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Versatile Role of Tocopherol (Vitamin E) on Human Health and Diseases: An Overview

Sohini Bhattacharyay[1], Srabasti Deb[1], Mainak Debnath[2], Sreyasree Basu[2], Indrajit Bhattacharyya[2] *

[1]Department of Food Technology, Guru Nanak Institute of Technology, West Bengal, India
[2]Department of Applied Science & Humanities, Guru Nanak Institute of Technology, West Bengal, India

ABSTRACT

The present article aims to highlight versatile functions and roles of Tocopherol (Vitamin E) on human health and diseases. Vitamin E is the generic descriptor for naturally occurring tocopherol and tocotrienol derivatives that qualitatively exhibit the biological activity of d-alpha-tocopherol. Vitamin E is highly soluble in fats and found to be an important component in the cell antioxidant defence system. Vitamin E is very popular not only for playing its fundamental role in the metabolism of cells and protecting the body tissues from damage caused by free radicals that can harm cells, tissues, and organs but also boost up the immune system against strong viral and bacterial attack. Primary dietary sources of vitamin E mostly include vegetable oils, seeds, and cereal grains. Study on the health reports across the globe clearly indicates that people who consume foods enriched with vitamin E or vitamin E dietary supplements experience lower chances of cardiovascular diseases, cancer, dementia, and skin diseases as well. Vitamin E deficit can result in various diseases such as peripheral neuropathy, myopathies, retinopathy that can lead to impaired immune responses.

Keywords: Vitamin E, antioxidant, immune system, tocopherol, tocotrienol

INTRODUCTION

Vitamin E was discovered in 1922 by Herbert Mclean E vans and Katharine Scott Bishop and in 1935, Evans and Gladys Anderson Emerson first isolated it as a micronutrient essential in the reproduction in rats at the University of California, Berkeley [**1**]. The chemical name of vitamin E "Tocopherol" had a Greek origin ("to'kos" means "child birth" and phe'rein means "to bear or to bring forth", i.e. to carry a pregnancy ending with "-ol" indicating an alocohol) and the biochemical importance of Vitamain E was first realized as a dietary fertility factor in the body of rats. [**2**].

A group of fat-soluble organic compounds having potential chain breaking antioxidant activities is commonly termed as Vitamin E [**3**]. Vitamin E is found to be present in fat-containing foods [**4**] and, the fat-soluble property of the vitamin allows it to be stored within the fatty tissues of animals and human beings. The vitamin E group (i.e. chroman-6-ols), collectively termed as tocochromanols (divided into tocopherols and tocotrienols), includes all of the tocol and tocotrienol derivatives that highlight the biological activity of d-alpha-tocopherol. It has been reported that the tocotrienol subfamily of natural vitamin E possesses powerful neuroprotective, anticancer, and cholesterol-lowering properties that are often not exhibited by tocopherols. Moreover at nanomolar concentration, α-tocotrienol, not α-tocopherol, prevents neurodegeneration [**5**].

Though it is not very clear why Tocopherol is considered as a Vitamin at all, the important health benefits of Vitamin E involve its antioxidant functions in cell membranes. Literature studies also reveal that vitamin E, specifically the RRR stereoisomer of alpha-tocopherol [**Fig. 1**] is popularly known for controlling gene expression and acting as an important factor in cell signal transduction and enzyme activity regulation [**6**].

Of the many different forms of vitamin E, gamma-tocopherol (γ-tocopherol) is the most common form that is found in the NorthAmerican diet, but alpha-tocopherol is the most biologically active species. Both the tocopherols and tocotrienols occur in α (alpha, where each of the three "R" sites has a methyl group (-CH3) attached)), β (beta, where R1= methyl group, R2=H, R3= methyl group), γ (gamma, where R1=H, R2=methyl group, R3=methyl group) and δ (delta, where R1=H, R2=H, R3=methyl group) forms, as determined by the number and position of methyl groups on the Chromanol ring. All eight of these vitamers feature a Chromane double ring, with a hydroxyl group that can donate

a hydrogen atom to reduce free radicals, and a hydrophobic side chain which allows for penetration into biological membranes [**6**].

FOOD SOURCES OF VITAMIN E

Variety of foods and plant oils, such as, soya, corn, olive oil, nuts and seeds, wheat germ found in cereals and cereal products, egg yolks, margarine, cheese, oatmeal, avocados and green leafy vegetables are considered to be common important sources of foods enriched with Vitamin E [**7**] (**Table 1**).

VITAMIN E DEFICIENCY

Various defects at various steps during delivery from the diet to the tissues, such as, malabsorption from the diet, defects in plasma lipoprotein transport, in delivery to cells and to sub-cellular sites, enhanced loss resulting from (oxidative) metabolism, result in Vitamin E deficiency in our body [**8**]. Deficiency of Vitamin E prevents our body from being able to absorb fats and fat soluble substances and thus results in several diseases, such as, chronic pancreatitis, Cholestasis, Cystic fibrosis, Short bowel syndrome, Crohn's disease etc. Since only a very small amount of vitamin E crosses the placenta, newborns, particularly premature ones, have been found to have an increased tendency of vitamin E deficiency that results in issues like haemorrhage in the brain and retinopathy of prematurity. However, infants usually get enough vitamin E through breast milk or milk with commercial formulas and thus the risk factor decreases with the age. On the other hand, deficiency of Vitamin E results in common symptoms like difficulty in waling, muscle weakness, coordination loss, and slow reflexes in children community. Adults can store large amounts of vitamin E in fat tissues, making the deficiency less likely. Excessive consumption of Vitamin E may found to be unsafe for the people who specially have heart disease or diabetes. Vitamin E plays an important role as an antioxidant especially for carrying mothers consuming Vitamin E supplements during initial periods of their pregnancy [**9, 10**].

ROLE OF α-TOCOPHEROL (VITAMIN E) ON HUMAN HEALTH

Research studies reveal that the biological activity of vitamin E is highly dependent upon regulatory mechanisms that serve to retain α-tocopherol and excrete the non-α-tocopherol forms [**3**]. The nutritional content of vitamin E is determined by comparing its equivalency to 100% RRR- configuration with α- tocopherol activity.[**11**] Vitamin E plays an important role as an efficient antioxidant that effectively scavenges radicals delivering hydrogen (H) atom to the peroxyl radicals as well as other free radicals and thus minimizes their damaging effect. The tocopherol radical thus-generated is recycled to tocopherol by a redox reaction in presence of a hydrogen donor, such as vitamin C. Due to very high solubility in fats; vitamin E can easily penetrate through the cell membranes and protect the membrane from oxidative damage. Thus alpha-tocopherol boosts our immune system and helps to resist blood clots to form [**12**]. Additionally α-tocopherol has very prominent effects on the immune system related to allergic airway disease (like rhinitis, atopic asthma) and lung functions. Higher serum α-tocopherol has been found to decline T cells that occurs with aging and thus considered to be a favourable spirometric marker in young adults [**13**]. In endothelial cells, α-tocopherol inhibits protein kinase C and thus inhibits the employment of leukocytes and altering the inflammatory immune response [**14, 15**]. It may also regulate the expression of immune-related genes in the heart as well as a group of genes related to inflammation.

Effect of Vitamin E as an antioxidant

Soon after the discovery of Vitamin E in 1922 [**1**], the antioxidant role of the vitamin E was explored [**16**], where vitamin E was described as a 'chain-breaking' antioxidant. The fact that vitamin E can efficiently inhibit lipid peroxidation was revealed during 1980 from physical organic chemistry approach [**17, 18**]. Most importantly Vitamin E functions as an antioxidant to protect lipids against oxidative damage [**17**]. It is observed from advanced studies that the rate of scavenging radicals decreases in the order of alpha, beta, gama and delta-tocopherol [**18**].

Vitamin E on the breast cancer

Breast cancer has been found a major health problem accounting for almost one – third of cancer related deaths in women across the globe. The prevention of breast cancer through dietary modification is an active area of clinical and epidemiologic research now a day. It has been proposed that the dietary supplementation of vitamin E, an important lipid-soluble antioxidant, may significantly reduce the risk of a woman in developing breast cancer. Experiments on animal body reveal that vitamin E can efficiently reduce the incidence of carcinogen-induced mammary tumors. Intake and serum levels of vitamin E and their relation to breast cancer have been evaluated in epidemiologic studies. In this regard, special attention should be paid to the interactions of other antioxidants with vitamin E and to the duration and timing (pre- vs. postmenopausal) of vitamin E in determining its preventive utility in breast cancer [**19, 20**].

Vitamin E and Cataract

Research and surveys have revealed that unstable molecular species such as free radicals effectively cause break down of healthy eye tissues and enhance possibilities of age-related macular degeneration (AMD) and cataract formation.

Vitamin E enriched food supplements like nuts, fortified cereals and sweet potatoes can efficiently protect eye cells from such kind damages and thus delay cataract formation [**21**]. Recent studies reveal that higher dietary intakes of lutein and zeaxanthin along with vitamin E significantly decrease the risk of cataracts and Vitamin E, accompanied with beta-carotene, vitamin C and zinc supplements, slows the progression of AMD by about 25 percent in individuals [**21**].

Cardiovascular Diseases

In addition to powerful antioxidant activity, Vitamin E exhibits potential preventive measures towards heart diseases. Alpha-tocopherol has been found to be the most active naturally abundant form of Vitamin E which is very popular for such preventive role. Oxidized low-density lipoprotein stimulates endothelial cells to produce inflammatory markers that is involved in foam cell formation and has cytotoxic effects on endothelial cells, inhibits the motility of tissue macrophages, and inhibits nitric oxide-induced vasodilatation. Vitamin E has been shown to increase oxidative resistance in vitro and thus can prevent atherosclerotic plaque formation in mouse models [**22, 23**].

Vitamin E and pregnancy

Vitamin E improves the blood circulation in placenta that offers the babies healthy wombs. Moreover, proper dosages of Vitamin E along with Vitamin C reduce the risk of high blood pressure (**pre-eclampsia**) during 16 to 22 weeks of pregnancy [**24**]. On the contrary, high Dosage of Vitamin E may cause complications during pregnancy. Medical studies reveal that children having higher concentration of Vitamin E at birth may have enhanced cognitive abilities at the age of two years [**7**].

Painful menstruation (dysmenorrhea)

Medical research shows that Vitamin E has an extremely important role in the regulation of Painful menstruation (dysmenorrhea). Taking vitamin E for 2 days before and for 3 days after bleeding begins decreases pain severity and duration, and thus reduces menstrual blood loss [**25**].

Vitamin E and skin

Being a powerful antioxidant Vitamin E supplements may be very much effective in regulating and reducing UV damages on skin. It has been studied that vitamin E applied topically may also help to nourish and protect our skin from damage issues resulting from harmful free radicals. Moreover, vitamin E effectively stops skin from losing moisture, protects cells from damage and softens the skin.

Figures and Tables

Table 1. Food sources of Vitamin E

Food Sources of Vitamin E	Milligrams of α-tocopherol (per serving)
Wheat germ oil, 1 tablespoon (tbsp)	20.3
Almonds, dry roasted, 1 oz.	7.4
Sunflower seed kernels, dry roasted, 1 oz.	6.0
Sunflower oil, over 60% linoleic, 1 tbsp	5.6
Safflower oil, over 70% oleic, 1 tbsp	4.6
Hazelnuts, dry roasted, 1 ounce	4.3
Peanut butter, smooth style, vitamin and mineral fortified, 2 tbsp	4.2
Peanuts, dry roasted, 1 oz.	2.2
Corn oil (salad or vegetable oil), 1 tbsp	1.9
Spinach, frozen, chopped, boiled, ½ cup	1.6
Broccoli, frozen, chopped, boiled, ½ cup	1.2
Soybean oil, 1 tbsp	1.3
Kiwi, 1 medium fruit without skin	1.1
Mango, raw, without refuse, ½ cup sliced	0.9
Spinach, raw, 1 cup	0.6
SOURCE: U.S. Department of Agriculture, Agricultural Research Service, 2004. USDA National Nutrient Database for Standard Reference, Release 16-.1. Nutrient Data Laboratory Home Page: www.nal.usda.gov/fnic/foodcomp.	

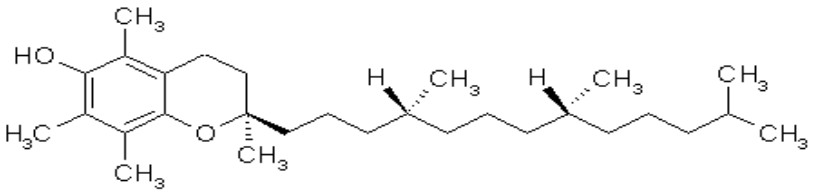

Figure 1. RRR Alpha-tocopherol form of Vitamin E

CONCLUSION

Vitamin E (alpha-Tocopherol) has been found to be an essential nutrient that functions as a peroxyl radical scavenger. The knowledge based on animal studies and human epidemiology thus suggests that tocopherols carry out essential functions in slowing or preventing degenerative disease processes. Though literature studies reveal vitamin E-specific pathways and molecular targets in several reports, the most important explanation as to why humans require Alpha-tocopherol is that it is a fat soluble antioxidant. Comparative functional studies explore that Alpha-Tocopherol is one of the important ingredients in regulating phosphorylation cascades and thus play unique role in case of heart diseases where cell adhesion, proliferation, and oxidant production may all be modified through vitamin E-sensitive pathways. Whereas, gama-Tocopherol is considered to be a unique potent nucleophile and generates a metabolite, gama-CEHC, with an intriguing pharmacological functions, natriuresis. Moreover, the former significantly contribute to the scavenging of electrophilic mutagens, whereas, the latter plays important roles to the prevention of cardiovascular disease by lowering blood pressure. Thus definite recommendation on the uses and dosages of tocopherols can only be expected from prospective intervention studies of individual tocopherols with defined isomers and stereochemistry.

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