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α-Tocopherol, Lipid Antioxidant

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Abbreviations:
$AscH^-$, ascorbate; $Asc^{\bullet-}$, semidehydroascorbate; $CoQH_2$, reduced ubiquinone 10, ubiquinol 10; $CoQ^{\bullet-}$, semiquinone radical of the $CoQ/CoQH_2$ system; GPx, glutathione peroxidase; LH, *bis*-allylic hydrogen; $L^{\bullet}$, lipid radical; $LOO^{\bullet}$, lipid peroxyl radical; LDL: low-density lipoprotein. NRP, nonradical produts; phGPx, phospholipid hydroperoxide glutathione peroxidase; $ROO^{\bullet}$, peroxyl radical; $TO^{\bullet}$, tocopheroxyl radical; TOH, tocopherol.

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Abstract

Vitamin E is the term for a group of tocopherols and tocotrienols, of which α-tocopherol has the highest biological activity. The natural stereo-isomer of α-tocopherol is (2R, 4'R, 8'R)-α-tocopherol or RRR-α-tocopherol. It is pale, yellow, viscous oil at room temperature, fat soluble and insoluble in water but dissolves in most organic solutions. α-Tocopherol functions as a chain-breaking antioxidant that prevents the propagation of free radical reactions. It can be recycled by coenzyme Q and ascorbate ($AscH^-$). Because of its antioxidant functions, some diseases have direct relationships with α-tocopherol.

Introduction

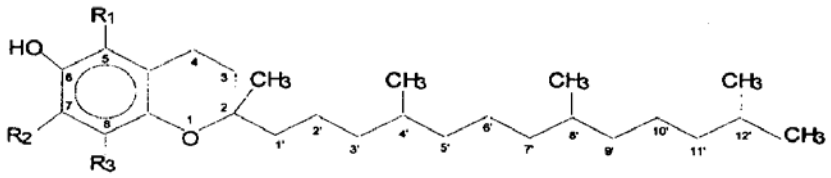
Vitamin E is a fat-soluble vitamin that exists in eight different forms. Each form has its own biological activity, the measure of potency or functional use in the body. α-Tocopherol is the most active form of vitamin E in humans, and is powerful biological antioxidant [1]. Because of the antioxidant function of α-tocopherol, it can scavenge free radicals that are potentially damaging by-products of the body's metabolism. To know the properties and antioxidant function of α-tocopherol is very important to human beings. The application of α-tocopherol can help human beings to prevent or delay the development of some chronic diseases and cancers caused by deficient of vitamin E (α-tocopherol).

Properties

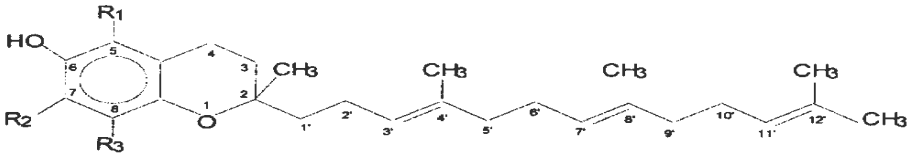
Nomenclature, structure and properties of α-tocopherol

Vitamin E was first characterized in wheat-germ oil and lettuce. It was composed by several similar substances. The name "tocopherol" was proposed by Evans *et al* in 1936, and the prefixes α, β, γ and δ were used to distinguish the family of substances [2]. Derivatives of α-tocopherol differ only in the number and arrangement of the methyl groups around the benzenoid ring of the chromanol structure. The natural stereo-isomer of α-tocopherol is (2R, 4'R, 8'R)-α-tocopherol or RRR-α-tocopherol. Vitamin E encompasses a group of eight isomeric molecules. The structure of tocol indicates that there are three centers of asymmetry; they are at C_2, C_4 ' and C_8 ' (Fig. 1). The tocotrienol possess only one center of asymmetry at C_2, in addition to sites of geometrical isomerism at C_3 ' and C_7 '. Thus, a number of stereo-isomers of the tocol and tocotrienol can exist. Natural α-tocopherol was shown conclusively to have the 2R, 4'R, 8'R configuration [3].

(a). Tocol, forms of vitamin E



(b). Tocotrienol, forms of vitamin E



Tocopherol/Tocotrienol	R_1	R_2	R_3
α–	CH_3	CH_3	CH_3
β–	CH_3	H	CH_3
γ–	H	CH_3	CH_3
δ–	H	H	CH_3

Figure 1. Chemical structure of tocopherol and tocotrienol analogs [2].

Physical properties of α-tocopherol

Tocopherol is pale, yellow viscous oil at room temperature, fat soluble and insoluble in water but dissolves in most organic solutions. The melting point of RRR-α-tocopherol is 2.5-3.58^{o}C. the compound is a viscous oil which is soluble in aprotic solvents at room temperature. The optical rotations of these tocopherols are very small and depend on the nature of the solvent. The ultraviolet absorption spectra of the tocol in ethanol show maxima in the range 292-298 nm; infrared spectra show OH (2.8-3.0 mm) and CH (3.4-3.5 mm) stretching and a characteristic band

at 8.6 mm. α-Tocopherol is fluorescent with an emission maximum about 325 nm in hydrophobic environments [2].

Antioxidant functions α-tocopherol

α-Tocopherol and γ-tocopherol are essential components of cellular defence mechanisms against endogenous and exogenous oxidants. The antioxidant reaction of α-tocopherol is nonenzymatic and fast. Reactions 1, 2 and 3 show us that α-tocopherol scavenge lipid peroxyl radicals, which are the chain-carrying species and propagate lipid peroxidation [2]. Reaction 4 show us a very fast radical-radical termination reaction [4].

$$LO_2^{\bullet} + LH \rightarrow LOOH + L^{\bullet} \qquad k \approx (10^1 - 10^2)\ M^{-1}\ S^{-1} \tag{1}$$

$$L^{\bullet} + O_2 \rightarrow LO_2^{\bullet} \qquad k \approx 3 \times 10^4\ M^{-1}\ S^{-1} \tag{2}$$

$$LO_2^{\bullet} + TOH \rightarrow LOOH + TO^{\bullet} \quad k = 2.5 \times 10^6\ M^{-1}\ S^{-1} \text{ (oleic acid solution)} \tag{3}$$

$$LOO^{\bullet} + TO^{\bullet} \rightarrow \text{NRP} \qquad k \approx 3 \times 10^8\ M^{-1}\ S^{-1} \tag{4}$$

Energetics for reactions 1 and reaction 3 are:

$LOO^{\bullet}, H^{+} / LOOH \qquad E^{o\,\prime} \cong + 1000$ mV

$TO^{\bullet}, H^{+} / TOH \qquad E^{o\,\prime} \cong + 480$ mV

Redox cycle

The redox cycles of α-tocopherol are important in the antioxidant function of the vitamin E. Regeneration of α-tocopherol *in vitro* from its tocopheroxyl radical form mediated by vitamin C and coenzyme Q have been demonstrated [2].

1). From the following reactions, they show us that coenzyme Q (CoQ) can independently react with peroxyl radicals and each antioxidant acts as a phenolic scavenger of radicals. Coenzyme Q also recycles α-tocopherol from its phenoxyl radical [5].

$$TO^{\bullet} + CoQH_2 \rightarrow TOH + CoQ^{\bullet-} + H^{+} \qquad k = 3 \times 10^{6}\ M^{-1}\ S^{-1} \tag{5}$$

$$TO^{\bullet} + CoQ^{\bullet-} + H^{+} \rightarrow TOH + CoQ \qquad k = 3.7 \times 10^{5}\ M^{-1}\ S^{-1} \tag{6}$$

2). From reaction 7, it shows us that ascorbate recycles tocopherol *via* $TO^{\bullet}$, producing the ascorbate radical [6].

$$AscH^{-} + TO^{\bullet} \rightarrow Asc^{\bullet-} + TOH \tag{7}$$

k=1.55 × 10^{6} M^{-1} S^{-1} Homogenous solution

k = 7.2 × 10^{7} M^{-1} S^{-1} + charged hexadecyl trimethyl NH_4^{+} micelles

k = 3.2 × 10^{2} M^{-1} S^{-1} Triton-X micelles

k = 3.8 × 10^{4} M^{-1} S^{-1} in sodium dodecyl sulfate micelles

This recycling is also shown in figure 2. The relatively stable tocopheroxyl radical formed in membrane-water interface, allowing water soluble ascorbate access to membrane-band $TO^{\bullet}$ for the repair reaction, thereby, recycling the tocopherol [7].

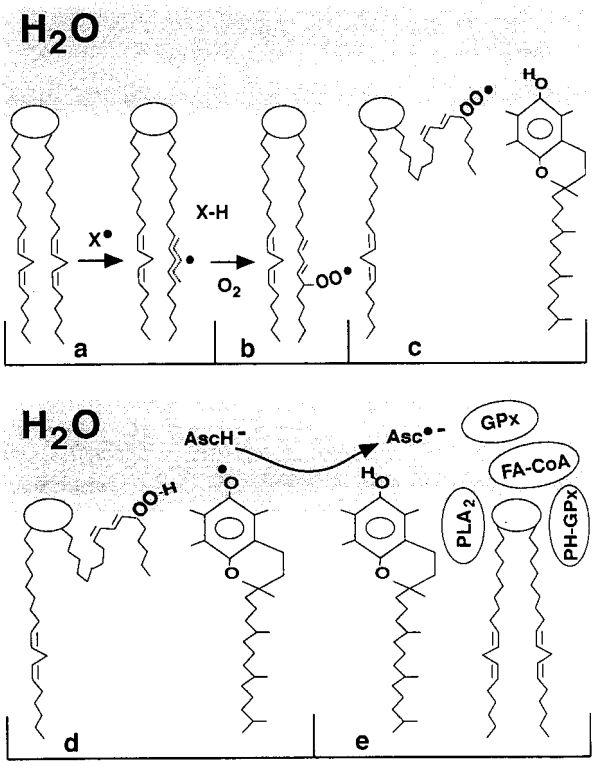


Figure 2. Membrane lipid peroxidation. Only one leaflet of the bilayer is represented. (a) Initiation of the peroxidation process by an oxidizing radical, $X^{\bullet}$, by abstraction of a *bis*-allylic hydrogen, thereby forming a pentadienyl radical. (b) Oxygenation to form a peroxyl radical and a conjugated diene. (c) The peroxyl radical moiety partitions to the water membrane interface where it is poised for repair by tocopherol. (d) The peroxyl radical is converted to a lipid hydroperoxide, and the resulting tocopheroxyl radical can be repaired by ascorbate. (e) Tocopherol has been recycled by ascorbate; the resulting ascorbate radical can be recycled by enzyme ststems. The enzymes phospholipase A2 (PLA2), phospholipid hydroperoxide glutathione peroxidase (ph-GPx), glutathione peroxidase repair the oxidized fatty acid chain of the phospholipid. [7]

Disease and α-tocopherol

Since its discovery in 1922, vitamin E supplementation has shown beneficial effects for numerous disorders, particularly atherosclerosis, ischemic heart disease, and development of different types of cancer [8]. Some studies have shown that α-tocopherol can significant decrease in release of reactive oxygen species, oxidation, IL-1 beta secretion and monocyte-endothelial cell adhesion, both in resting and activated cell. Due to this function, vitamin E or α-tocopherol participate the treatment of certain breast cancers, diabetes and inflammations.

The deficiency of vitamin E also can cause diseases. The disease that has best been directly linked with an α-tocopherol deficiency is ataxia (AVED) [9]. Other diseases have a less clear relationship. AVED is caused by mutations in the gene for α-tocopherol transfer protein (α-TTP). Therapeutic and prophylactic vitamin E supplementation prevents the onset of the disease before irreversible damage development.

Summary

α-Tocopherol is one form of vitamin E; it has highest biological antioxidant activity of eight forms. It is fat- soluble oil at room temperature. The natural stereo-isomer of α-tocopherol is (2R, 4'R, 8'R)-α-tocopherol or RRR-α-tocopherol. Due to the antioxidant function of α-tocopherol, it can scavenge free radicals that are potentially damaging by-products of the body's metabolism. It also can be recycled by vitamin C and coenzyme Q. The disease that has been directly linked with an α-tocopherol deficiency is ataxia (AVED), and application of α-tocopherol contribute to the therapy of some chronic diseases and cancer.

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