Vitamin E Deficiency

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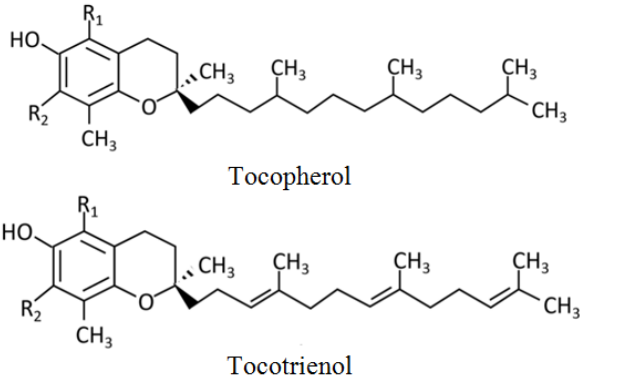
INTRODUCTION

Vitamins, unlike macronutrients, do not serve structural functions, nor does their catabolism provide significant energy, but they can still be considered crucial for essential metabolic functions [1]. In fact, the common forms of most vitamins require some metabolic activation to their functional bioactivity. Although the vitamins share these general characteristics, they display chemical and functional similarities. Briefly, vitamins are emphatically grouped into fat-soluble vitamins (A, D, E, and K) and water-soluble vitamins (B-complex and C) based on their absorption potential in either fat or water, in addition to the region of their physiological activity. For instance, several vitamins act as enzymatic cofactors (vitamins A, K, and C; thiamin; niacin; riboflavin; vitamin B6; biotin; pantothenic acid; folate; and vitamin B12). Others are natural antioxidants (vitamins E and C) orcan act as cofactors in metabolic oxidation-reduction reactions (vitamins E, K, and C, niacin, riboflavin, and pantothenic acid) [2]. Vitamins A and D have been reported to exhibit properties of skin hormones, such as organized metabolism, activation, inactivation, and elimination in specialized cells of the tissue, exertion of biological activity, and release in the circulation [3]. Also, vitamin A serves as a photoreceptive cofactor in vision [4]. On the other hand, water-soluble vitamins movement freely through the body, and excessive amounts usually are excreted by the kidneys through urine. Human body requires water-soluble vitamins in recurrent small doses. These vitamins are not as likely as fat-soluble vitamins to reach toxic levels. However, niacin, vitamin B6, folate, choline, and vitamin C have higher consumption limits. Fat-soluble vitamins are stored in the body's fat cells and are not excreted as easily as water-soluble vitamins [5]. Taking into consideration, understanding the significance as well as the magnitude of the severity of this micronutrient's malnutrition, and providing adequate control and preventive measures is very crucial for human health promotion.

VITAMIN E

Vitamin E is a lipid-soluble compound whose molecular structure contains a chromanol ring with a side chain located at the C2 position. This vitamin comprises a group of eight different compounds: α-, β-, γ-, and δ-tocopherols and the corresponding four tocotrienols (Figure 1). These forms present antioxidant activities, but cannot be interconverted, and only α-tocopherol meets the human vitamin E requirement. In recent years an enzymatic synthesis of vitamin E ester derivatives forms of tocopherol and tocotrienols, including acetate, nicotinate, succinate, and phosphate, has received

increasing attention due to its prospective applications and higher oxidation resistance [6]. As is common knowledge, vitamin E it is a compound easily oxidized when subjected to heat, light, and alkaline conditions, while esters are less susceptible to oxidation and therefore more appropriate for food, cosmetic, and pharmaceutical applications compared to the free form.



	α	β	γ	δ
R1	CH_3	CH_3	H	H
R2	CH_3	H	CH_3	H

Figure 1: Chemical structure of vitamin E homologues.

Vitamin E can be considered as the major lipid-soluble component in the cell antioxidant defense system, and it can only be obtained from the diet [7]. Vitamin E comprises important biological functions within the body due to its role as an antioxidant agent [8]. This vitamin protects the Polyunsaturated Fatty Acids (PUFAs) in the membrane from oxidation, regulate the production of Reactive Oxygen Species (ROS) and Reactive Nitrogen Species (RNS), and modulate signal transduction. Immunomodulatory effects of vitamin E have been observed in animal and human models under normal and disease conditions [9]. As is common knowledge, oxidation has been linked with the increase and development of inflammatory processes. Inflammation is a common pathogenesis of many chronic diseases, including cardiovascular and bowel diseases, diabetes, arthritis, and cancer [10]. Also, platelet hyperaggregation, that originate atherosclerosis, can also be avoided by vitamin E intake. Also, platelet hyper aggregation has been detected in psoriatic patients, promoting thrombus formation [11]. The current literature review discusses the importance of vitamin E, considering the diseases that may result from the lack of this vitamin.

NATURAL SOURCES OF VITAMIN E

For a better understanding of the consequences of vitamin E deficiency, it is imperative to address exogenous natural sources recognized for their high levels of this vitamin. Humans cannot synthesize vitamin E, so enough quantity must be obtained through the diet. Notably, the occurrence of vitamin E malnutrition in an individual could be an indication of vitamin deficiency, attributable not only to poor consumption of vitamin-rich diets but also due to factors influencing vitamin absorption. As a fat-soluble natural compound, vitamin E is found in plant-based oils, nuts, seeds, fruits, and vegetables. The proportion of the four tocopherols (Figure 1) varies in plant organs. In leaves, for example, the most abundant vitamer is α-tocopherol [12], while β-, γ-, and δ-tocopherols and tocotrienols tend to predominate in plant seeds [13]. Additionally, the proportion of these vitamin E isomers substantially differs between the same plant varieties, oil extraction method or even the cooking method [14]. Safflower oil, coconut oil, rapeseed oil, palm oil, olive oil, almonds, peanuts, pistachio, walnuts, and acorns are recognized as natural sources of vitamin E [15,16]. Some fruits and vegetables also contain significant amounts of vitamin E (more than 1 mg/100 g edible weight), such as avocado, blackberries, cranberries, kiwi, and green leafy vegetables [13,17]. Animal products, including meat, milk, and eggs are valuable sources of vitamin E [18]. According to some authors, vitamin E supplementation in animal diet has been reported to be effective in reducing lipid oxidation in meat [19], eggs [20], and milk [21], as well as lowering serum and egg yolk cholesterol concentrations and improving antioxidant status of the animal [21]. These results allow us to affirm that the increase in vitamin E supplementation in animal feed enhances them as animal foods.

VITAMIN E DEFICIENCY

To understand the consequences of vitamin E deficiency, it is important to highlight its main functions. Vitamin E is recognized as potent biological antioxidant, being considered the most important compound of defense against lipid peroxidation. Also, it is important for normal function of the immune cells, for modulatory effects regarding signal transduction, cellular

pathways (e.g., NF-KB signaling), and gene expression (e.g., pro-inflammatory cytokines). Besides its immunomodulatory effects, vitamin E also plays an important role in carcinogenesis with its antioxidant properties against cancer, and ischemic heart disease with limiting the progression of atherosclerosis.

Despite vitamin E deficiency be considered extremely rare in humans, most cases of hypervitaminosis are related to dietary pattern. Rather, it tends to be caused by irregularities in dietary fat absorption or metabolic disorders. For instance, the lack of fruit and vegetable intake by pregnant women without immunity to toxoplasmosis, may provide scarcity of vitamin E in premature infants. Also, severe acute respiratory syndrome SARS-CoV-2 reached pandemic status perhaps because of poor eating habits and, consequently, lack of an effective immune system which is strengthened by vitamin E. According to Ferro et al. [22] as an immunological response to SARS-CoV-2 a high concentration of cytokine over stimulates the body's immune response to microorganisms because of the increasement of inflammatory factors levels. Vitamin E deficiency cannot activate apoptotic pathways in neoplastic cells [23]. Ling et al. [24] described tocotrienols as the most chemopreventive agents. In contrast to the effects of α-tocopherol in animal carcinogenesis models (colon, prostate, mammary and lung) tocotrienols have demonstrated higher positive chemopreventive effects. However, the levels of tocotrienols described in foods are significantly lower than tocopherols levels, showing, once again, the negative effects of vitamin E deficiency.

Several diseases are caused by oxidative stress. Low contents of vitamin E can promote elevated oxidative stress with high production of Reactive Oxygen Species (ROS), Malondialdehyde (MDA), 8-Hydroxy-2-deoxyguanosine (8-OHdG) and isoprostanes. Thus, various transcription factors can be activated, increasing expression of genes encoding growth factors, inflammatory cytokines, and chemokines. Oxidative stress is associated with the pathogenesis of multiple diseases, such as, cardiovascular disease, cancer, diabetes, hypertension, aging, and atherosclerosis. Therefore, oxidative stress products as well as serum vitamin E levels can also be used as markers of the inflammatory response.

CONCLUSION

More studies are now focusing on vitamin E as an anti-inflammatory agent duo to its antioxidant activity. Current studies suggest that increasing vitamin E intake might be a suitable candidate as an alternative treatment for chronic degenerative diseases. Moreover, inflammaging is a highly significant risk factor for both morbidity and mortality in the elderly people, as most if not all age-related diseases. Vitamin E deficiency will provide elevated levels of inflammatory biomarkers such as C-reactive protein and interleukin-6 (IL-6), which are linked to many aging phenotypes, for example, changes in body composition, energy production and utilization, metabolic homeostasis, immune senescence, and neuronal health. Currently, studies are being conducted against COVID-19 using a group of phytochemicals, including vitamin E. Although the group of phytochemicals is diverse, a small number of them have been qualified for clinical trials and are commercially available. To improve the knowledge of vitamin E and its pharmacological properties, structure-activity relationship, identification of its molecular mechanism and evaluation of biological properties should be carried out.

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