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A REVIEW ABOUT VITAMIN E AND ITS EFFECTS

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Review
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Abstract

Vitamin E is a tocol due to its chemical structure, and a fat-soluble vitamin. It can be isolated from various plant sources. Vitamin E is an antioxidant and, since it is fat-soluble, it possesses important functions, especially in cell membranes and lipoproteins. It was first discovered as a micronutrient by Evans and Bishop in 1922. Its effects subsequently began being investigated. Different tocol compounds (tocopherol and tocotrienol) exhibit vitamin E activity. The most active form is alpha-tocopherol. Research shows that vitamin E reduces the risk of and ameliorates cardiovascular diseases, many types of cancer, and various chronic diseases. Studies of the effects of vitamin E on physiological and pathological states are still ongoing, and its protective and curative effects are being investigated. The purpose of this article is to highlight some of the effects on the body of vitamin E based on the available literature.

Key Words: Vitamin E, Antioxidant, Cancer, Chronic diseases, Apoptosis.

Özet

E vitamini, kimyasal yapısı nedeniyle bir tokol ve yağda çözünen bir vitamindir. Çeşitli bitki kaynaklarından izole edilebilir. E vitamini bir antioksidandır ve yağda çözünmesi nedeniyle özellikle hücre zarları ve lipoproteinlerde önemli fonksiyonlara sahiptir. İlk olarak 1922 yılında Evans ve Bishop tarafından bir mikro besin maddesi olarak keşfedildi. Daha sonra etkileri araştırılmaya başlandı. Farklı tokol bileşikleri (tokoferol ve tokotrienol) E vitamini aktivitesi gösterir. En aktif olanı alfa-tokoferoldür. Araştırmalar, E vitamininin kardiyovasküler hastalıklar, birçok kanser türü ve çeşitli kronik hastalıkların riskini azalttığını ve bu hastalıkları iyileştirdiğini göstermektedir. E vitamininin fizyolojik ve patolojik durumlar üzerindeki etkileri ile ilgili çalışmalar devam etmekte olup, koruyucu ve tedavi edici etkilerinin araştırılmasına yönelik çalışmalar yapılmaktadır. Bu makalenin amacı, mevcut literatürden yola çıkarak E vitamininin vücut üzerindeki bazı etkilerini vurgulamaktır.

Anahtar Kelimeler: E Vitamini, Antioksidan, Kanser, Kronik hastalıklar, Apoptoz.

1. Introduction

Vitamin E was discovered in 1922 by Herbert McLean Evans and Katharine Scott Bishop, and later isolated in pure form in 1935 by Evans and Gladys Anderson Emerson at the University of California, Berkeley (Oakes, 2007), It is a fat-soluble vitamin and has 8 isoforms, including four tocopherols (α, β, δ, γ) and four tocotrienols (α, β, δ, γ) (Zingg, 2007; Constantinou et al., 2008). Alpha-tocopherol is the most abundant form of vitamin E in nature. This substance occurs naturally as the D isomer; the racemic form is made synthetically, and this form is used as a medicine. In nature, vitamin E is found in vegetables, herbs and vegetable oils. In plants, tocopherol is found in green leafy plants as α-tocopherol and in fruits and seeds as γ-tocopherol (Zielinski, 2008; Akman, 2021).

Since there are established methods for the chemical measurement of alpha-tocopherol and others are difficult to measure chemically, only the amount of α-tocopherol is measured when evaluating the vitamin E activity of foods (Kayaalp, 2002).

Absorption and transport to the liver are like fat-soluble vitamins. It is mostly collected in the adipose tissue in the body; its stored amount is not much (Kayaalp, 2002; Kalaycıoğlu et al., 2006). Vitamin E, a fat-soluble vitamin, is absorbed by lipids, packaged into chylomicrons and

transferred to the liver, then transported in the plasma via the TTP (alpha-tocopherol transfer protein) in the liver (Herrera & Barbas, 2001). It hardly crosses the placenta. It is secreted in a relatively large amount into milk by the mammary glands in lactating women. Its concentration in normal plasma varies between individuals and averages 0.4-0.5 mg/dl. Changes in the total lipid level in the plasma are also reflected in the vitamin E level. Therefore, in evaluating the adequacy of the plasma vitamin E level, the plasma vitamin E/total lipid ratio is considered rather than the absolute vitamin E concentration. A rate below 0.8mg/dl is considered a deficiency (Herrera & Barbas, 2001; Kayaalp, 2002).

2. Material and Methods

This review was organized by searching the literature. The history, metabolism and effects of vitamin E on the body were investigated. Research papers on these topics were published between 1995 and 2021.

3. Results and Discussion

3.1. Vitamin E and antioxidant effect

The most important feature of vitamin E is its antioxidant activity. Unsaturated fatty acids of membrane phospholipids in cells can be easily oxidized and transformed into peroxide derivatives, either spontaneously or because of the challenging reaction of oxidant molecules. This event is called lipid peroxidation (Kayaalp, 2002; Kumar, 2017). Vitamin E shows its antioxidant effect by preventing lipid peroxidation and cell death according. It is known as a chain-breaking antioxidant (Kanter et al., 2007).

It has also been reported that it has antioxidant properties by reducing singlet oxygen, superoxide and hydroxyl radicals (Kumar, 2017). It is reported that vitamin E creates an extremely strong antioxidant effect by using all of the mechanisms of radical removal, suppression, repair and increase of endogenous defense (Stratton & Liebler,1997).

Vitamin E attracts and binds to itself to free oxygen radicals; before damaging cell organelles, cell membranes and nucleic acids. It prevents oxidative damage by settling on cellular membranes containing unsaturated fatty acids and other fats. It has been reported that in the deficiency of vitamin E, cellular membranes are damaged by free radicals and there is an increase in the passage of calcium ions into the cell (Kayaalp, 2002; Harrison et al., 2003; Jordão et al., 2004).

In addition, the protective or curative effects of vitamin E against the toxic effects of many drugs have been shown in various studies. A recent study investigated the effects of vitamin E against methotrexate-induced hepatotoxicity. In the histopathological analysis of liver tissue, the number of congestions, sinusoidal dilatation, activated Kuppffer cells and mononuclear cells increased in the methotrexate group. Vitamin E treatment after methotrexate reduced this histopathological damage compared to the methotrexate group. In the methotrexate group, oxidative stress increased in the liver, but vitamin E reduced oxidative stress with the help of its free radical scavenging property (Kurt et al., 2020). In a study examining the curative effects of vitamin E against cisplatin-induced nephrotoxicity; renal injury biomarkers (uric acid, urea, and creatinine) and tumor necrosis factor-a (TNF-a) were significantly higher in the cisplatin group, while these markers were decreased in the cisplatin+vitamin E group. Therefore, it was suggested that vitamin E might improve nephrotoxicity (Abdel-Daim et al., 2019). In a recent study, the potential cytoprotective effect of vitamin E on monosodium glutamate-induced testicular toxicity was demonstrated by various parameters. In addition, in histological examinations, it was observed that monosodium glutamate-induced pycnotic nucleus, irregular germinal epithelium, separation of spermatogenic cells from the basal lamina, and vacuolization findings were greatly improved with the application of vitamin E (El Kotb et al., 2020).

3.2. Effects of vitamin E on carcinogenesis and apoptosis

The role of vitamins in cancer treatment has been widely studied so far, and it is known that vitamins with high antioxidant capacity, such as vitamin E, play important roles in adjuvant therapy and as cancer-protective agents (Mamede et al., 2011). There are many studies on the applicability of vitamin E and its derivatives such as α, β, γ and δ tocopherols in cancer treatment (Wada, 2012; Yang et al., 2012). Although classical chemotherapeutic agents have toxic effects on non-cancerous normal tissues, some forms of vitamin E have been shown to have very low side effects on healthy tissues, making vitamin E advantageous (Zhao et al., 2009).

While α-tocopheryl succinate (α-TOS) caused apoptotic death of various neoplastic cell lines, redox-active α-tocopherol (α-TOH) and its uncharged ester α-tocopheryl acetate (α-TOA) were not as effective as α-TOS. Therefore, the proapoptotic activity of α-TOS draws attention (Yamamoto et al., 2000; Neuzil et al., 2001).

Various studies have been shown that vitamin E inhibits the growth of melanoma, colon, breast cancers (Malafa et al., 2001; Barnett et al., 2002; Weber et al., 2003; Lawson et al., 2004).

Weber et al. said that mitochondria play a central role in apoptosis induced by α-tocopheryl succinate, an agent with anticancer activity (Weber et al., 2003). Malafa et al. observed that melanoma growth was inhibited in mice that given vitamin E (Malafa et al., 2001). Barnett et al. observed that liver metastases in colon cancer were prevented by vitamin E (Barnett et al., 2002). Lawson et al. discovered that a novel vitamin E analog administered as liposome aerosols reduced mammary tumor burden and inhibited metastasis in mouse (Lawson et al., 2004).

In vivo and in vitro studies over the past few years have shown that tocotrienols can effectively inhibit the growth of many types of cancer or prevents cancer formation. In a recent study; δ-tocotrienol has been shown that blocked human bladder cancer cell growth by inhibition of the STAT3 pathway (Ye et al., 2015). Gamma-tocotrienol reversal of the epithelial-mesenchymal transition in human breast cancer cells was associated with inhibition of canonical Wnt signaling (Ahmed et al., 2016). Xu et al. observed in their studies that γ-tocotrienol administration inhibited proliferation and induced apoptosis in human cervical cancer HeLa cells via the mitochondrial pathway (Xu et al., 2017). In a recent study, it was observed that Tocotrienol-rich fraction (TRF) can suppress colon cancer via Wnt pathway (Zhang et al., 2015). In a study in human gastric cancer cells, γ-tocotrienol was shown to inhibit the invasion and migration of human gastric cancer cells through down-regulation of cyclooxygenase-2 expression. (Zhang et al., 2018). Lim et al. reported that administration of β-tocotrienol in human lung and brain cancer cell lines causes antiproliferation and induction of caspase-8-dependent mitochondria-mediated apoptosis (Lim et al., 2014). Gamma-tocotrienol treatment increased the expression of peroxiredoxin-4 in a study in HepG2 liver cancer cell line (Sazli et al., 2015). In a different study, the role of the EGR-1/Bax pathway in δ-tocotrienol-induced apoptosis in pancreatic cancer cells has been demonstrated (Wang et al., 2015). Tocotrienol has been shown to play a role in inhibiting human prostate tumor growth in conjunction with epigenetic modifications of cyclin-dependent kinase inhibitors p21 and p27 (Huang et al., 2017). An in vitro study showed that; α-tocotrienol induces endoplasmic reticulum stress-mediated apoptosis in human melanoma cells (Marelli et al., 2016).

3.3. Effects of vitamin E on the cardiovascular system

Alpha-tocopherol is the most naturally abundant and active form of vitamin E, a fat-soluble antioxidant vitamin. Oxidation is an important cause of atherogenesis. The oxidized low-density lipoprotein stimulates endothelial cells to produce inflammatory markers, has cytotoxic

effects on endothelial cells, inhibits the motility of tissue macrophages, and inhibits nitric oxide-induced vasodilation. Vitamin E has been shown to increase oxidative resistance in vitro and prevent atherosclerotic plaque formation in mouse models. Consumption of foods rich in vitamin E has been associated with a lower risk of coronary heart disease in middle-aged to older men and women (Saremi & Arora, 2010).

Cell culture studies have shown that vitamin E (α-tocopherol) inhibits the activation of endothelial cells stimulated by high levels of low-density lipoprotein cholesterol and proinflammatory cytokines. With this inhibition, it was predicted that the development of lesions on the arterial wall could be prevented (Meydani, 2004).

In the study investigating the effects of dietary intake of vitamins C and E on plasma antioxidant levels and oxidative stress in elderly subjects; they found that plasma levels of vitamins C and E were inversely related to coronary heart disease (Singh et al., 1995).

3.4. Neurological diseases associated with vitamin E deficiency

Vitamin E is a fat-soluble antioxidant essential for human health. Studies with vitamin E deficiency in humans and animal models have revealed that vitamin E plays critical role in protecting the central nervous system and especially the cerebellum from oxidative damage and motor coordination deficiencies (Ulatowski & Manor, 2015).

The biological half-life of vitamin E in the brain is extremely slow compared to other tissues, and the concentrations of α-tocopherol vary widely in different parts of the brain. For these reasons, we can say that vitamin E exhibits behaviors specific to the central nervous system tissue (Gohil et al., 2008). The expression level of TTP was markedly elevated in brain samples from patients affected by Alzheimer's disease, the oxidative stress-related neurodegenerative disease (Copp et al., 1999). However, it has been reported in studies that the use of vitamin E does not affect the regression of Alzheimer's disease and the improvement of mild cognitive disorders (Isaac et al., 2008; Boothby et al., 2005).

Vitamin E deficiency ataxia (AVED) is a rare autosomal recessive neurodegenerative disease due to mutations in the TTPA gene. In addition to symptoms such as ataxia, dysarthria, and hyporeflexia, cardiomyopathy and retinitis pigmentosa findings are also observed (Di Donato et al., 2010).

3.5. Use of vitamin E in chronic diseases

In a randomized controlled study, it was determined that the use of vitamin E in Type 2 diabetes mellitus patients with nonalcoholic hepatosteatosis improves the picture of nonalcoholic hepatosteatosis, and the use of combined or single vitamin E improves the deteriorated histology of the liver (Bril et al., 2019). In streptozocin-induced diabetic rats, blood glucose levels decreased, and blood and tissue MDA levels were significantly decreased after vitamin E administration (Daniel et al., 2018).

Vitamin E levels of pregnant women who developed pregnancy-induced hypertension and normal pregnant women in the third trimester were examined, and it was found that vitamin E levels were significantly lower in the group with pregnancy-induced hypertension (Sahu et al., 2009).

Studies in the literature say that vitamin E can reduce the incidence and severity of some autoimmune diseases through the regulation of the immune system (Rezaieyazdi et al., 2018). In an in vivo study examining the curative effects of vitamin E on autoimmune arthritis disease, it was concluded that oral nutrition rich in tocotrienol obtained from palm oil was effective on histopathological and radiological improvements (Zainal et al., 2019).

3.6. Effects of vitamin E deficiency in childhood

Vitamin E is known to prevent oxidative stress due to its antioxidant activity (Ghaffari et al., 2014). It also plays a role in improving nerve conduction, integrating the hemoglobin membrane, and is necessary for normal vision (Okebukola et al., 2020).

The erythrocytes of patients with hereditary hemolytic anemia are prone to an increased risk of chronic oxidative stress-induced membrane lipid peroxidation resulting in a shortened half-life of developing erythroblasts and circulating erythrocytes. Vitamin E deficiency is a common feature seen in some of these hereditary hemolytic anemias (Ren et al., 2008). Various studies in the literature; revealed that α-tocopherol supplementation significantly reduced red blood cell deformity, reduced erythrocyte osmotic fragility and early hemolysis, and therefore increased hemoglobin levels in patients with sickle cell anemia, beta-thalassemia, and glucose-6-phosphate dehydrogenase deficiency (Jaja et al., 2005; Sutipornpalangkul et al., 2012). Vitamin E deficiency in premature infants has been associated with hemolytic anemia. Although formulas and parenteral nutrition are supported by vitamin E; since some preterm babies can still develop

hemolytic anemia, it was thought that those with anemia, reticulocytosis and oxygen need could benefit from additional vitamin E (Gomez-Pomar et al., 2018).

As a result, in this review article, some of the effects of vitamin E on the body and its protective/healing effects on tissues were discussed. Studies on the physiological effects of vitamin E and its possible protective/healing effects in diseases are still ongoing. We believe that the unclear points on this subject and the role of vitamin E in the events will be explained together with its mechanisms.

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