Vitamins as Antioxidants

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Abstract

Oxidative stress is a significant factor in the development of chronic diseases. An improved antioxidant potential in the body can reduce oxidative stress and prevent or improve disease conditions. Some food nutrients, especially vitamin C, E, and carotenoids are well-known antioxidants; however, other vitamins such as Vitamin K, Vitamin D, Niacin, Pyridoxine and Riboflavin that may have antioxidant potential are usually not put into consideration. This review entails studies that have investigated the antioxidant properties of other vitamins with the known antioxidants inclusive and their effect in reducing oxidative stress. The reviewed studies suggest that other vitamins possess antioxidant nature, and they can improve oxidative stress, ranging from lipid peroxidation, protein carbonylation, and reduction of advanced glycated end-products. Therefore, proper attention should be given to these neglected vitamins in research activities on oxidative stress, nutrition and the management of diseases related to oxidative stress.

Keywords: Antioxidants; Chronic diseases; Oxidative stress; Vitamins

1. Introduction

Oxidative stress is a condition characterised by a high rate of reactive oxygen species or reduced capacity to neutralise them. Oxidative stress is responsible for the development of many chronic diseases like cardiovascular diseases [1], cancer [2], and diabetes [3]. Several researchers have given close attention to the connection between oxidative stress and these mentioned diseases because they are of public health importance. Increasing antioxidant capacity is one of the ways of reducing oxidative stress. Many studies have examined the antioxidant potential of
some vitamins such as vitamin E, vitamin C, and Carotenoids and their role in human health. It has almost become a well-established fact that the vitamins mentioned above possess the antioxidant capacity. Even though the possible part of other vitamins on oxidative stress has received little attention, these vitamins have not been well appraised for their role in health as an antioxidant or in their deficiency state. Some of the ignored antioxidant vitamins are Vitamin K, Vitamin D, Niacin, Pyridoxine, and Riboflavin, which act as co-enzyme in many cases to attack free radicals and, their deficiency states precipitate oxidative stress. Numerous studies have reported the effect of these vitamins such as vitamin K on neuroprotection [4], riboflavin on lipid peroxidation and protein carbonyls in rats [5], vitamin B12 on ganglion cells of the retina [6] to mention a few. A deficiency of these vitamins is also associated with oxidative stress-induced conditions like atherogenesis [7], and increased homocysteine, which increases cardiovascular risk [8]. The examples mentioned above point out that these vitamins possess antioxidant property, but more investigations should be carried out on these vitamins. This review evaluates studies that have investigated the antioxidant properties of these vitamins and their effect on oxidative stress.

2. Oxidative Stress

Oxidative stress is a condition caused by an imbalance between the free radicals and antioxidant defence system of the body. In health, free radicals and antioxidants remain in balance state [9], but in conditions of oxidative stress, there is a large number of reactive oxygen species and reactive nitrogen species than the antioxidant. Some atoms are unstable and highly reactive due to the presence of unpaired electrons in valence orbitals. They attain stability by acquiring electrons from nearby molecules in the body, causing a cascade of reactions resulting in cellular damage and diseases [9, 10]. Event leads to the accumulation of peroxides and free radicals that can damage different components of the cell, including nucleic acids, proteins, lipids, carbohydrates, and other molecules [9, 11]. The two primary forms of radicals or reactive oxygen species and reactive nitrogen species include superoxide radical, hydrogen peroxide (H$_2$O$_2$) and hydroxyl radical [12] and the reactive nitrogen species include nitric oxide and its metabolites [9]. Oxidative stress has been reported to play a significant role in the pathogenesis of diseases like Diabetes mellitus, renal failure, cardiovascular diseases, cancer, polycystic ovary syndrome, neurodegenerative diseases, [13-16]. Antioxidants neutralise excess free radicals. Antioxidants are produced in the body (endogenous) or acquired from the diet (exogenous). Many studies have reported a decrease in endogenous antioxidants in many disease conditions. Therefore, intake of exogenous antioxidants in the diet becomes vital to improve the dangerous effect of reduced antioxidants and increased free radicals in disease conditions.

3. Vitamins

Vitamins are groups of complex organic compounds found in foodstuffs and essential for a healthy metabolism. Their deficiency can cause disorders, whereas resupply of these nutrients can alleviate deficiency symptoms [17]. Vitamins are different from other food nutrients due to their distinct organic nature, and their classification depends on their chemical nature and function [18]. Growth, development, health, and reproduction require minute amounts of vitamins [19]. Some vitamins synthesised from other sources in the body deviate from the usual definition of vitamins. For instance, Animals integrate ascorbic acid, tryptophan an essential amino acid produce niacin, while UV radiation from sunlight synthesises vitamin D [20]. Generally, classification of Vitamins is into two groups:
Example of water-soluble vitamins is: Vitamins B complex and C and that of fat-soluble vitamins include: A, D, E, and K. Fat-soluble vitamins are associated with fats and are absorbed with dietary fats. The absorption of fat-soluble vitamins is like the absorption of fats. Water-soluble vitamins are not associated with fats and are unaffected by alterations in fat absorption [20, 21]. Vitamin A is a fat-soluble vitamin obtained both from plant and animal sources. Vitamin A from animal sources is known as retinoid, whereas, the vitamin A from the plant source is called provitamin A carotenoids [22]. They are essential for vision, cell growth and development, antioxidant activity, and promotion of proper cell communication [23]. Provitamin A carotenoid are mainly present in sweet potato, carrots, spinach, kale, mustard greens, collard greens, turnip greens, Swiss chard, winter squash, Romaine lettuce, cantaloupe, broccoli, asparagus, sea vegetables, chili peppers, tomatoes, basil, papaya, shrimp, eggs, Brussels sprouts and grapefruit while Pre-formed vitamin A sources are- shrimp, eggs, cow’s milk, cheese, yoghurt, salmon, sardines, chicken, turkey, beef and lamb [23].

Vitamin D is vital for the human body health, but the exact body intake amount varies and has an inconsistent pattern because exposure to sunlight also produces vitamin D in human skin [24]. Vitamin D is vital for normal body functioning as its deficiency cause the malformation and softening of bones. Vitamin D deficiency is associated with many disorders like osteoporosis, rickets, osteomalacia, loss of balance, diabetes, rheumatoid arthritis, asthma, depression, epilepsy, and lowered immune function. Calcitriol is essential for the maintenance of healthy calcium homeostasis [25]. It is also involved in the maturation of white blood cells, which is a Frontline player in immunity responses [26]. Vitamin D is present in Egg yolks, tuna, salmon, sardines, mushrooms, cow’s milk, soy milk, orange juice, and fortified foods [24].

Vitamin E comprises of four forms of tocopherols and tocotrienols, forming eight naturally occurring forms of vitamin E, which include alpha, beta, gamma, and delta classes of tocopherol and tocotrienol [27]. Collectively the eight compounds are called “tocochromanols,” and they are fat-soluble antioxidants. Present in the serum and red blood cells among the tocopherols are the alpha- and gamma-tocopherols, with the alpha-tocopherol present in a higher concentration [28]. Vitamin E shields the body structures from oxidative damage. A deficiency of vitamin E protects low-density lipoproteins against oxidative damage. Vitamin E deficiency is also associated with heart attack, cancer, stroke, fibrocystic breast disease, epilepsy, PMS, diabetes, Parkinson’s disease, cataract, Alzheimer’s disease [29]. Dietary sources of vitamin E includes Sunflower seeds, spinach, turnip greens, asparagus, beet greens, mustard greens, chili peppers, almonds, broccoli, bell peppers, kale, tomatoes, avocado, peanut, shrimp, olives, olive oil, collard greens, cranberries, raspberries, kiwifruit, carrots, and green beans [23].

Vitamin K is known as Blood clotting factors because the name derived from the German word “koagulation” means blood clotting. Three different types of Vitamin K are known, namely; K1 (Phylloquinone), K2 (Menaquinone) and K3 (Menadione). K1 form is most prevalent and needed for photosynthesis in plants.
Synthesised from K1 is the K2 type. Bacteria and other microorganisms form vitamin K3. In the human body, by the biological conversion of K1 and K3 produce K2. While, K2 is not present in plants, but the fermentation of bacteria produces it through the transformation of K1 into K2 [30]. Vitamin K is essential for blood clotting activity [31, 32], helps in the maintenance of bone health by keeping demineralisation under control [32, 33]. Food sources for Vitamin K1 are dark green leafy vegetables, while sources of Vitamin K2 include: eggs, meat, fish, dairy, fermented animal foods, and fermented plant foods and vitamin K3 is not naturally present in dietary foods [31, 32]. Generally nutritional sources for vitamin K are: spinach, mustard greens, beet greens, Swiss chard, turnip greens, parsley, broccoli, Brussels sprouts, romaine lettuce, asparagus, basil, cabbage, celery, kiwifruit, green beans, cucumber, tomatoes, black pepper, green peas, blueberries, carrots, soybeans, avocado, raspberries, winter squash, pear, cranberries, bell peppers, plum, cantaloupe and eggplant [30].

Water-soluble Vitamins includes Vitamin B1, Vitamin B2, Vitamin B3, Vitamin B5, Vitamin B6, Vitamin B9, Vitamin B12, Biotin and Vitamin C [21]. Vitamin B1 belongs to the group of vitamin B complex and known as thiamin. Vitamin B1 plays essential roles in human health. It is involved in energy production from carbohydrates and fats [34]. Vitamin B1 acts as a co-enzyme precursor of some key enzymes of carbohydrate metabolism [35]. It also helps in the structural development of brain cells [36], and it is involved in the detoxification of alcohol [35]. The dietary sources of vitamin B1 are: asparagus, sunflower seeds, green peas, flax seeds, Brussels sprouts, beet greens, spinach, cabbage, eggplant, romaine lettuce, mushrooms, navy beans, black beans, barley, dried peas, lima beans, oats, sesame seeds, kidney beans, peanuts, sweet potato, tofu, tuna, pineapple, oranges, broccoli, green beans, onions, collard greens, fortified cereals, dried beans, lean meats, soy foods and whole wheat grain.

Vitamin B2 is also known as riboflavin. It is involved in energy metabolism. Vitamin B2 recycles glutathione, which is the most crucial antioxidant which protects against free radicals in the body. It also promotes iron metabolism, and its deficiency increases the risk of anaemia as iron is an essential element for red blood cell production [37]. The dietary sources of Vitamin B2 are spinach, beet greens, asparagus, sea vegetables, eggs, cow’s milk, collard greens, broccoli, Swiss chard, green beans, mushrooms, turnip greens, kale, mustard greens, soybeans, yogurt, almonds, turkey, green peas, sweet potato, sardines, tuna, carrots and cabbage [23].

Vitamin B3 is also known as Niacin. Niacin is a group of compounds having vitamin activity. Vitamin B3 comprised of nicotinic acid, nicotinamide, and numerous enzymatic forms [38]. Nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADP) are two distinct forms of vitamin B3, and they are primarily involved in the production of energy from dietary proteins, carbohydrates, and fats [39]. NAD, NADP, and niacin-containing enzymes are scavengers of free radicals and protect tissues from oxidative damage [40]. Dietary sources of vitamin B3 are: mushrooms, cauliflower, sweet potato, broccoli, beet greens, asparagus, turnip greens, bell peppers, cucumber, celery, avocado, lentils, dried peas, chicken, turkey, yogurt, salmon, rye, beef, eggs, potatoes, wheat, corn, shrimps, papaya, winter squash, and cow milk.
Vitamin B5 or Pantothenic acid is from the Greek word “pantothen,” which means "on all sides" or "from all quarters." The frequent presence of this vitamin in foods is the reason for naming it as pantothenic acid. Pantothenic acid, incorporated into Coenzyme A (CoA), has a central position for energy metabolism [41]. Dietary sources of vitamin B5 are fish, cauliflower, sweet potato, broccoli, beet greens, asparagus, turnip greens, bell peppers, cucumber, celery, avocado, lentils, dried peas, chicken, turkey, yogurt, salmon, rye, beef, eggs, potatoes, wheat, corn, shrimps, papaya, winter squash, cow's milk, mustard greens, tomatoes, sea vegetables, romaine lettuce.

Vitamin B6 exists in different forms which are pyridoxal (PL), pyridoxine (PN), pyridoxal 5’-phosphate (PLP), pyridoxamine (PM), pyridoxine-5’-phosphate (PNP) and pyridoxamine 5’-phosphate (PMP) [42]. Vitamin B6 is involved in red blood cell production, carbohydrate metabolism, liver detoxification, brain, and nervous system health [43]. Vitamin B6 involved in the generation of neurotransmitters in the brain and nervous system (43). Vitamin B6 helps in liver detoxification, and its deficiency causes liver dysfunction [44]. Furthermore, Vitamin B6 deficiency can cause attention deficit disorder. Dietary sources of vitamin B6 are: Tuna, spinach, cabbage, bell peppers, turnip greens, garlic, cauliflower, turkey, beef, chicken, salmon, sweet potato, potatoes, banana, winter squash, broccoli, Brussels sprouts, collard greens, beet greens, kale, carrots, swiss chard, asparagus, mustard greens, tomatoes, leeks, summer squash, chili peppers, sunflower seeds, pinto beans, avocado, lentils, green peas, lima beans, onions, shrimps, and pineapple [41].

Vitamin B9 is also known as folate. It has critical importance for human health. There are different forms of flutes present in dietary sources dihydrofolates, methyl folate, poly glutamyl folates, and mono glutamyl folates [45]. Vitamin B9 is vital for brain health and provides support for the cardiovascular and nervous system in human [45]. Folate regulates homocysteine level, which is a marker for cardiovascular diseases as a higher level of homocysteine showed an increased risk of cardiovascular diseases. Folate is a central nutrient for cardiovascular health [45, 46]. Folate is essential in the synthesis of erythrocytes. Risk of cancer is lower in human by higher intake of folates, especially in females, risk of breast cancer is reduced [45]. Food sources of folates include Lentils, asparagus, spinach, turnip greens, broccoli, beets, romaine lettuce, bok Choy, cauliflower, parsley, pinto beans, garbanzo beans, black beans, navy beans, kidney beans, papaya, and Brussels sprouts.

Vitamin B12 also known as cobalamin, has cobalt in its structure [8]. This vitamin is essential for energy metabolism and other biological processes, but differently, from B complex vitamins, it has some unique functions [8]. Vitamin B12 can be stored in the body for many years, whereas most of the other B vitamins cannot allow long-time storage. It also has a larger molecule and a complex structure. Microorganisms like bacteria and fungi synthesise vitamin B12, and it is difficult to absorb. Vitamin B12 is essential for erythrocyte maturation during the production of red blood cells, and it is necessary for the maintenance of cardiovascular health of human by preventing an increase in the level of homocysteine. Vitamin B12 also maintains bone health as the incidence of osteoporosis is increased with deficiency of this vitamin. Dietary sources of Vitamin B12 include sardines, salmon, tuna, cod, lamb, scallops, shrimps, beef, yoghurt, cow’s milk, eggs, turkey, chicken, cheese, mushrooms, and breakfast cereals.
Biotin was formerly known as coenzyme R, vitamin H, or vitamin B7, but now in recent times, it is known as Biotin. It is a member of B-complex vitamins, and most importantly, Biotin plays a crucial role in sugar and fat metabolism. Biotin is essential for fat deposition in the skin as biotin deficiency causes skin rashes. Increasing intake of biotin in the food of lactating mothers can reduce the symptoms of cradle cap in infants [47]. Food sources of biotin include tomatoes, almonds, eggs, onions, carrots, romaine lettuce, cauliflower, sweet potato, oats, peanuts, walnuts, salmon, yoghurt banana, raspberries, cow’s milk, strawberries, watermelon, grapefruit, and cucumber.

Vitamin C (ascorbic acid) is a prevalent nutritional supplement [48]. Vitamin C possesses antioxidant potentials, protecting cellular structures from the harmful effects of free radicals. Its significant iron absorption in transforming iron into a form easily absorbed into the intestines. Vitamin C is vital in the production of collagen, which is a structural component of the human body. The synthesis of certain neurotransmitters is also dependent on vitamin C, especially neurotransmitters involved in signalling of feelings, thoughts, and commands throughout the brain and nervous system. Vitamin C is also prerequisite for the synthesis of serotonin, a hormone needed for the proper functioning of the endocrine system, nervous system, digestive system, and immune system. Dietary sources of vitamin C includes papaya, bell peppers, broccoli, Brussels sprouts, strawberries, pineapple, oranges, kiwifruit, cantaloupe, cauliflower, kale, cabbage, Bokchoy, grapefruit, parsley, turnip greens, beet greens, mustard greens, collard greens, raspberries, Swiss chard, tomatoes, lemons and limes, spinach, asparagus, sea vegetables, fennel, and sweet potatoes [49].

4. Vitamins and Oxidative Stress

The knowledge of free radicals and reactive oxygen species (ROS) in biology has given a new understanding of the pathogenesis of diseases, and it promises new insights into health and disease management [50]. Free radicals are any molecular species that contains an unpaired electron in an atomic orbital. The presence of unpaired electron results in specific common properties that are shared by most radicals [51]. Many chemical species are unstable and highly reactive; they can either donate an electron to another molecule or accept an electron from other molecules, therefore behaving as oxidants or reducing agents [52]. The most critical oxygen-containing free radicals in many disease states are hydroxyl, superoxide anion, hydrogen peroxide, oxygen singlet, hypochlorite, nitric oxide radical, peroxynitrite radicals [53], these are highly reactive species in the nucleus and in the membranes of cells capable of damaging biologically relevant molecules such as DNA, proteins, carbohydrates, and lipids [54]. Free radicals attack essential macromolecules leading to cell damage and homeostatic disruption.

The formation of free radicals occurs continuously in the cells because of both enzymatic and non-enzymatic reactions. Enzymatic reactions serve as a source of free radicals, include those involved in the respiratory chain, phagocytosis, prostaglandin synthesis, and the cytochrome P-450 system [55]. Production of free radicals is in non-enzymatic reactions of oxygen with organic compounds as well as those initiated by ionising reactions. Generation of free radicals in the body occurs in cellular structures like Mitochondria and Peroxisome. Processes like Xanthine oxidase, Inflammation, Phagocytosis, Arachidonate pathways, Exercise, Ischemia/reperfusion injury can also result
in the production of free radicals [51]. Free radicals are generated externally from cigarette smoke, Environmental pollutants, Radiation, Pesticides, Industrial solvents, and Ozone [51].

4.1 Vitamin A and oxidative stress
Vitamin A is also called retinoic acid, and it possesses the ability to inhibit viral hepatitis [56]. Even though vitamin A is not a popular antioxidant, few studies reported a likely antioxidant role in an indirect way. All-trans retinoic acid was reported to play a key role in the inhibition of hepatic stellate cells (an effector of hepatocellular carcinoma) activation via suppressing thioredoxin-interacting protein and reduces oxidative stress levels [57]. Also, retinoic acid, which is a metabolite of vitamin A, was reported to upregulate expression of anti-oxidant related genes in in-vitro mature buffalo oocytes [58]. Furthermore, all-trans retinoic acid-induced superoxide dismutase and glutathione transferase activities, while it decreased malondialdehyde and reactive oxygen species in both healthy and varicocele sperm, which suggests that retinol enhances antioxidant enzyme activity [59]. Therefore, there is growing evidence suggesting that vitamin A could play a role in protecting the body against oxidative stress damage.

4.2 Vitamin D and oxidative stress
Vitamin D exists in three forms, which are 7-dehydrocholesterol, ergocalciferol, and cholecalciferol. All these three forms have been reported to inhibit iron-dependent lipid peroxidation [60], and the antioxidant ability of vitamin D was reported to be comparable to the anticancer drug Tamoxifen [60]. Numerous evidence is supporting the antioxidant activity of Vitamin D3 (cholecalciferol) in oxidative stress diabetes. Some experimental studies reported that vitamin D3 administration in diabetic mice helps to diminish the ROS formation by the suppression of the gene expression of NADPH oxidase [61, 62]. Furthermore, Vitamin D supplementation has been suggested to provide significant protection against oxidative stress-mediated vascular complications in diabetes [63]. Also, a study proposed that vitamin D is an antioxidant because of an increase in hepatic GSH amounts in rats that have gotten cholecalciferol [64]. Vitamin D supplementation for nine weeks among pregnant women has beneficial effects on biomarkers of oxidative stress. It caused a significant increase in total antioxidant capacity and glutathione activity, among other metabolic enzymes [65]. The evidence in the literature implies a significant antioxidant role of Vitamin D3 in mature erythrocytes without a nucleus, this result not only verify that cholecalciferol has an antioxidant effect [66], but also suggest that 1,25-dihydroxycholecalciferol could be like a direct antioxidant of the membrane, via stabilizing and protecting the membrane from lipid peroxidation through the relationship with their hydrophobic parts [60].

4.3 Vitamin E and oxidative stress
Vitamin E discovered in 1922, together with its physiological functions, and its anti-oxidative effects, have been studied for nearly a century now [67]. Vitamin E is fat-soluble compounds divided into tocopherols and tocotrienols each occurring in the alpha, beta, gamma, and delta forms. Alpha-Tocopherol received the most attention among the vitamin E with antioxidant potentials, but some studies suggested that tocotrienols may have different health-promoting capacities. An increased concentration of alpha-tocopherol in the liver was found to exert a protective
effect against oxidative damage in exercise-induced oxidative stress [68]. Also, Alpha-Tocopherol protects cell membranes from lipid peroxidation by superoxide radical anion and lipid peroxyl free radical scavenging [69]. Also, alpha-tocopherol was reported to reduce oxidative stress in workers exposed to lead, and the administration of alpha-tocopherol reversed adverse health effects of lead exposure, which induced oxidative stress [70]. Alpha-tocopherol, in combination with alpha-lipoic acid, was also found to be beneficial in preventing BPA-induced oxidative stress [71]. Another form of vitamin E like the Gamma tocopherol has been shown to improve inflammation, oxidative stress, and apoptosis in diabetic wounds by nuclear factor kappa B, nuclear factor (erythroid-derived 2)-like 2, and sirtuin-1 [72].

4.4 Vitamin K and oxidative stress
Vitamin K occurs in three forms, which are K1 (Phylloquinone), K2 (Menaquinone) and K3 (Menadione). Leafy plants produce Phylloquinone (vitamin K1). In contrast, menaquinone is a product of bacterial from the gut or conversion of phylloquinone derived from the diet. Hence, menaquinone is the most abundant form of vitamin K in animal tissues [73]. One of the mechanisms for ROS production in the body is through activation of 12-lipoxygenase an enzyme involved in arachidonic acid metabolism. Vitamin K has been reported to block the activation of 12-lipoxygenase in arachidonic acid-induced oxidative injury to developing oligodendrocytes [74], a report from the same research group showed that phylloquinone (vitamin K1) and menaquinone 4 (MK-4; a vitamin K) protect developing oligodendrocytes and immature neurons against glutathione depletion induced oxidative injury and generation of ROS [75]. Also, vitamin K hydroquinone (KH2) was a potent biological antioxidant [76], there is a shortage of information on the regenerative antioxidative enzymatic mechanisms for this required trace nutrient [75] which could be an area of research interest.

4.5 Vitamin C and oxidative stress
Vitamin C serves as an important nutrient for the body. Ascorbate is a powerful antioxidant with the ability to mop up free radicals within, and outside the cell which is by acting directly on peroxyl radicals or indirectly by boosting the antioxidant properties of vitamin E, this helps to control lipid peroxidation of cellular membranes and nuclear materials of the cell. Ascorbate, due to its well-known antioxidant property, ameliorates DNA damage by decreasing reactive oxygen species or protects proteins involved in DNA repair [77]. Ascorbate also prevents the formation of nitrosamine, which produces reactive nitrogen species [78]. Vitamin C, in combination with L-carnitine, was reported to improve cisplatin-induced nephrotoxicity due to their antioxidant and anti-inflammatory property [79].

Conversely, Vitamin C can behave as a pro-oxidant in certain conditions. High-dose vitamin C has been reported to induce ROS production inside the cells and cause impairment of the mitochondrial membrane potential [80]. Vitamin C has also been reported to generate ascorbate radicals and Hydrogen peroxide in pharmacological doses [81]. Therefore, Ascorbic acid in high doses has been suggested to kill cancer cells by inducing pro-oxidant effects selectively. One of the mechanisms suggested for its anti-cancer effect is through the induction of hydrogen peroxide in cell and depleting Nicotinamide Adenine Dinucleotide [82].
4.6 B Complex vitamins and oxidative stress

4.6.1 Vitamin B2 and oxidative stress: Riboflavin (Vitamin B2) is vital for the metabolism of nutrients and antioxidant protection [83]. Riboflavin can be regarded as one of the neglected antioxidant nutrients, because primarily, vitamin C, E, and Carotenoids are mainly known to be antioxidants. Riboflavin possesses some antioxidant property as a result of the glutathione redox cycle and its conversion from reduced riboflavin to its oxidised form [84]. Riboflavin acts as coenzymes for redox enzymes in its FAD and FMN forms. In this state, they act as antioxidants [85] because FAD coenzyme is essential for glutathione reductase activity in converting oxidised glutathione to its reduced form [83, 86, 87]. Reduced glutathione acts as an antioxidant in the intracellular milieu by deactivating reactive oxygen species during the conversion to its oxidised form [87]. FAD needed to re-convert the oxidised glutathione to its reduced form, thereby regaining its antioxidant potential. Glutathione is crucial to its ability to deactivate peroxides, especially hydroperoxides [88]. Therefore it is expected that riboflavin deficiency may increase lipid peroxidation. Several animal studies indicated the negative effects of riboflavin deficiency on lipid metabolism as well as the desired effect of riboflavin administration [89-93]. A similar study reported reduced lipid peroxides like malondialdehyde and protein carbonyls in diabetic rats after riboflavin administration [94].

4.6.2 Vitamin B6 and oxidative stress: Vitamin B6 (Pyridoxine), is one of the water-soluble B vitamins that are essential for protein, fat, and carbohydrate metabolism [42]. Pyridoxine possesses some antioxidant property, even though it is not a classical antioxidant compound. The report shows that pyridoxine acts as an active hydroxyl radical (-OH) scavenger with the ability to mop-up to eight -OH molecules [95]. An in-vitro study reported that vitamin B6 prevented the generation of oxygen radicals and lipid peroxidation in U937 monocytes, which may occur via alteration of mitochondrial function [96]. Vitamin B6 deficient rats developed peroxidative stress because of increased thiobarbituric acid activity in the rat liver and heart [97] suggesting a pivotal role for pyridoxine in preventing peroxidation. Deficiency of vitamin B6 has a connection with atherogenesis by influencing the biosynthesis of long-chain polyunsaturated fatty acids, increase lipid peroxidation, and affect antioxidant defence [7]. Furthermore, pre-treatment of rats with vitamin B6 was effective in treating chromium-induced oxidative stress by improving antioxidant enzymes like catalase, superoxide dismutase, glutathione peroxidase, glutathione reductase and glutathione S- transferase (GST) which demonstrates the antioxidant property of vitamin B6 [98]. A theoretical study of the scavenging capacity of pyridoxine on different reactive oxygen species viz. hydroxyl, superoxide, and oxygen radical showed that pyridoxine reacts more strongly with hydroxyl radicals through binding with pyridoxine aromatic ring or the abstraction of hydrogen from the groups attached to the ring [99].

4.6.3 Vitamin B12 and oxidative stress: Vitamin B12 is also known as cobalamin, is a water-soluble vitamin that is essential in maintaining neuronal health and haematopoiesis. Cobalamin may possess some antioxidant property due to some evidence from in-vitro studies. Some authors suggest that vitamin B12 possess a direct super-oxide scavenger mechanism [6, 100]. Administration of cyanocobalamin on human aortic cells lowered the level of superoxide in the intracellular fluid and mitochondrion [100]. Similar results occurred in cell-free systems and neuronal cells. Furthermore, some in-vivo studies have also reported results with a reduced superoxide burst in the ganglion cells of the retina after vitamin B12 administration [6]. Also, the antioxidant property of vitamin B12 has a
relationship with its ability to preserve glutathione. However, the reactions involved in this are under investigation [101, 102]. Vitamin B12 may protect against oxidative stress by altering the activity of nuclear factor-KB, which may modulate the expression of cytokines and growth factors, thereby protecting against inflammation-induced oxidative stress [103], this is because studies with Vitamin B12 deficient rats reported decreased epidermal growth factor levels compared to control [103]. Vitamin B12 stimulates the conversion of homocysteine to methionine, and a deficiency of vitamin B12 will imply increase homocysteine levels [8]. Homocysteine is readily oxidised to hydrogen peroxide, thereby increasing reactive oxygen species in the body [104, 105]. Therefore, it indirectly protects against oxidative stress due to its role in homocysteine metabolism. Vitamin B12 may play a key role in oxidative stress cycle. Subclinical deficiency of vitamin B12 causes the generation of reactive oxygen species, which in turn impairs the uptake of vitamin B12. Oxidative stress can contribute to the formation of advanced glycated end products, which could reduce vitamin B12 uptake [106, 107].

4.6.4 Vitamin B3 and oxidative stress: Reduction of oxidative stress is by increasing the antioxidant potential through improved endogenous antioxidants, such as the enzymes Superoxide Dismutase (SOD), Catalase (CAT) and Glutathione Reductase (GR) [108], and exogenous antioxidants like nutritional antioxidants including tocopherols, ascorbic acid, carotenoids, niacin, and some trace elements [109]. Niacin (vitamin B3) acts as a coenzyme of redox enzymes in Nicotinamide Adenine Dinucleotide (NAD) and Nicotinamide Mononucleotide (NMN) forms [109]. A study on the possible beneficial effect of Niacin administration in rats exposed to methyl mercury demonstrated that niacin ameliorated the adverse effect produced by methyl mercury, the mechanism behind its useful role was suggested to relate to the inherent antioxidant potential of Niacin [110]. Niacin was also reported to improve lipid peroxidation, protein carbonylation, DNA damage, and tissue injury caused by reactive oxygen species in alloxan-induced diabetic rats [111]. Niacin also decreased glycation in human serum albumin and reduced DNA damage in in-vitro studies on glycated human serum albumin [112].

4.6.5 Vitamin B5 and oxidative stress: Pantothenic acid (PA) which is also known as vitamin B5 is a water-soluble vitamin that is involved in several intermediary metabolic reactions as a constituent of coenzyme A (CoA), while Coenzyme A plays a crucial role in glucose, fatty acids, and amino acids reactions like the tricarboxylic acid cycle, acetylation of choline to form acetylcholine and biosynthesis of fatty acids [113]. Administration of pantothenic acid has been reported to significantly reduce oxidative stress and improved damage to the brain in gamma-irradiated rats [114].

4.6.6 Vitamin B9 and oxidative stress: Vitamin B9 is also called Folates and exists in the following reduced forms viz: 7, 8-dihydrofolate (DHF), 5, 6, 7, 8-tetrahydrofolate (THF) and 5-methyltetrahydrofolate (5-MTHF), they are significant vitamins of medical importance because of their potential to improve cardiovascular disease due to the ability to reduce plasma homocysteine level [115, 116]. However, folates may have a direct antioxidant effect in-vivo, which has no connection to its homocysteine-lowering effect [117]. The reduced forms of folic acid were found to have a comparable antioxidant property with vitamin C and vitamin E [118]. THF exhibits the most protective effect against lipid peroxidation while DHT is very effective against ABTS+ cations. Folate has also been
reported by several studies to be beneficial in improving haematological disease [119, 120], cancer [121-124], neurological disorders [125], and neural tube defects [126, 127]. The protective role of folates in these diseases was suggested to be due to its antioxidant property [117, 128]. A Summary of vitamins biological roles and sources is given in Table 1.

|   | VITAMIN A | They are essential for vision, cell growth and development, antioxidant activity and promotion of proper cell communication [23]. | sweet potato, carrots, spinach, kale, mustard greens, collard greens, turnip greens, Swiss chard, winter squash, Romaine lettuce, cantaloupe, broccoli, asparagus, sea vegetables, chili peppers, tomatoes, basil, papaya, shrimp, eggs, Brussels sprouts and grapefruit while Pre-formed vitamin A sources are- shrimp, eggs, cow’s milk, cheese, yoghurt, salmon, sardines, chicken, turkey, beef and lamb [23]. |
|---|-----------|-------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 2. | VITAMIN D | Vitamin D is vital for the maintenance of healthy calcium homeostasis [25]. It is also involved in the maturation of white blood cells, which is a frontline player in immunity responses [26]. | Vitamin D is present in Egg yolks, tuna, salmon, sardines, mushrooms, cow’s milk, soy milk, orange juice and fortified foods [24]. |
| 3. | VITAMIN E tocopherols and tocotrienols. | Vitamin E shields the body structures from oxidative damage Vitamin E deficiency is also associated with heart attack, cancer, stroke, fibrocystic breast disease, epilepsy, PMS, diabetes, Parkinson’s disease, cataract, Alzheimer’s disease [29]. | Dietary sources of vitamin E includes Sunflower seeds, spinach, turnip greens, asparagus, beet greens, mustard greens, chili peppers, almonds, broccoli, bell peppers, kale, tomatoes, avocado, peanut, shrimp, olives, olive oil, collard greens, cranberries, raspberries, kiwifruit, carrots, and green beans [23]. |
| 4. | VITAMIN K Phylloquinone), (Menaquinone) (Menadione). | Vitamin K is essential for blood clotting activity [31, 32], helps in the maintenance of bone health by keeping demineralisation under control [32, 33] | eggs, meat, fish, dairy, fermented animal foods, and fermented plant foods, spinach, mustard greens, beet greens, Swiss chard, turnip greens, parsley, broccoli, Brussels sprouts, romaine lettuce, asparagus, basil, cabbage, celery, kiwifruit, green beans, cucumber, tomatoes, black pepper, green peas, blueberries, carrots, soybeans, avocado, raspberries, winter squash, pear, cranberries, |
|   | VITAMIN B1 | Thiamine | It is involved in energy production from carbohydrates and fats [34]. Vitamin B1 acts as a co-enzyme precursor of some key enzymes of carbohydrate metabolism [35]. It also helps in the structural development of brain cells [36], and it is involved in the detoxification of alcohol [35]. | Asparagus, sunflower seeds, green peas, flax seeds, Brussels sprouts, with beet greens, spinach. Cabbage, eggplant, romaine lettuce, mushrooms, navy beans, black beans, barley, and dried peas. Also, we have lima beans, oats, sesame seeds, kidney beans, peanuts, sweet potato, tofu, tuna, pineapple, oranges, broccoli, green beans, onions, collard greens, fortified cereals, dried beans, lean meats, soy foods and whole wheat grain. |
|---|---|---|---|---|
| 5. | VITAMIN B2 | Riboflavin | It is involved in energy metabolism. Vitamin B2 recycles glutathione which is the most crucial antioxidant which protects against free radicals in the body. It also promotes iron metabolism and its deficiency increases the risk of anaemia as iron is an essential element for red blood cell production [37]. | spinach, beet greens, asparagus, sea vegetables, eggs, cow’s milk, collard greens, broccoli, Swiss chard, green beans, mushrooms, turnip greens, kale, mustard greens, soybeans, yogurt, almonds, turkey, green peas, sweet potato, sardines, tuna, carrots and cabbage [23] |
| 6. | Vitamin B3 | Niacin Nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADP) | They are primarily involved in the production of energy from dietary proteins, carbohydrates, and fats [39]. NAD, NADP, and niacin-containing enzymes are scavengers of free radicals and protect tissues from oxidative damage [40]. | Mushrooms, cauliflower, sweet potato, broccoli, beet greens, asparagus, turnip greens, bell peppers, cucumber, celery, avocado, lentils, dried peas, chicken, turkey, yogurt, salmon, rye, beef, eggs, potatoes, wheat, corn, shrimps, papaya, winter squash, and cow milk. |
| 7. | VITAMIN B5 | PANTOTHENIC ACID | Pantothentic acid incorporated into Coenzyme A (CoA) has a central position for energy metabolism [41]. | fish, cauliflower, sweet potato, broccoli, beet greens, asparagus, turnip greens, bell peppers, cucumber, celery, avocado, lentils, dried peas, chicken, turkey, yogurt, salmon, rye, beef, eggs, potatoes, wheat, corn, shrimps, papaya, winter squash, cow’s milk, mustard greens, tomatoes, sea vegetables, |
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|---|---|---|
| 9. | Vitamin B6 | Pyridoxine | Vitamin B6 is involved in red blood cell production, carbohydrate metabolism, liver detoxification, brain and nervous system health [43]. It is also involved in the production of neurotransmitters in the brain and nervous system [43]. Vitamin B6 helps in liver detoxification and its deficiency cause the liver dysfunctioning [44]. Vitamin B6 deficiency was found to be linked with attention deficit disorder. | Tuna, spinach, cabbage, bell peppers, turnip greens, garlic, cauliflower, turkey, beef, chicken, salmon, sweet potato, potatoes, banana, winter squash, broccoli, Brussels sprouts, collard greens, beet greens, kale, carrots, swiss chard, asparagus, mustard greens, tomatoes, leeks, summer squash, chili peppers, sunflower seeds, pinto beans, avocado, lentils, green peas, lima beans, onions, shrimps, and pineapple [41]. |
| 10. | VITAMIN B9 | Folate | Vitamin B9 is essential for brain health and provides support for the cardiovascular and nervous system in human [45]. It is also vital for the production of red blood cells. | Lentils, asparagus, spinach, turnip greens, broccoli, beets, romaine lettuce, bok choy, cauliflower, parsley, pinto beans, garbanzo beans, black beans, navy beans, kidney beans, papaya, Brussels sprouts |
| 11. | Vitamin B12 | Cobalamin | It plays an essential role in energy metabolism. Vitamin B12 needed for erythrocyte maturation during the production of red blood cells, and it plays a role in the maintenance of cardiovascular health of human by preventing an increase in the level of homocysteine. Vitamin B12 also maintains bone health as the incidence of osteoporosis is increased with deficiency of this vitamin. | Sardines, salmon, tuna, cod, lamb, scallops, shrimps, beef, yoghurt, cow’s milk, eggs, turkey, chicken, cheese, mushrooms and breakfast cereals. |
| 12. | BIOTIN | | It is a member of B-complex vitamins, and most importantly, Biotin plays a crucial role in sugar and fat metabolism. Biotin is needed for fat deposition in tomatoes, almonds, eggs, onions, carrots, romaine lettuce, cauliflower, sweet potato, oats, peanuts, walnuts, salmon, yoghurt banana, raspberries, cow’s milk, strawberries, watermelon, grapefruit and | 226 |
the skin as biotin deficiency causes skin rashes.

13. VITAMIN C
   Ascorbic acid

Vitamin C is well known for its antioxidant properties protecting cellular structures from harmful effects of free radicals. It also plays a role in iron absorption by transforming iron into a form which can be easily absorbed into intestines. Also, Vitamin C is needed for collagen production, which is a structural component of the human body. The synthesis of certain neurotransmitters is also dependent on vitamin C, especially neurotransmitters involved in signalling of feelings, thoughts, and commands throughout the brain and nervous system. Vitamin C is also prerequisite for the synthesis of serotonin, a hormone needed for the proper functioning of the endocrine system, nervous system, digestive system and immune system.

Papaya, bell peppers, broccoli, Brussels sprouts, strawberries, pineapple, oranges, with kiwifruit. Cantaloupe, cauliflower, kale, cabbage, Bok choy, grapefruit, parsley, turnip greens, beet greens, mustard greens, collard greens, raspberries, Swiss chard, tomatoes, lemons and limes, spinach, asparagus, sea vegetables, fennel, and sweet potatoes [49].

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Table 1: Summary of Vitamins Biological Roles and Sources.

5. Conclusion

This review discusses both in-vivo and in-vitro studies on the antioxidant properties of vitamins. It has also been able to call attention to other vitamins (Vitamin K, Vitamin D, Niacin, Pyridoxine and Riboflavin) aside classical antioxidants (Vitamin C, E and carotenoids) which play vital roles in defending the body against free radicals by potentiating enzyme antioxidants, acting as co-enzymes, in their reduced physiological forms or by directly attacking free radicals. More studies using improved techniques should be carried out on these vitamins to delineate their role to allow their incorporation as nutritional supplementation for the management and prevention of human diseases.

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