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STRUCTURAL FEATURES AND PHARMACOLOGICAL IMPORTANCE OF VITAMIN E AS AN ANTIOXIDANT IN HUMANS

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Abstract

Oxidative stress, resulting from an imbalance between reactive oxygen species production and antioxidant defense mechanisms, plays a central role in the pathogenesis of numerous chronic and degenerative diseases. Vitamin E represents a major group of lipid-soluble antioxidants that protect cellular membranes and lipoproteins from oxidative damage. This review comprehensively summarizes the chemistry, structural classification, transport mechanisms, and pharmacological roles of vitamin E, with particular emphasis on its antioxidant function in human health. Vitamin E encompasses eight naturally occurring tocochromanols, including four tocopherols and four tocotrienols, each exhibiting distinct biological activities influenced by their chemical structure, stereochemistry, and metabolism. The review highlights dietary sources, physicochemical characteristics, and the preferential biological activity of α-tocopherol mediated through the α-tocopherol transfer protein. Furthermore, the mechanistic role of vitamin E as a chain-breaking antioxidant in preventing lipid peroxidation is discussed, along with its synergistic interaction with other antioxidants such as vitamin C. The pharmacological significance of vitamin E in the prevention and modulation of cardiovascular diseases, cancer, cataracts, neurodegenerative disorders such as Alzheimer's disease, immune dysfunction, and infectious diseases is critically evaluated. Despite promising mechanistic and observational evidence, clinical outcomes of vitamin E supplementation remain inconsistent, emphasizing the importance of isoform specificity, dosage, and population characteristics. Overall, this review underscores the multifaceted biological roles of vitamin E and highlights future research directions necessary to optimize its therapeutic and preventive applications.

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INTRODUCTION

An excessive accumulation of oxidants and free radicals poses a serious threat to human health when endogenous defense mechanisms fail to neutralize them effectively, leading to a condition known as oxidative stress. This imbalance between the generation of reactive oxygen species (ROS) and antioxidant defenses plays a central role in the initiation and progression of numerous chronic disorders, including cancer, cardiovascular diseases, rheumatoid arthritis, autoimmune conditions, and age-related degeneration (Langseth, 1995). Oxidative stress contributes to cellular dysfunction by inducing structural and functional damage to essential biomolecules such as nucleic acids, lipids, and proteins (Valko et al., 2007). To counteract oxidative damage, the human body employs a complex antioxidant defense system consisting of both endogenously synthesized antioxidants and exogenous antioxidants obtained from dietary sources and supplements (Alin & Hakkarainen, 2011; Finley et al., 2011). Dietary antioxidants are abundant in foods rich in vitamins A, C, and E, essential minerals, and polyphenolic compounds. Consequently, diets enriched with antioxidant-containing foods have been widely suggested to reduce the risk or delay the onset of chronic diseases, including cancer and neurodegenerative disorders such as Alzheimer's disease. Among dietary antioxidants, vitamin E has received considerable attention due to its proposed role in mitigating oxidative stress caused by free radical activity (Davì et al., 2005; Nunomura et al., 2006).

Vitamin E refers to a group of lipid-soluble compounds first identified in 1922 by Evans and Bishop, which possess distinct antioxidant properties essential for normal physiological function (Niki & Traber, 2012). It is predominantly found in fat-containing foods, and owing to its fat-soluble nature, vitamin E can be stored in adipose tissues, reducing the need for daily intake (Zingg, 2007). Chemically, vitamin E belongs to the family of tocochromanols, which includes tocopherols and tocotrienols, collectively derived from homogentisic acid in plants. There are eight naturally occurring isoforms: α-, β-, γ-, and δ-tocopherols, along with their corresponding tocotrienols. Among these forms, α- and γ-tocopherols are the most abundant in human diets, with their relative proportions varying according to food sources. Vegetable oils represent the richest dietary sources, containing multiple homologues in differing concentrations. In human circulation, α-tocopherol is

the predominant form present in serum and erythrocytes, whereas β- and δ-tocopherols occur in much lower concentrations. The preferential retention of α-tocopherol is attributed to its high affinity for the α-tocopherol transfer protein (α-TTP), which selectively facilitates its incorporation into circulating lipoproteins. In contrast, other tocopherol forms are more rapidly metabolized and excreted via bile and feces. α-Tocopherol is also widely distributed in non-hepatic tissues, particularly in organs with high oxidative activity, such as the heart and lungs, where it accumulates in mitochondrial and endoplasmic reticulum membranes (Chow, 1997).

As a potent antioxidant, vitamin E protects cellular membranes from oxidative damage by scavenging free radicals generated during metabolic processes or environmental exposure, including tobacco smoke and radiation. Such protective effects are associated with a reduced risk of conditions such as cardiovascular disease, cancer, and inflammatory disorders. In addition to its antioxidant activity, vitamin E plays a vital role in maintaining immune function, skin integrity, and visual health (Rizvi et al., 2012). Common dietary sources include nuts, seeds, and vegetable oils, making adequate intake achievable through balanced nutrition. Although vitamin E deficiency is rare, excessive supplementation can result in tissue accumulation and potential adverse effects (Pham-Huy et al., 2008). This review highlights recent advances in vitamin E research, emphasizing its biological significance, antioxidant potential, and implications for human health. It aims to provide a comprehensive overview of the beneficial effects of vitamin E and its prospective role in disease prevention and therapeutic strategies.

SOURCES OF VITAMNIN E

Dietary Sources include nuts, seeds, vegetable oils, and several fruits and vegetables are among the foods that provide vitamin E. The largest natural concentration of vitamin E is found in wheat germ oil, which is followed by almonds and sunflower seeds. **Nuts and seeds**, such as hazelnuts, peanuts, pumpkin seeds, pine nuts, Brazil nuts, and pistachios, are additional foods rich in vitamin E. Sunflower, safflower, corn, and soybean oils are examples of vegetable oils. **Vegetables:** butternut squash, turnip greens, red bell pepper, spinach, and broccoli. **Seafood:** abalone, trout, and salmon.

Fruits: Kiwi fruit, avocados, mangoes, and mamey sapote. Fruit juices, spreads, margarines, and breakfast cereals are examples of fortified foods. Additionally, because they include all of the many homologues in variable amounts, edible vegetable oils are the richest dietary sources of vitamin E (**Table 1**). Because of its antioxidant and moisturising qualities, vitamin E is usually thought to be good for hair health, with potential advantages like encouraging hair growth, lowering breakage, and enhancing scalp health. As an antioxidant that shields skin cells and hydrates the skin, vitamin E is beneficial for skin. It can alleviate excessive pigmentation, UV damage, and dry skin (Bartolini et al., 2022).

Table 1: Vitamin E content in vegetable oils (in mg of tocopherol per 100 g) (Drotleff and,Ternes 2001).

Oil	α-tocopherol	γ-tocopherol	δ-tocopherol	α-tocotrienol
Coconut	0.5	0	0.6	0.5
Maize (corn)	11.2	60.2	1.8	0
Palm	25.6	31.6	7.0	14.3
Olive	5.h	Trace amounts	0	0
Peanut	13.0	21.4	2.1	0
Soybean	10.1	59.3	26.4	0
Wheatgerm	133.0	26.0	27.	2.6
Sunflower	48.7	5.1	0.8	0

CHEMISTRY OF VITAMIN E

The eight fat-soluble molecules that make up vitamin E include four tocopherols (α, β, γ, and δ) and four tocotrienols (α, β, γ, and δ). The most physiologically active form of vitamin E is α-tocopherol, which has a chromanol ring and a phytyl-like side chain. Natural tocochromanols are classified into two homologous series: tocopherols with a saturated side chain and tocotrienols with an unsaturated side chain. The word "tocopherol" refers to the methyl-substituted derivatives of tocol and is not the same as "vitamin E." A lengthy isoprenoid side chain attached at position two of a 6-

chromanol ring characterises the basic chemical structure shared by tocopherols and tocotrienols (**Figure 1**) (Ball, 1997).

Tocochromanols: Tocopherols and tocotrienols are subtypes of tocochromanols, which are a group of vitamin E molecules (**Figure 1.A**). Whereas tocotrienols contain an unsaturated side chain with three double bonds, tocopherols have a saturated side chain. **Chroman Ring:** A substituted 6-chromanol ring, which is a six-membered ring with a hydroxyl group, is the structure shared by both tocopherols and tocotrienols. **Phytyl-like Side Chain:** The 6-chromanol ring has a lengthy isoprenoid side chain connected to it. **Methylation Pattern:** Tocopherol or tocotrienol is classified as α, β, γ, or δ based on the methylation pattern of the chromanol ring. Positions 5, 7, and 8 of the chromanol ring are methylated in α-tocopherol, the most physiologically active form. **Other variant:** Include β-tocopherol alone at position 8, γ-tocopherol at positions 7 and 8, and β-tocopherol that is methylated at locations 5 and 8. **Figure 1.C** illustrates tocotrienols, which are comparable to tocopherols but have three double bonds in their side chain (Mohd et al., 2020).

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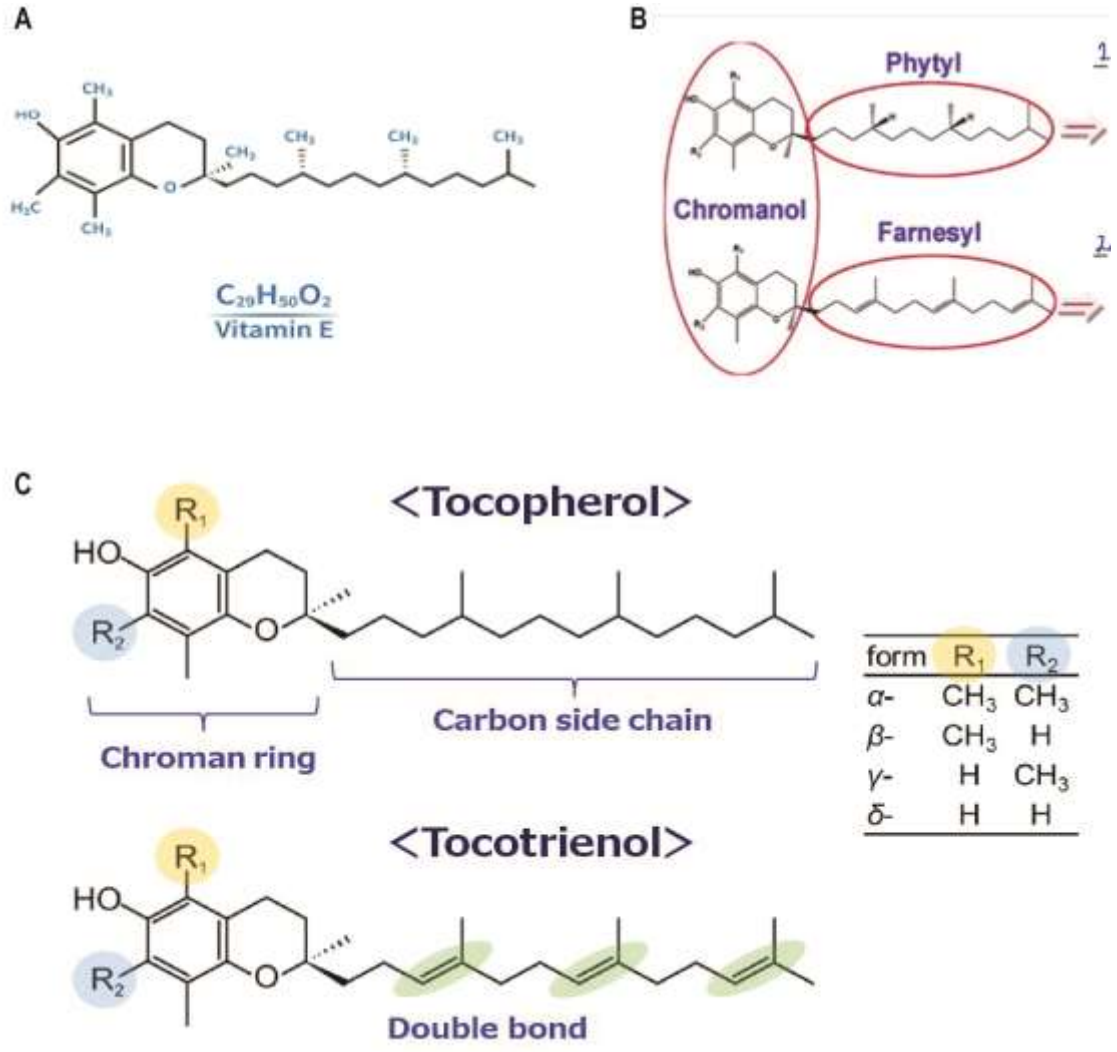

Figure 1: Chemical structure of vitamin E.

CLASSIFICATION OF VITAMIN E

Vitamin E refers to a group of fat-soluble compounds with biological activity that share a common 6-hydroxychroman ring structure. These compounds, collectively known as tocols, include both tocopherols and tocotrienols. Structurally, tocols are derivatives of 2-methyl-2-(4,8,12-trimethyltridecyl)-chroman-6-ol and differ mainly in the saturation and substitution pattern of their side chains and chromanol rings. Tocopherols are characterized by a chromanol ring that is variably

methylated at the 5, 7, and 8 positions and a fully saturated C16 phytyl side chain attached at position 2. In contrast, tocotrienols possess an unsaturated isoprenoid side chain containing three double bonds at the 3, 7, and 11 positions. The degree and position of methyl groups on the chromanol ring determine the individual homologs within each group. Accordingly, α-tocotrienol contains three methyl groups (5,7,8-trimethyl), β-tocotrienol has two methyl groups at positions 5 and 8, γ-tocotrienol is dimethylated at positions 7 and 8, and δ-tocotrienol contains a single methyl group at position 8.

Although tocopherols and tocotrienols share identical chromanol ring methylation patterns and nomenclature (α, β, γ, and δ), they differ structurally in the saturation of their hydrophobic side chains. Tocopherols contain a saturated phytyl tail, whereas tocotrienols possess an unsaturated tail with three isolated double bonds. This unsaturation reduces the number of stereogenic centers in tocotrienols, resulting in fewer possible stereoisomers compared with tocopherols. Tocotrienols have only one chiral carbon at position 2 of the chromanol ring, giving rise to two stereoisomers (2R and 2S), although only the naturally occurring 2R configuration with trans double bonds at the 3 and 7 positions is biologically relevant. Vitamin E activity is influenced by the degree of methylation on the chromanol ring, with higher methylation—particularly in the α-form—being associated with greater biological potency. Overall, vitamin E comprises eight naturally occurring compounds, including four tocopherols (α-, β-, γ-, and δ-tocopherol) and four tocotrienols (α-, β-, γ-, and δ-tocotrienol). All eight forms consist of a polar chromanol head and a hydrophobic isoprenoid-derived side chain. Chemically, tocopherols and tocotrienols are closely related, differing only in the saturation of their side chains. Despite the structural diversity among vitamin E homologs, α-tocopherol (RRR-α-tocopherol) is often considered the reference form due to its superior bioavailability and preferential retention in human tissues. For this reason, α-tocopherol is commonly regarded as the standard against which the biological activity of other vitamin E forms is evaluated, even though it represents only one of the eight naturally occurring vitamin E compounds.

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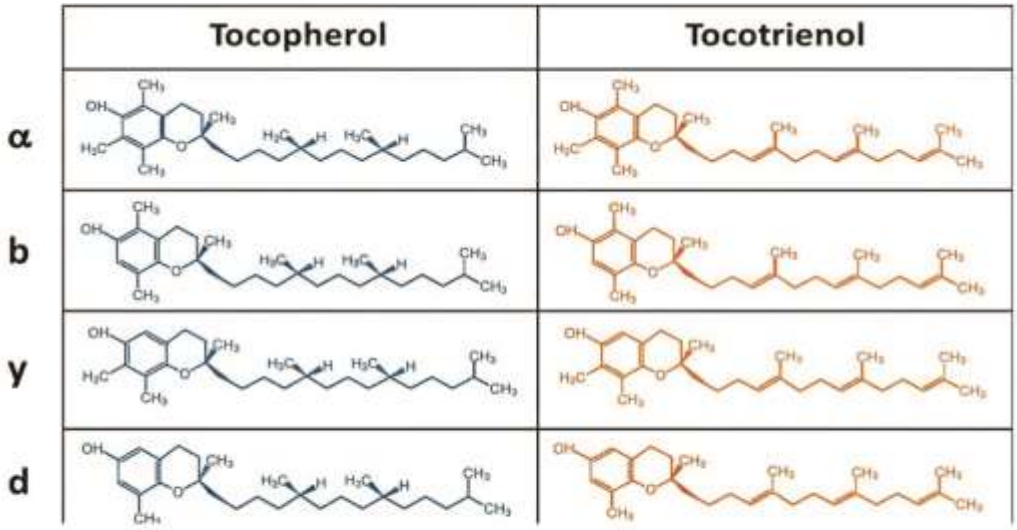

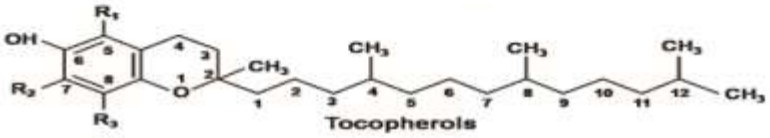

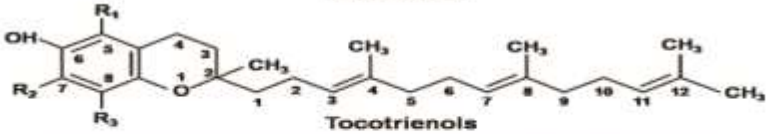

Tocopherols / Tocotrienols	R_1	R_2	R_3
α-Tocopherol / Tocotrienol	CH_3	CH_3	CH_3
β-Tocopherol / Tocotrienol	CH_3	H	CH_3
γ-Tocopherol / Tocotrienos	H	CH_3	CH_3
δ-Tocopherol / Tocotrienol	H	H	CH_3

Figure 2: Classification of vitamin E.

CHEMICAL CHARACTERISTICS

Antioxidant Activity: As a lipid-soluble antioxidant, vitamin E guards against free radical damage to cell membranes and other lipids. Free radicals are extremely reactive oxygen species that are produced during regular metabolism and inflammatory processes because they have one or more unpaired electrons. Free radicals can bind to any adjacent normal cellular component, including polyunsaturated fatty acids (PUFAs) or DNA, and oxidize or "steal" an electron, causing damage to that component. Free radicals attacking polyunsaturated fatty acids (PUFA) produce lipid peroxyl radicals, which can spread endlessly in a chain reaction (Diplock, 1991). Vitamin E is said to as a

"chain-breaking" antioxidant because it can preserve fatty acids by scavenging the peroxyl radical and halting this process. Vitamin C and selenium are two more important minerals that are a part of the antioxidant defence system. By replenishing depleted vitamin E, vitamin C seems to work in tandem with vitamin E (Niki, 1991). It seems that beta-carotene can quench singlet oxygen.

However, there has been no discernible effect from beta carotene supplementation in randomised studies, and smokers have a higher risk of lung cancer and overall mortality (Virtamo et al., 1998; Omenn et al., 1996). **Hydrogen Donation:** To stabilise free radicals and stop the chain reaction of lipid peroxidation, vitamin E donates a hydrogen atom from its phenolic group. **Solubility:** Alcoholic beverages, vegetable oils, and organic solvents all dissolve vitamin E, but water does not. **Stability:** Light, oxygen, and transition metal ions can oxidise and degrade vitamin E (Maeda et al., 2006; Li et al., 2012).

TRANSPORT OF VITAMIN E (Alpha-TOCOPHEROL)

Lipoproteins are plasma lipid transporters that have an amphipatic surface made up of phospholipids, unesterified cholesterol, and a wide range of apolipoproteins, and a hydrophobic core that contains triacylglycerol and cholesterol ester. The size, chemical makeup, and function of lipoproteins vary widely. Chylomicrons, very low density lipoprotein (VLDL), low density lipoprotein (LDL), and high density lipoprotein (HDL) are the four main groups of lipoproteins that are distinguished by their differences in density. Lipoproteins are dynamic structures that undergo molecular transfer between their surface and core, as well as between themselves and tissues (Norum et al., 1984).The lipoproteins are mostly produced in the intestine (chylomicrons and HDL) or liver (VLDL and HDL), or they are created in plasma (HDL and LDL) when triacylglycerol-rich lipoproteins are metabolised. A majority of apolipoproteins are produced in the intestine and liver73a. They may also act as ligands recognised by various cellular receptors and regulate various enzymes involved in the metabolism of lipoproteins. a-Tocopherol is transported in blood associated with lipoproteins in both rats and humans; no particular plasma transport protein has been identified (Behrens et al., 1986; Bjerneboe et al., 1987; Lambert et al., 1984).

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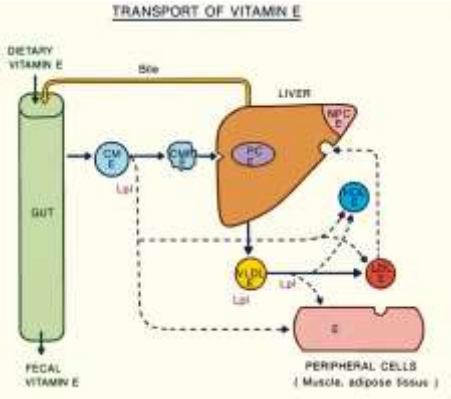

Figure 3: Transport of vitamin E.

Transportation of vitamin E from one tissue to another. The small intestine absorbs the unesterified form of vitamin E that has been hydrolysed from dietary esters, incorporates it into chylomicrons (CM), and secretes it into the intestinal lymph. Chylomicron remnants (CMR) are created when the triacylglycerols in the core of chylomicrons are hydrolysed by lipoprotein lipase (Lpl), which is found on the luminal side in capillaries of various tissues. During lipolysis, some vitamin E may be transported to various peripheral tissues along with the free fatty acids. Through an uncontrolled CMR-receptor, parenchymal cells (PC) in the liver absorb CMR. While parenchymal cells store the majority of vitamin E, nonparenchymal cells (NPC) also contain part of it. The parenchymal cells release vitamin E in conjunction with very low density lipoproteins (VLDL). Similar to chylomicrons, these particles are broken down by lipoprotein lipase. Due to their transformation into plasma, low density lipoproteins (LDL) contain some of the vitamin E found in VLDL particles. Via the LDL-receptor (also known as the apoB/E-receptor), vitamin E in LDL may be absorbed through receptor-mediated endocytosis. During lipolysis, lipoprotein lipase most likely transfers some of the vitamin E linked to chylomicrons and VLDL to peripheral cells and high density lipoproteins (HDL). Vitamin E is either metabolised or released in large quantities into the bile. The intestine does not absorb a significant portion of vitamin E. Dotted lines indicate paths of unknown or negligible significance (**Figure 3**).

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PREVENTION OF OXIDATIVE STRESS

Vitamin E functions as a highly effective chain-breaking antioxidant that suppresses the generation of reactive oxygen species (ROS) during lipid oxidation and the propagation phase of free-radical reactions (Burton et al., 1983). It is predominantly localized within cellular and organelle membranes, where it provides optimal protection even at very low concentrations, with approximately one vitamin E molecule present per 2,000 phospholipid molecules. Acting as a primary defensive barrier against lipid peroxidation, vitamin E preserves membrane integrity by preventing oxidative damage caused by free radicals. Evidence indicates that combinations of tocopherol isomers exhibit greater inhibitory effects on lipid peroxidation in human erythrocytes than α-tocopherol alone (Howard et al., 2011). Through its peroxyl radical–scavenging capacity, vitamin E safeguards polyunsaturated fatty acids within membrane phospholipids as well as circulating plasma lipoproteins (Tran et al., 1996). The tocopheroxyl radicals generated during this process may follow several pathways: they can oxidize other lipid molecules, undergo further oxidation to form tocopheryl quinones, combine with another tocopheroxyl radical to yield non-reactive dimers, or be regenerated back to tocopherol through interaction with other antioxidants. Notably, α-tocopherol is primarily involved in preventing the initiation of new free-radical reactions, whereas γ-tocopherol is more effective in capturing and neutralizing pre-existing radicals. Oxidative stress has been implicated in the development of numerous disorders, including cancer, ageing-related degeneration, arthritis, and cataracts. Consequently, vitamin E may play a protective role in reducing the risk or delaying the onset of chronic diseases associated with excessive ROS activity.

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PHARMACOLOGICAL ROLE OF VITAMIN E

Because of its antioxidant properties, anti-inflammatory properties, ability to suppress platelet aggregation, and immune-boosting properties, vitamin E has been shown to be highly helpful in the prevention and reversal of a number of disease problems (Paolisso et al., 1993).

Cardiovascular diseases

Cardiovascular disorders largely develop due to oxidative modification of low-density lipoproteins, which subsequently triggers vascular inflammation (McAnally et al., 2007). Among vitamin E isoforms, γ-tocopherol has been shown to enhance cardiovascular function by upregulating nitric oxide synthase activity, thereby increasing the production of nitric oxide and promoting vasodilation (Sesso et al., 2008). This effect is attributed to its ability to neutralize reactive nitrogen species, particularly peroxynitrite, leading to improved endothelial performance. Human supplementation studies have demonstrated that a daily intake of 100 mg of γ-tocopherol can significantly reduce key risk factors associated with arterial thrombosis, including platelet aggregation and elevated cholesterol levels (Shklar & Oh, 2000). Furthermore, combinations of tocopherols exhibit greater efficacy in suppressing lipid peroxidation and inhibiting platelet aggregation compared with individual tocopherol forms, indicating a synergistic antiplatelet effect (Singh et al., 2000). In addition to tocopherols, tocotrienols have been reported to decrease endogenous cholesterol synthesis by downregulating hepatic 3-hydroxy-3-methylglutaryl-CoA reductase activity (Ricciarelli et al., 1999). However, despite these mechanistic benefits, several large-scale clinical intervention trials have failed to demonstrate consistent cardiovascular protection from vitamin E supplementation and have instead linked its use to an increased incidence of haemorrhagic stroke. Consequently, it has been proposed that the cardioprotective potential of vitamin E may be better evaluated through long-term studies involving younger populations (McIntyre et al., 2000).

Cancer

Vitamin E has been widely reported to exhibit anti-cancer potential, which is attributed to its diverse biological activities. These include activation of the wild-type p53 tumor suppressor gene, suppression of mutant p53 expression, induction of heat shock proteins, and inhibition of angiogenesis through interference with transforming growth factor-α signaling. Importantly, different isoforms of vitamin E—namely α-, γ-, and δ-tocopherols—demonstrate distinct anti-cancer functions. α-Tocopherol has been shown to suppress protein kinase C (PKC) activity and collagenase production, both of which are involved in tumor progression. In contrast, γ-tocopherol exhibits stronger growth-inhibitory effects than α-tocopherol in human prostate cancer cell lines, while δ-tocopherol has demonstrated significant antiproliferative activity in mouse mammary cancer models. γ-Tocopherol inhibits cancer cell proliferation through multiple mechanisms. It effectively scavenges free radicals, including reactive nitrogen species that can induce DNA damage and promote malignant transformation. Additionally, γ-tocopherol modulates cell cycle progression by downregulating cyclins, thereby arresting cancer cells and preventing uncontrolled division. Compared with α-tocopherol, γ-tocopherol is more potent in inducing apoptosis, activating multiple programmed cell death pathways, enhancing peroxisome proliferator-activated receptor-γ (PPAR-γ) activity—particularly in colon cancer cells—and reducing tumor angiogenesis, which limits nutrient supply to cancerous tissues. Furthermore, tocotrienols have also been reported to exert strong antiproliferative and pro-apoptotic effects in both normal and malignant human cells. These effects are mediated through mitochondrial apoptosis pathways, suppression of cyclin D–dependent cell cycle progression, inhibition of tumor vascularization, and downregulation of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase activity, collectively contributing to the prevention of malignant cell growth (Wang et al., 2012).

Cataracts

Cataracts are among the leading causes of visual impairment in the elderly and are largely attributed to oxidative damage that results in the aggregation of altered lens proteins. A number of

observational investigations have suggested an association between vitamin E intake and a reduced likelihood of cataract formation. For instance, Leske and colleagues reported better lens transparency in individuals using vitamin E supplements as well as in those with elevated circulating levels of the vitamin. Similarly, prolonged vitamin E supplementation has been linked with a reduced rate of age-related lens opacity progression. In contrast, findings from the randomized Age-Related Eye Disease Study (AREDS) demonstrated no significant influence of vitamin E on cataract onset or progression during a mean follow-up period of 6.3 years. Taken together, current evidence does not provide conclusive support for the use of vitamin E supplements, either alone or in combination with other antioxidants, in preventing cataract development (Braakhuis et al., 2019).

Alzheimer's disease

Alzheimer's disease (AD) is strongly associated with oxidative damage, particularly protein oxidation and lipid peroxidation mediated by free radical reactions. The accumulation of β-amyloid peptides contributes to neuronal toxicity by promoting oxidative stress and the generation of hydrogen peroxide, which ultimately leads to neuronal degeneration and disease progression. Vitamin E has been shown to counteract these processes by inhibiting hydrogen peroxide formation and reducing oxidative-stress–induced cytotoxicity. Experimental studies demonstrate that vitamin E significantly decreases β-amyloid–induced neuronal death in rat hippocampal cultures and PC12 cells, and also mitigates excitatory amino acid–mediated toxicity in neuroblastoma cell lines. Clinical evidence further supports a protective role for vitamin E in AD. Alzheimer's Disease Cooperative Study (1997) reported that vitamin E supplementation slowed functional decline in patients with moderately severe AD, delaying the loss of daily living abilities and postponing institutional care. Additional studies have revealed that individuals with AD often exhibit lower plasma levels of antioxidant micronutrients, indicating that impaired antioxidant defense may contribute to disease development. Elevated plasma vitamin E concentrations have been associated with a reduced risk of AD in older adults, with neuroprotection appearing to depend on a combination of tocopherols and tocotrienols rather than α-tocopherol alone.

A large-scale study published in 2009 involving 847 participants showed that administration of 2,000 IU of vitamin E, particularly when combined with a cholinesterase inhibitor, produced greater clinical benefits than either treatment alone. At the biomarker level, combined plasma measurements of tocopherols and tocotrienols, together with automated magnetic resonance imaging (MRI) analyses, have been shown to distinguish patients with AD and mild cognitive impairment (MCI) from healthy controls and to predict the progression from MCI to AD. These findings highlight the potential value of plasma vitamin E isoforms as indirect nutritional biomarkers of AD pathology. Nevertheless, despite these promising effects, high-dose vitamin E supplementation should only be used under medical supervision, as it may interact adversely with other medications, including lipid-lowering agents (Butterfield and Lauderback, 2002).

Human immunodeficiency virus and acquired immunodeficiency syndrome

Vitamin E is an important anti-inflammatory agent that is often found to be deficient in human immunodeficiency virus (HIV)-positive individuals; however, it is not known whether vitamin E supplementation is beneficial either at every or any stage of HIV infection. At a dose of 400 IU, vitamin E was shown to restore delayed skin hypersensitivity reactions and interleukin-2 production, and at high doses it was shown to stimulate T helper cell (CD4 T-cell) proliferation. In 1997, Tang *et al.* studied the association between serum vitamin A and E levels with HIV-1 disease progression. In this study, it was found that men with serum vitamin E levels above 23.5 µm/L had a significantly reduced risk of disease progression. A strong correlation was noted in this cohort between the intake of supplements containing vitamin E at the point of entry into the study and high blood levels of vitamin E. A study on murine acquired immunodeficiency syndrome (AIDS) using a 15-fold increase in dietary vitamin E showed the normalisation of immune parameters that are altered in HIV/AIDS. Apart from this, an increase in dietary vitamin E has also been shown to protect against the side-effects of azidothymidine, such as bone marrow toxicity. Related studies on bone marrow cultures from stage IV AIDS patients using d-alpha-tocopherol supplementation revealed similar results. Nevertheless, it has also been reported that higher vitamin E levels pre-infection were found to be

associated with increased mortality. Thus, further research is needed to elucidate the role vitamin E plays in the pathogenesis of HIV-1 (Itinoseki et al., 2014).

Immunity

Evidence indicates that vitamin E plays an important role in strengthening host defense mechanisms by modulating immune function. It has been shown to improve both humoral and cellular immune responses, particularly by enhancing phagocytic activity. Its immunomodulatory effects are most pronounced in infectious conditions where phagocytosis is a key component, while its influence on purely cell-mediated immunity appears comparatively limited. Nevertheless, supplementation with vitamin E has been reported to significantly improve both humoral and cell-mediated immune responses in humans, with especially notable benefits observed in elderly populations.

Daily supplementation of approximately 200 mg of vitamin E has been associated with enhanced antibody responses to various vaccines in healthy individuals, without producing adverse effects. Moreover, increased plasma concentrations of vitamin E in older adults have been correlated with greater resistance to viral infections and a reduced incidence of infectious episodes over extended follow-up periods. Recent findings further suggest that regular vitamin E intake can augment immune responsiveness to specific antigens. In addition to its immunological benefits, vitamin E—particularly when combined with vitamin C—has demonstrated therapeutic potential in conditions such as photodermatitis, dysmenorrhea, pre-eclampsia, and tardive dyskinesia (Lewis et al., 2019).

CONCLUSION

Vitamin E is a vital lipid-soluble antioxidant with diverse biological functions that extend beyond its classical role in scavenging free radicals. Its structural diversity, encompassing tocopherols and tocotrienols, contributes to distinct pharmacokinetic behaviors and biological activities, influencing membrane stability, immune regulation, inflammatory pathways, and cellular signaling mechanisms. Evidence presented in this review demonstrates that vitamin E plays a significant role in protecting against oxidative stress-mediated damage implicated in cardiovascular diseases, cancer,

neurodegenerative disorders, ocular diseases, and immune dysfunction. However, results from large-scale clinical trials remain conflicting, highlighting that the health benefits of vitamin E are highly dependent on its molecular form, dosage, duration of intake, and individual physiological status. Importantly, mixed tocopherols and tocotrienols appear to exert broader and more potent protective effects compared to α-tocopherol alone. Future research should focus on isoform-specific actions, personalized supplementation strategies, and long-term clinical evaluations to clarify therapeutic efficacy and safety. A deeper understanding of vitamin E metabolism, transport, and molecular targets will be essential for translating its antioxidant potential into effective clinical and nutritional interventions aimed at disease prevention and health promotion.

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