Handbook of PHARMACEUTICAL EXCIPIENTS

Second Edition

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Contents

Alpha Tocopherol

1. Nonproprietary Names

BP: Alpha tocopherol
PhEur: α-Tocopherolum
USP: Vitamin E
See also Sections 3, 9 and 18.

2. Synonyms

(±)-3,4-Dihydro-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)-2*H*-1-benzopyran-6-ol; E307; synthetic alpha tocopherol; *all-rac*-α-tocopherol; *dl*-α-tocopherol; 5,7,8-trimethyltocol.

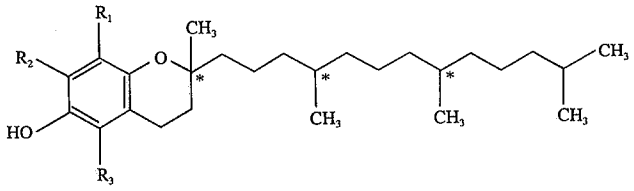
3. Chemical Name and CAS Registry Number

(±)-(2*RS*,4′*RS*,8′*RS*)-2,5,7,8-Tetramethyl-2-(4′,8′,12′-trimethyltridecyl)-6-chromanol
[10191-41-0]
Note that alpha tocopherol has three chiral centres giving rise to eight isomeric forms. The naturally occurring form is known as *d*-alpha tocopherol or (2*R*,4′*R*,8′*R*)-alpha-tocopherol. The synthetic form, *dl*-alpha tocopherol or simply alpha tocopherol, occurs as a racemic mixture containing equimolar quantities of all the isomers.
Similar considerations apply to beta, delta and gamma tocopherol and tocopherol esters.
See Section 18 for further information.

4. Empirical Formula Molecular Weight

$C_{29}H_{50}O_2$ 430.69

5. Structural Formula



Alpha tocopherol: $R_1 = R_2 = R_3 = CH_3$.
Beta tocopherol: $R_1 = R_3 = CH_3$; $R_2 = H$.
Delta tocopherol: $R_1 = CH_3$; $R_2 = R_3 = H$.
Gamma tocopherol: $R_1 = R_2 = CH_3$; $R_3 = H$.
* Indicates chiral centres.

6. Functional Category

Antioxidant; therapeutic agent.

7. Applications in Pharmaceutical Formulation or Technology

Alpha tocopherol is primarily recognised as a source of vitamin E and the commercially available materials and specifications reflect this purpose. Whilst alpha tocopherol also exhibits antioxidant properties, the beta, delta and gamma tocopherols are considered to be more effective as antioxidants.
Of widespread regulatory acceptability, tocopherols are of value in oil or fat-based pharmaceutical products and are normally used in the concentration range of 0.001-0.05%. There is frequently an optimum concentration; thus the autoxidation of linoleic acid and methyl linolenate is reduced at low concentrations of alpha tocopherol but accelerated by higher concentrations. Antioxidant effectiveness can be increased by the addition of oil soluble synergists such as lecithin and ascorbyl palmitate.[1]

8. Description

Alpha tocopherol is a practically odorless, clear, colorless, yellow, yellowish-brown or greenish-yellow colored viscous oil.
See also Section 18.

9. Pharmacopeial Specifications

Test	PhEur 1990	USP XXII
Identification	+	+
Acidity	—	+
Acid value	⩽ 2	—
Heavy metals	⩽ 20 ppm	—
Sulfated ash	⩽ 0.1%	—
Assay	96.0-102.0%	96.0-102.0%

Note that the USP XXII describes vitamin E as comprising *d*- or *dl*-alpha tocopherol; *d*- or *dl*-alpha tocopheryl acetate; or *d*- or *dl*-alpha tocopheryl acid succinate. However, the PhEur 1990 and the BP 1993 describe alpha tocopherol and alpha tocopheryl acetate in separate monographs.
The diversity of the tocopherols described in the various pharmacopeial monographs makes a comparison of specifications difficult.

10. Typical Properties

Solubility: practically insoluble in water; freely soluble in acetone, ethanol, ether and vegetable oils.

11. Stability and Storage Conditions

Tocopherols are slowly oxidized by atmospheric oxygen and rapidly by ferric and silver salts. Oxidation products include tocopheroxide, tocopherylquinone and tocopherylhydroquinone, as well as dimers and trimers. Tocopherol esters are more stable to oxidation than the free tocopherols but are in consequence less effective antioxidants. *See also* Section 18.
Tocopherols should be stored under an inert gas, in an airtight container in a cool, dry, place and protected from light.

12. Incompatibilities

Tocopherols are incompatible with peroxides and metal ions especially iron, copper and silver. Tocopherols may be absorbed into plastic.[2]

13. Method of Manufacture

Naturally occurring tocopherols are obtained by the extraction or molecular distillation of steam distillates of vegetable oils, e.g. alpha tocopherol occurs in concentrations of 0.1-0.3% in corn, rapeseed, soybean, sunflower and wheat germ oils.[3] Beta tocopherol and gamma tocopherol are usually found in natural sources along with alpha tocopherol. Racemic synthetic tocopherols may be prepared by the condensation of the appropriate methylated hydroquinone with racemic isophytol.[4]

14. Safety

Tocopherols (vitamin E) occur in many food substances that are consumed as part of the normal diet. The daily nutritional

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