routinely can support body's natural defence mechanism by enhancing the immune response.

Keywords: Vitamin A; Folate; Vitamin C, D, E; Humoral immune response; Cell mediated response

Structure of Review

Vitamins being natural components that carry out various important biochemical activities in our body are required in appropriate amounts in our daily diet, if not taken properly or if their concentration in our body gets reduced due to any known or unknown causes then it may lead to a number of unpleasant health conditions. Researches related to intake of vitamins have been increased since last decade due to their vital importance in boosting the innate immunity of our body. Some major vitamins like A, B, C, D, and E have been reported to boost up the immune system by strengthening the activity of immune cells during any pathogen attack or in the case of the intrusion of some toxic materials either inhaled from air or that may be present in the foods. This review focuses on the compilation of some of the previous and recent studies regarding the role of vitamins that they play in boosting or enhancing the immune system. With the compilation of these studies in a review, it will be helpful for the future scientists to get the sufficient information from this review regarding the role of vitamins in enhancing the immunity.

Introduction

Vitamins are vital organic nutrients in our meal that are utilized by the cells of our body for proper growth, development, disease prevention like deficiency disorders, and to improve immune system efficacy. Vitamins are taken routinely along with diet and are required in proper trace amounts so that all the barriers of the immune system such as skin, cell-mediated and humoral immune response etc. could be sustained. The immune system helps in preventing the active tissues of the body from the agents that lead to diseases [1]. Bioavailability of vitamins varies with age, sex, and physiological conditions. Their quantities within the body are mostly regulated by the type of dietary intakes and eating habits. Vitamin supply can also be affected by drugs, tea or caffeine, smoking, alcohol abuse, dietary fibers (phytates) etc., This review focuses on almost all vitamins either water/fat-soluble vitamins, in context with the human immune system. Vitamin deficiency suppresses overall immunity by affecting cell-mediated and adaptive immune response, leading to impaired regulation of the balanced immune response with increased morbidity, malnutrition, and mortality. Vitamins A, C, and E mainly aid in enhancing the skin epithelium barrier function. With the exception of vitamin C, all the vitamins are claimed to be essential for antibody production [2]. Vitamins are also vital for developing innate immunity and adaptive immunity in the body [3]. Most of the vitamins like, B_6, B_9, B_{12}, A and D are also applied in our body to boost-up the cell-mediated immune response with the production of cytokines and T-lymphocytes. Overall, inadequate intake and lowered nutritional status of these vitamins and trace elements may lead to suppressed immunity, which predisposes to infections and aggravates malnutrition. Therefore, the intake of appropriate amounts of all such essential vitamins in our daily diet can help in supporting the cognitive power of the body leading to well-being of health [4].

Bioavailability

Bioavailability means availability of vitamins in blood circulation and their effect in our body as we understand it commonly. In broader spectrum, bioavailability is defined as the proper absorptivity and uptake of various nutrients by the cells [5,6]. Factors that affect bioavailability vary by age, sex, and physiological conditions, like pregnancy [7]. Vitamin deficiency occurs more commonly either due

to insufficient intake of the vitamins or due to disturbances in absorption and utilization of these vitamins from the gut. Malnutrition results in weakened immunity and hence people are attacked by chronic infections due to weak immune response. Many types of eating disorders like anorexic/bulimic condition and binge eating and problems in ingestion or engulfing food reduce total dietary intake of vitamins. Vitamin bioavailability also depends on the type and amount of nutrients digested along with the body, such as phytates present in beans and veggies, and caffeine in tea/coffee reduces vitamin and mineral absorption. Sometimes increase or decrease of one vitamin may also affect vitamin absorption, for example, vitamin B_6, B_9, and B_{12} work together to enhance its absorption but if any vitamin is reduced then it may affect others. Some drugs like antibiotics, anti-inflammatory, histamine, anti-seizures etc. decrease vitamin B complex, vitamin D and C levels within the body cells. Few well-known diseases like as "celiac disease" and "lactose intolerance" lessens the vitamin absorption by affecting the digestive processes, like incomplete digestion.

β-carotenes and retinol (a precursor of vitamin A) are the major precursors of vitamin A [8], (Figure 1) Vitamin A occurs naturally in food stuffs like fish, beef liver, eggs, and dairy products which are the animal sources for vitamin A precursors such as retinol and palmitate, whereas green leafy vegetables and fruits serve as plant sources for carotenoids that can be converted into retinol. Vitamin A plays a key role in enhancing eye sight, growth, reproduction, blood cells formation and it also improves body's immune response [9]. β-carotenes function as an antioxidant when it comes to the enhancement of immune response [10], like, for example, in an experiment, when dairy cows were given 300 mg-600 mg β-carotene/day, this supplementation resulted in the reduction of the incidence of retained placenta and metritis as compared to control cows [11]. Retinoic acid which acts as vitamin A metabolite, derived from retinol enhances the lymphocyte proliferation [12] and mitogen stimulation. In the case of innate immunity vitamin A is essential for maintaining and recovery of epithelial structures at the skin, urinary tract and lungs epithelium. According to Villamor and coworkers [13], vitamin A supplementation shows no effect on the concentration of immune factors in cervicovaginal fluids of HIV-infected pregnant women. However, Vitamin A supplementation imparts beneficial effects on intestinal integrity among children suffering from severe infections or to those who are malnourished [13]. It has also been known that vitamin A derivative called retinoic acid also plays an important function of allowing the proper migration of T-cells to the site of inflammation or infection in the gut [14] and this dispatching of immune cells to the proper sites in the gut is referred as gut homing, which is brought about by the presence of certain codes present on the receptors of T-cells [15]. Derivative of retinol (retinoic acid) is involved in the proper migration of the, cytotoxic killer cells (CD8 or T-lymphocytes), CD4 (helper T cells), and immunoglobulins involved in the immune response through mucous membrane (IgA) antibody producing cells.

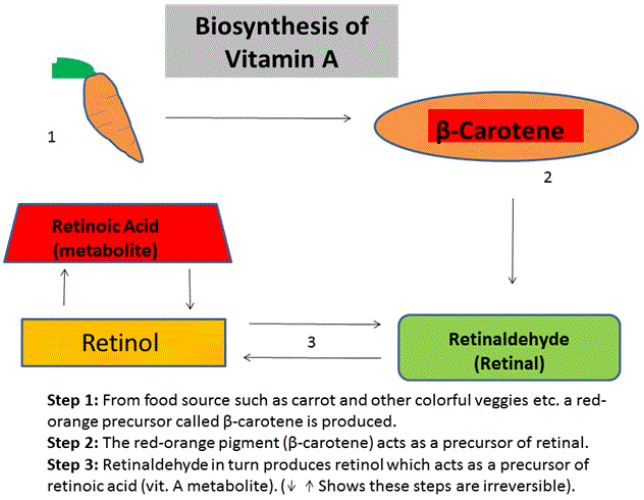

Figure 1: A brief and general schematic of Vitamin A biosynthesis.

Anti-HCV Role of Retinol (Vitamin A)

Slow deterioration of liver and hepatic cancer due to the hepatitis C virus is one of the leading causes of final phase of hepatic disease called hepatitis C [16]. Recent studies have shown that the derivative of vitamin A called retinoic acid has the role of viral inhibition [17]. Liver is the main site of detoxification of alcoholic compounds and poisons. Cho [16] hypothesized that in the people who abuse alcohol in their diets suffer from liver cancer or their liver undergoes cirrhotic conditions due to the impairment of vitamin A in their hepatic cells, thus providing the evidence of relationship between vitamin A reduction and HCV attack. In such people or patients, liver starts to deteriorate slowly due to reduced or suppressed retinol conversion to retinoic acid. In the liver cells, the alcohol in the form ethanol is converted into acetate through the activity of certain enzymes that convert the alcohol in the form that can be easily flushed out from the body, the enzymes that play such role are, the alcohol dehydrogenase and aldehyde dehydrogenase; the process starts by the metabolization of alcohol into acetaldehyde in the presence of alcohol dehydrogenase enzyme, which is further converted into acetate by the activity of aldehyde dehydrogenase [18]. Besides this ethanol neutralizing activity, both of these enzymes also play vital role in the conversion of retinol to retinoic acid. In the liver cells of people who use alcohol routinely beyond their optimum requirements, the concentration of ethanol often increases beyond the concentration of alcohol dehydrogenase being produced in their hepatic cells and this increase in ethanol also causes the decreased retinoic acid production leading to vitamin deficiency in hepatic cells [19]. During hepatitis C virus (HCV) attack the host cells start producing interferons which are the natural viral replication inhibitors and these interferons also lead to the activation of the interferon genes of the nearby cells which are called as interferon stimulated genes [20]. It has also been found that some of these genes activated by interferons also include certain genes that are activated or expressed in the presence of retinoic acid or they can be said to be the genes whose transcription is induced by retinoic acid [21]. All these studies provide evidence that improper vitamin A (retinol) conversion to retinoic acid by the alcohol dehydrogenase and aldehyde dehydrogenase leads to the decreased interferon production due to the

inactivation of interferon producing genes which causes the liver cells to become susceptible to alcohol dependent HCV attack.

According to WHO, the vitamin A deficiency is a serious public health problem that affects 127 million preschool children and in recent results, it leads to the deaths of approximately 20 million people in the low income countries which is estimated to be the 2.4% of the total deaths due to vitamin A deficiency worldwide. In children, vitamin A deficiency results in increased risks of mortality and morbidity from measles and diarrheal infections, night blindness, and anemia, and among women it is likely to be associated with high mortality related to pregnancy. So, its consumption in daily diet should be increased according to Dietary Reference Intake's (DRI) recommended values.

Mentioned in Table 1 is the USDA National Nutrient Database for vitamin A intake recommended for different age groups along with the natural sources of vitamin A.

Sources of Vitamin A	Vitamin A Deficiency Causes	Recommended Dietary Intake of Vitamin A for Male and Female per day	
		Male	Female
Sweet potato, spinach, carrots, pistachio nuts, broccoli, peppers, egg, cheese, apricots	Night Blindness (xerophthalmia), diarrhea, anemia, measles	300 mcg (for age 1-3 years)	300 mcg (for age 1-3 years)
		600 mcg (for age 9-13 years)	600 mcg (for age 9-13 years)
		900 mcg (for adults)	700 mcg (for Adults) 770 mcg (for pregnant) 1300 mcg (for lactating)
mcg=Microgram=(1×10^{-6}) of a gram			

Table 1: Recommended Dietary Allowance (RDA) for Vitamin A.

Vitamin B Complex and Immunity

Vitamin B complex was historically supposed to be the single vitamin but later it was found that it consists of several different compounds that can be grouped into different categories according to their functional distinctions [22], members of B complex include thiamine (B_1), riboflavin (B_2), niacin (B_3), pantothenic acid (B_5), pyridoxine (B_6), biotin (B_7), folic acid (B_9) and cobalamins (B_{12}) [23]. Several members of vitamin B complex are used in our body to promote the defensive role for better health and prevention of diseases by boosting-up the immune system. Types of vitamins that fall in this category of vitamin B complex play a key role by acting as antioxidants in the body thus enhancing the efficiency of the immune response [24]. Members of vitamin B complex that have such roles in immune response efficacy include vitamin B_6, B_9 and B_{12}.

Vitamin B_6

Vitamin B_6 actually acts as co-factor for certain enzymes that helps the in carrying out their respective functions [22]. B_6 contains 3 pyridine derivatives therefore it is named as pyridoxine. Vitamin B_6 helps control levels of homocysteine in the blood. Homocysteine is a common amino acid [25]. Higher level of homocysteine (hyper-homosysteinaemia) is associated with heart diseases like Acute Coronary Syndrome (ACS) and cardiovascular death, collectively called athero-thrombosis [26,27]. The body needs B_6 in order to absorb vitamin B_{12} and to make red blood cells and cells of the immune system. Vitamin B_6 helps the body to make several neurotransmitters like serotonin, chemicals that carry signals from one nerve cell to another. Serotonin is only synthesized by the tryptophan and this conversion of tryptophan to serotonin occurs in the presence of pyridoxal phosphate which is a vitamin B_6 derivative [28]. Vitamin B_6 is needed for normal brain development and function, and helps the body to make nor-epinephrine, which influences the mood, and melatonin, that helps in regulating the body clock. Symptoms of serious deficiency included muscle weakness, nervousness, irritability, depression, difficulty concentrating and sometimes short-term memory loss. According to National Institute of Health in USA, the Recommended Dietary Allowance of vitamin B_6 for adults should be 2 mg per day [22]. Vitamin B_6 helps to improve immune response to the increase in production of antibodies and also helps in communicative interactions between cytokines and chemokines [29]. Vitamin B_6 deficiency reduces the lymphocyte growth and proliferation, antibody formation and T-cell activity [30].

Sources of Pyridoxine (B_6)	Deficiency of B_6 Causes	Recommended Dietary Intake of Vitamin B_6 per day	
		Males	Females
Beef liver, chickpeas, tuna, salmon, rice, cereals, onions	Depression, weak immunity, dermatitis, anemia, confusion.	0.5 mg (age 1-3 years)	0.5 mg (age 1-3 years)
		1 mg (age 9-13 years)	1 mg (age 9-13 years)
		1.3 mg (adults)	1.3 mg (adults) 1.9 mg (pregnant) 2.9 mg (lactating)

Table 2: Recommended Dietary Allowance (RDA) For Pyridoxine (B_6).

Table 2 shows the USDA National Nutrient Database for vitamin B_6 intake recommended for different age groups along with the natural sources.

Vitamin B_9

Vitamin B_9 or Folic acid (folate) also plays a role in immunity enhancement. It is commonly a key role player in the biosynthesis of nucleic acids, proteins [31] blood cells and nervous tissues [25]. Rich sources of folic acid include, poultry, shellfish, salmon, tuna, dark leafy

vegetables, whole grains, beans, orange juice, citrus fruits, cantaloupes, asparagus, milk etc. Folic acid is crucial for proper brain function and plays an important role in mental and emotional health. Its deficiency in central nervous tissue may lead to depression, insomnia, fatigue, anxiety etc., [32]. For adults, Reference Dietary Intake of folate is 400-600 mcg/day for pregnant and for lactating it is 500 mcg/day.

Table 3 shows the USDA National Nutrient Database for vitamin B_9 intake recommended.

Sources of Vitamin B_9	Deficiency of Folic Acid Causes	Recommended Dietary Intake of B_9 Per Day	
Lettuce, avocado, spinach, kidney beans, shellfish, salmon, egg, rice, peanuts	Elevated blood homocysteine levels, megaloblastic anemia, fingernail pigmentation, tongue ulcers.	Males	Females
		150 mcg (age-1-3 years)	150 mcg (age 1-3 years)
		300 mcg (age 9-13 years)	300 mcg (age 9-13 years)
		400 mcg (adults)	400 mcg (adults) 600 mcg (pregnant), 500 mcg (lactating)

Table 3: Recommended Dietary Allowance (RDA) for Folate (B_9).

Vitamin B_{12}

They are also known as cobalamins because they contain cobalt [25]. Normally, 2.4-2.6 mcg for pregnant women and 2.8 mcg/day intake of vitamin B_{12} for lactating women is recommended. It aids in the metabolism of every cell of the human body, especially affecting DNA synthesis, fatty acid, and amino acid metabolism. It is also involved in B-cell synthesis and T-cell multiplication [33]. According to Vellema [34], in animal models, when they were devoid of vitamin B_{12} in their diets, as a result, deficiency of B_{12} caused immune response reduction during viral and bacterial infections in those model animals. This experimentation gave the proof of importance of vitamin B_{12} in boosting body's immunity. Vitamin B_{12} cannot be synthesized naturally in humans and plants. Only bacteria have the enzymes needed for B_{12} synthesis. Food sources of vitamin B_{12} are animal products that include meat, fish, poultry and dairy products. In Table 4 is the USDA National Nutrient Database for vitamin B_{12} intake recommended for different age groups along with the natural sources.

Sources of B_{12} (Cobalamins)	Deficiency of B_{12} Causes	Recommended Dietary Intake of B_{12} per day	
Milk, yogurt, cheese, egg, trout, cereals	Megaloblastic anemia, weight loss, fatigue, confusion, weakness, depression	Males	Females
		0.9 mcg (age 1-3 years)	0.9 mcg (age 1-3 years)
		1.8 mcg (9-13 years of age)	1.8 mcg (9-13 years of age)
		2.4 mcg (14 years and +)	2.4 mcg (14 years and +) 2.6 mcg (pregnant) 2.8 mcg (lactating)

Table 4: Recommended Dietary Allowance (RDA) for Cobalamins (B_{12}).

Vitamin C and Immunity

It is commonly known as the L-ascorbic or simply ascorbic acid found in almost every type of body tissue but in pituitary gland and in central nervous system, it is present in higher concentrations, approximately up to 400 mg/kg [25]. Ascorbic acid stimulates iron absorption from the intestine and modulates iron transport for storage and is also involved in cellular growth and differentiation and collagen formation, also helps in the formation of catecholamine and carnitine [35], in the brain it aids in natural synthesis of vital neurotransmitters like dopamine and noradrenalin [25]. Vitamin C boosts up human immunity towards infections and cold illnesses by increasing phagocytosis, lymphocyte proliferation and neutrophil chemotaxis against exogenous pathogens. It neutralizes reactive oxygen species (ROS) formed in immune cells, without vitamin C, reactive oxygen species couldn't have been removed from immune cells which would lead to the destruction of immune cells, these reactive oxygen species are necessary to kill foreign invaders but they may also damage the cell itself if not taken care of at the meantime, this essential role is played by antioxidants like vitamin C [2]. Vitamin C is found in higher concentrations within the leukocytes and it has been found that it also aids in chemotaxis of neutrophils and monocytes.

During any kind of infection vitamin C concentrations the immune cells (e.g., leukocytes) falls rapidly to lower concentrations due to its utilization and then after eradicating the cause of infection it again restores back to normal, this proves that vitamin C actively takes part in warding off the infectious agents during an infection [36]. Deficiency of ascorbic acid in the body leads to suppressed immune response, susceptibility to infections, weak collagen formation and in case of an injury wound healing process gets delayed [37]. It also acts as a reducing agent and thus reduces oxidase enzymes that play an important part in metabolizing various kinds of drugs, ascorbic acid

deficiency leads to the lower drug metabolization and also the lowered activity of electron transporters like cytochrome P-450 occurs [38]. It is evident that ascorbic acid also has antiviral activity, as according to Siegel and Morton [39] when in lab, mouse cells were cultured with ascorbic acid they started producing interferons.

In Table 5 is the USDA National Nutrient Database for vitamin C intake recommended for different age groups along with the natural sources.

Sources	Deficiency Causes	Recommended Dietary Intake of Vitamin C per day	
Tomato, cabbage, oranges, cantaloupes, green and red pepper, spinach, green peas	Scurvy, weak immunity	Males	Females
		15 mg (age-1-3 years)	15 mg (age-1-3 years)
		45 mg (9-13 years of age)	45 mg (9-13 years of age)
		90 mg (adults)	75 mg (adults) 85 mg (pregnant) 120 mg (lactating)

Table 5: Recommended Dietary Allowance (RDA) for Vitamin C.

Vitamin D and Immunity

It is composed of two main groups that contain vitamin D_2 and vitamin D_3 [35]. Vitamin D_2 is commonly known as ergocalciferol and D_3 as cholecalciferol. They are found mainly in the bones and teeth and help in their maintenance [40]. Main food sources of vitamin D include, fish liver oils, eggs of hen but the common source of vitamin D present in nature is the sunlight [35]. Lower concentrations of this vitamin in the body have been found to be the cause of increase in infection rates and apart from rickets, and other bone and joint disorders, now the lack of this vitamin has lead to the increased death rates due to cancers, heart diseases and other microbial infections [40]. In humans both types of vitamins (D_2 and D_3) are utilized but vitamin D3 is naturally produced by the human cells in the presence of ultraviolet radiations from the sunlight whereas the ergocalciferol or vitamin D_2 is not synthesized in humans but it is synthesized in the plants and can also be utilized [41]. Vitamin D_3 (1, 25-dihydroxyvitamin) plays an important part in regulating human immune response [3]. Vitamin D is also best known for its activity in the expression of those genes that produce proteins which are toxic to a number of foreign microbes. According to Maggini and Wintergerst [2], vitamin D receptors (VDRs) are present in the monocytes, macrophages and thymus tissues which indicates their role in immunoregulation. They can regulate the immune response as well and can also modulate the innate and adaptive immunity of the human body [42]. Conversion of vitamin D, synthesized in the skin cells by the absorption of ultraviolet rays from sunlight, to vitamin D_2 (25-hydroxyvitamin) takes place inside the liver cells as a result of the action of certain enzymes, such as, CYP27A1 in mitochondria and another is the microsomal enzyme CYP2R1, this hydroxylated form of vitamin D_2 then circulates to the kidneys where it gets converted to vitamin D_3 (1, 25-dihydroxyvitamin) via the action of mitochondrial CYP27B1 also known as 1-α-hydroxylase, and microsomal CYP2R1 enzymes [43]. Cholecalciferol/D_3 is the steroidal form of vitamin D and it starts circulating in the body and is transported via certain D3-binding proteins to the specific tissues or cells where required [44], such as to the VDRs of macrophages and dendritic cells in order to activate various immune responsive actions [43], refer to Figure 2. It also has positive effects on the synthesis of immunoglobulins and cytokines and also has proved its activity against multiple sclerosis, arthritis rheumatoid arthritis etc., [1]. It also enhances the regulation of T-lymphocytes lipopolysaccharide surface receptors and also down-regulates expression of immunoglobulin E (IgE) initiated by vitamin A [45]. Ergocalciferol (D_3) provides protection against inflammation of adipose tissues [46]. Role of vitamin D against the tuberculosis bacteria has also been of importance and was reported in 1980s. Monocytes encounter the Mycobacterium tuberculosis by the activation of Vitamin D_3 [47]. It is also essential in overcoming inflammation and other chronic diseases like diabetes that are caused due to inflammation. Obesity is the mainly due to the inflammation and so is the diabetes, common of which is type II diabetes [48]. Vitamin D also acts and modulates the inflammations that may lead to chronic disease development [49,50].

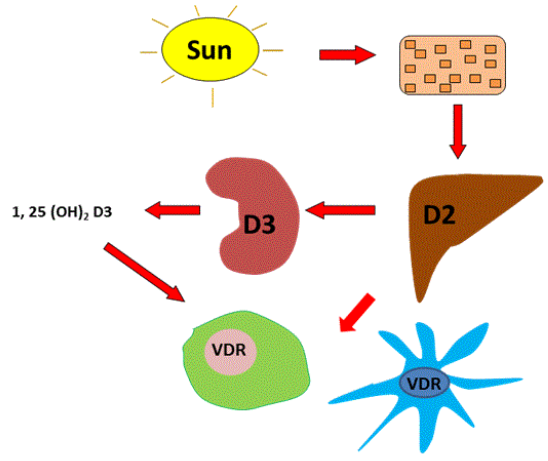

Figure 2: Vitamin D Biosynthesis and its Immunoregulatory response.

Given below in Table 6 is the USDA National Nutrient Database for vitamin D intake recommended for different age groups along with the natural sources.

Sources	Deficiency Causes	Recommended Dietary Intake of Vitamin D per day	
Milk, yogurt, egg, cheese, cod liver oil, orange juice, salmon, tuna	Rickets, Osteomalcia, reduced absorption, increased in excretion	Males	Females
		15 mcg (1-13 years of age	15 mcg (1-13 years of age
		15 mcg (adults)	15 mcg (adults) 15 mcg (for lactating and pregnant women)
		15 mcg (old-51+ years)	15 mcg (old-51+ years)

Table 6: Recommended Dietary Allowance (RDA) for Vitamin D.

Vitamin E and Immunity

Regarded as the derivative of tocol or tocotrienol and among them α-tocopherol is best known for its role in maintaining health in the humans. α-tocopherol, in the form of lipoproteins is secreted by the liver and plays its part as the protector of certain proteins and fatty acids present in the membrane from free radicals by acting as an antioxidant [51]. Vitamin E molecules produced in plants are also of key importance to humans as there are approximately 8 different kinds of molecules in human body that are obtained from plant sources [52]. Niki and Traber [52] described that, at the start, the concentrate containing antioxidant molecules was referred to as the 'inhibitols' because it resembled to the inhibitols obtained from different plant sources like lettuce, wheat, palm oils etc. and these inhibitols were neutralized by the agents that destroy the hydroxyl (OH) groups. In 1940s, the α-tocopherols were known to be the key role players in neutralizing and destroying free radicals that form within the different cells of tissues and this role of vitamin E gained extreme importance and interest. α-tocopherols do not have any role in the signaling pathway rather it changes the chemical composition of the environment where the process of signaling needs to be carried out [51]. Vitamin E is also known to be the immunoregulator and plays an important role in enhancing immune response [53] by inactivating and inhibiting the free radicals as a result of antioxidant activity [2]. When the diet is supplemented with vitamin E intake, it results in the mitogen stimulated increased T-lymphocyte multiplication, increased cytotoxic cell activity and maximize the action of macrophages against the intruders thus providing the strong basis of action against infections [54,55]. An increase in vitamin E is also known for inhibiting the activation of protein kinase C (PKC) enzyme which in turn leads to the reduced platelets, nitric oxide and also the shows reduced superoxide accumulation in macrophage cells and neutrophils [56]. The deficiency of vitamin E in the body leads to the development of a disease called ataxia [57].

Given below in Table 7 is the USDA National Nutrient Database for vitamin E intake recommended for different age groups along with the natural sources.

Sources	Deficiency Causes	Recommended Dietary Intake of Vitamin E Per Day	
Sunflower, safflower, wheat germ, peanuts, tomato, spinach, broccoli.	Ataxia, impaired immune response, retinopathy, peripheral neuropathy	Males	Females
		6 mg (1-3 years of age)	6 mg (1-3 years of age)
		11 mg (9-13 years of age)	11 mg (9-13 years of age)
		15 mg (14 years and + age)	15 mg (14 years and + age) 15 mg (pregnant) 19 mg (lactating)

Table 7: Recommended Dietary Allowance (RDA) for Vitamin E.

Conclusion

Adequate intake of micronutrients, especially vitamins are required and considered mandatory for healthy immune system and its optimal functionality. Immunity is the natural defense mechanism in biological systems to fight against infections, diseases or other unwanted biological invasions and autoimmune diseases. Immunity provides protection to life through three different kinds of barriers including,

Skin/epithelial barrier, 2. Cellular response (T lymphocytes and cytokines) and last one are

Humoral immune response (antibodies).

Vitamins are a group of substances that are needed for normal cell function, growth, and development. We can obtain them from fruits, vegetables, beans, lentils, whole grains and fortified dairy foods. Vitamins have the properties to help the body in fighting against a variety of illnesses and protect the body from damage to cells. Many foods contain vitamins that promote, enhance and regulate the immune system. Some vitamins have more immune protection power than others. Vitamins A, C, and E mainly aid in enhancing the epithelium/skin barrier function. With the exception of vitamin C, all the vitamins are claimed to be essential for antibody production. Most of the vitamins like (vitamin B_6, B_9, B_{12}, A and D) are also applied in our body (orally) to produce a cell-mediated response with the production of cytokines and T-lymphocytes. Comprehensively, inadequate intake and lowered nutritional status of these vitamins and trace elements may lead to suppressed immunity, which predisposes to infections and aggravates malnutrition. Therefore, supplementation with selected vitamins can support the body's natural defence system by enhancing all three levels of immunity.

Acknowledgement

I really want to thank all the contributing authors who contributed different portions regarding their fields of expertise and made this article to come into originality and lead to the completion of this

article. There are no funders for this review paper as it is a combined effort of all the group mates linked to each other professionally.

References

1. Ibrahim KS, El-Sayed EM (2015) Potential role of nutrients on immunity. International Food Research Journal 23: 464-474.
2. Maggini S, Wintergerst ES, Beveridge S, Hornig DH (2007) Selected vitamins and trace elements support immune function by strengthening epithelial barriers and cellular and humoral immune responses. British Journal of Nutrition 98: S29-S35.
3. Mora JR, Iwata M, Andrian UH (2008) Vitamin effects on the immune system: vitamins A and D take centre stage. Nature Reviews Immunology 8: 685-698.
4. Comerford KB (2013) Recent developments in multivitamin/mineral research. Advances in Nutrition: An International Review Journal 4: 644-656.
5. Krebs NF (2001) Bioavailability of dietary supplements and impact of physiologic state: infants, children and adolescents. The Journal of nutrition 131: 1351S-1354S.
6. Fairweather-Tait SJ (1997) From absorption and excretion of minerals to the importance of bioavailability and adaptation. British Journal of Nutrition 78: S95-S100.
7. Yetley EA (2007) Multivitamin and multimineral dietary supplements: definitions, characterization, bioavailability, and drug interactions. The American journal of clinical nutrition 85: 269S-276S.
8. Tanumihardjo SA (2002) Factors influencing the conversion of carotenoids to retinol: bioavailability to bioconversion to bioefficacy. International Journal for vitamin and nutrition research 72: 40-45.
9. Hinds TS, West WL, Knight EM (1997) Carotenoids and retinoids: a review of research, clinical, and public health applications. The Journal of Clinical Pharmacology 37: 551-558.
10. Chew BP, Park JS (2004) Carotenoid action on the immune response. The Journal of Nutrition, 134: 257S-261S.
11. Spears JW, Weiss WP (2008) Role of antioxidants and trace elements in health and immunity of transition dairy cows. The Veterinary Journal 176: 70-76.
12. Ertesvag A, Engedal N, Naderi S, Blomhoff HK (2002) Retinoic acid stimulates the cell cycle machinery in normal T cells: involvement of retinoic acid receptor-mediated IL-2 secretion. The Journal of Immunology 169: 5555-5563.
13. Villamor E, Fawzi WW (2005) Effects of vitamin A supplementation on immune responses and correlation with clinical outcomes. Clinical microbiology reviews 18: 446-464.
14. Bono MR, Tejon G, Santibañez FF, Fernandez D, Rosemblatt M, et al. (2016) Retinoic acid as a modulator of T cell immunity. Nutrients 8: 349.
15. Mora JR, von Andrian UH (2006) T-cell homing specificity and plasticity: new concepts and future challenges. Trends in immunology 27: 235-243.
16. Cho NE (2016) Retinoid regulation of antiviral innate immunity in hepatocytes. Hepatology.
17. Villamor E, Koulinska IN, Aboud S, Murrin C, Bosch RJ, et al. (2010) Effect of vitamin supplements on HIV shedding in breast milk. The American journal of clinical nutrition 92: 881-886.
18. Crabb DW, Matsumoto M, Chang D, You M (2004) Overview of the role of alcohol dehydrogenase and aldehyde dehydrogenase and their variants in the genesis of alcohol-related pathology. Proceedings of the Nutrition Society 63: 49-63.
19. Chase JR, Poolman MG, Fell DA (2009) Contribution of NADH increases to ethanol's inhibition of retinol oxidation by human ADH isoforms. Alcoholism: Clinical and Experimental Research 33: 571-580.
20. Schoggins JW, Rice CM (2011) Interferon-stimulated genes and their antiviral effector functions. Current opinion in virology 1: 519-525.
21. Saito T, Owen DM, Jiang F, Marcotrigiano J, et al. (2008) Innate immunity induced by composition-dependent RIG-I recognition of hepatitis C virus RNA. Nature 454: 523-527.
22. Hellmann H, Mooney S (2010) Vitamin B6: a molecule for human health? Molecules 15: 442-459.
23. Roje S (2007) Vitamin B biosynthesis in plants. Phytochemistry 68: 1904-1921.
24. Pleiner J (2008) Intra-arterial vitamin C prevents endothelial dysfunction caused by ischemia-reperfusion. Atherosclerosis 197: 383-391.
25. Huskisson E, Maggini S, Ruf M (2007) The influence of micronutrients on cognitive function and performance. Journal of International Medical Research 35: 1-19.
26. Vermeulen EG, Stehouwer CDA, Valk J, Knaap MVD, Van Den Berg M, et al. (2000) Effect of homocysteine-lowering treatment with folic acid plus vitamin B6 on progression of subclinical atherosclerosis: a randomised, placebo-controlled trial. The Lancet 355: 517-522.
27. McCully KS, Ragsdale BD (1970) Production of arteriosclerosis by homocysteinemia. The American journal of pathology 61: p. 1.
28. Shabbir F (2013) Effect of diet on serotonergic neurotransmission in depression. Neurochemistry international 62: 324-329.
29. Kunisawa J, Kiyono H (2013) Vitamin-mediated regulation of intestinal immunity. Frontiers in immunology 4: p. 189.
30. Rail LC, Meydani SN (1993) Vitamin B6 and immune competence. Nutrition reviews 51: 217-225.
31. Stover PJ (2004) Physiology of folate and vitamin B12 in health and disease. Nutrition reviews, 62: S3-S12.
32. Intakes (1998) Dietary reference intakes for thiamin, riboflavin, niacin, vitamin B6, folate, vitamin B12, pantothenic acid, biotin, and choline. National Academies Press (US).
33. Sakane T, Takada S, Kotani H, Tsunematsu T (1982) Effects of methyl-b12 on the in vitro immune functions of human T lymphocytes. Journal of clinical immunology 2: 101-109.
34. Vellema P (1996) The effect of cobalt supplementation on the immune response in vitamin B12 deficient Texel lambs. Veterinary immunology and immunopathology 55: 151-161.
35. Kraemer K (2012) Introduction: The diverse and essential biological functions of vitamins. Annals of Nutrition and Metabolism 61: 185-191.
36. Hume R, Weyers E (1973) Changes in leucocyte ascorbic acid during the common cold. Scottish Medical Journal 18: 3-7.
37. Wintergerst ES, Maggini S, Hornig DH (2006) Immune-enhancing role of vitamin C and zinc and effect on clinical conditions. Annals of Nutrition and Metabolism 50: 85-94.
38. Carr AC, Frei B (1999) Toward a new recommended dietary allowance for vitamin C based on antioxidant and health effects in humans. The American journal of clinical nutrition 69: 1086-1107.
39. Siegel BV, Morton JI (1977) Vitamin C and the immune response. Experientia 33: 393-395.
40. Gombart AF (2009) The vitamin D-antimicrobial peptide pathway and its role in protection against infection. Future microbiology 4: 1151-1165.
41. Bikle D (2009) Nonclassic actions of vitamin D. The Journal of Clinical Endocrinology & Metabolism 94: 26-34.
42. Aranow C (2011) Vitamin D and the immune system. Journal of Investigative Medicine 59: 881-886.
43. Sadarangani SP, Whitaker JA, Poland GA (2015) Let there be light: the role of vitamin D in the immune response to vaccines. Expert review of vaccines 14: 1427-1440.
44. Haussler MR, et al. (2013) Molecular mechanisms of vitamin D action. Calcified tissue international 92: 77-98.
45. Zhang Y, Donald YM, Richers BN, Liu Y, Remigio LK, et al. (2012) Vitamin D inhibits monocyte/macrophage proinflammatory cytokine production by targeting MAPK phosphatase-1. The Journal of Immunology 188: 2127-2135.
46. Gao D, Trayhurn P, and Bing C (2013) 1, 25-Dihydroxyvitamin D3 inhibits the cytokine-induced secretion of MCP-1 and reduces monocyte

recruitment by human preadipocytes. International journal of obesity 37: 357-365.

47. Hewison M (2012) An update on vitamin D and human immunity. Clinical endocrinology 76: 315-325.
48. Pickup JC (2004) Inflammation and activated innate immunity in the pathogenesis of type 2 diabetes. Diabetes care 27: 813-823.
49. Nezhad HA (2013) Evidences of dual role of vitamin D through cellular energy homeostasis and inflammation pathway in risk of cancer in obese subjects. Minerva medica 104: 295-307.
50. Molero GI (2013) Hypovitaminosis D and incidence of obesity: a prospective study. European journal of clinical nutrition 67: 680-682.
51. Traber MG, Atkinson J (2007) Vitamin E, antioxidant and nothing more. Free Radical Biology and Medicine 43: 4-15.
52. Niki E, Traber MG (2012) A history of vitamin E. Annals of Nutrition and Metabolism 61: 207-212.
53. Maslova E, Hansen S, Strøm M, Halldorsson TI, Olsen SF, et al. (2014) Maternal intake of vitamins A, E and K in pregnancy and child allergic disease: a longitudinal study from the Danish National Birth Cohort. British Journal of Nutrition 111: 1096-1108.
54. Meydani SN, Han SN, Wu D (2005) Vitamin E and immune response in the aged: molecular mechanisms and clinical implications. Immunological reviews 205: 269-284.
55. Pae M, Meydani SN, Wu D (2014) The role of nutrition in enhancing immunity in aging. Aging and disease 3: 91-129.
56. Azzi A, Ricciarelli R, Zingg JM (2002) Nonantioxidant molecular functions of αtocopherol (vitamin E). FEBS letters 519: 8-10.
57. Jiang Q (2014) Natural forms of vitamin E: metabolism, antioxidant, and anti-inflammatory activities and their role in disease prevention and therapy. Free Radical Biology and Medicine 72: 76-90.