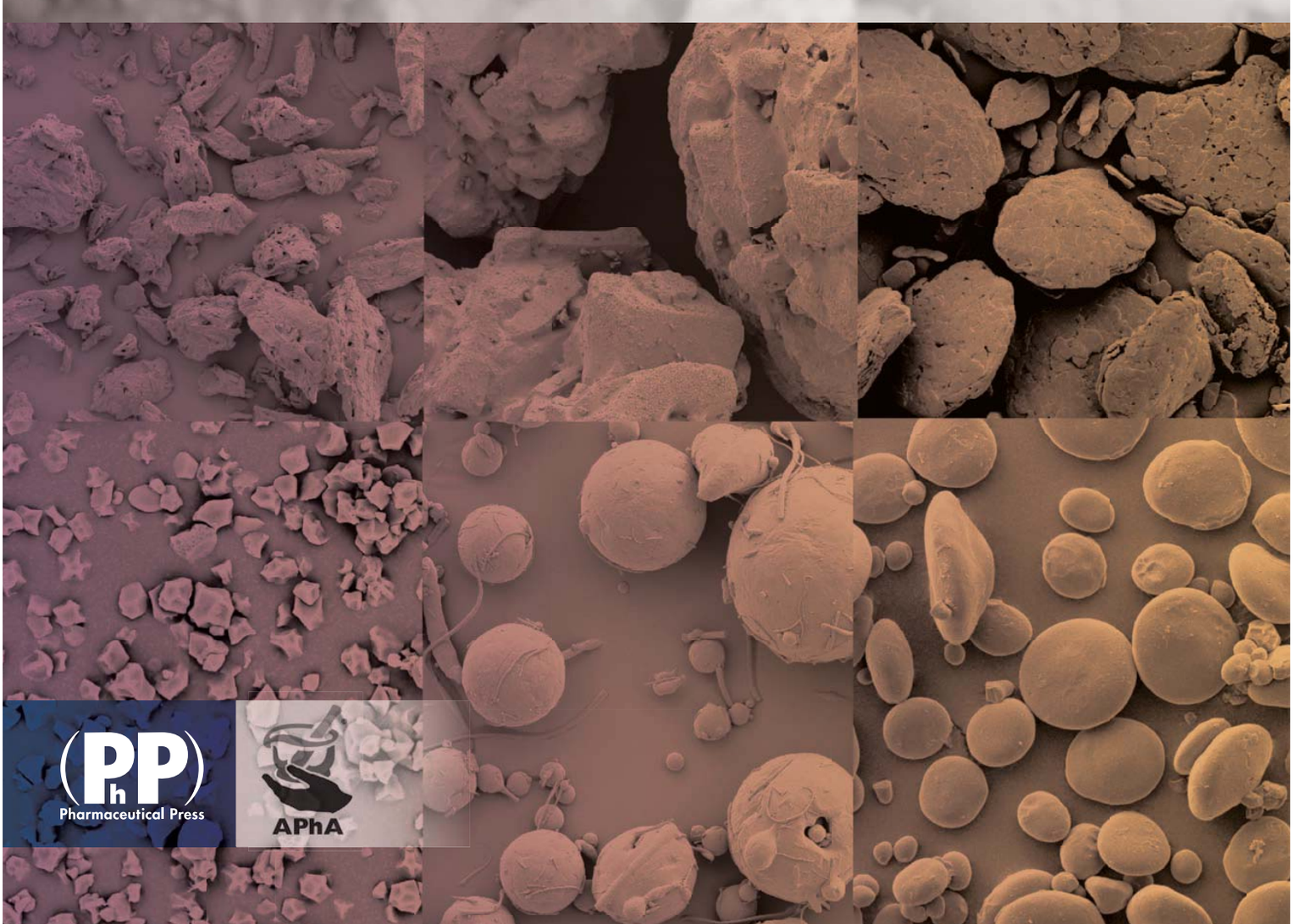
Handbook of Pharmaceutical Excipients

Sixth edition

Edited by
Raymond C Rowe, Paul J Sheskey and Marian E Quinn



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SIXTH EDITION

Edited by

Raymond C Rowe BPharm, PhD, DSC, FRPharmS, FRSC, CPhys, MInstP

Chief Scientist

Intelligensys Ltd, Stokesley, North Yorkshire, UK

Paul J Sheskey BSc, RPh

Application Development Leader

The Dow Chemical Company, Midland, MI, USA

Marian E Quinn BSc, MSc

Development Editor

Royal Pharmaceutical Society of Great Britain, London, UK

London • Chicago

Pharmaceutical Press

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Alcohol

1 Nonproprietary Names

BP: Ethanol (96%)

JP: Ethanol

PhEur: Ethanol (96 per cent)

USP: Alcohol

2 Synonyms

Ethanolum (96 per centum); ethyl alcohol; ethyl hydroxide; grain alcohol; methyl carbinol.

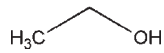
3 Chemical Name and CAS Registry Number

Ethanol [64-17-5]

4 Empirical Formula and Molecular Weight

C_2H_6O 46.07

5 Structural Formula



6 Functional Category

Antimicrobial preservative; disinfectant; skin penetrant; solvent.

7 Applications in Pharmaceutical Formulation or Technology

Ethanol and aqueous ethanol solutions of various concentrations (*see* Sections 8 and 17) are widely used in pharmaceutical formulations and cosmetics; *see* Table I. Although ethanol is primarily used as a solvent, it is also employed as a disinfectant, and in solutions as an antimicrobial preservative.[1,2] Topical ethanol solutions are used in the development of transdermal drug delivery systems as penetration enhancers.[3–10] Ethanol has also been used in the development of transdermal preparations as a co-surfactant.[11–13]

Table I: Uses of alcohol.

Use	Concentration (% v/v)
Antimicrobial preservative	⩾10
Disinfectant	60–90
Extracting solvent in galenical manufacture	Up to 85
Solvent in film coating	Variable
Solvent in injectable solutions	Variable
Solvent in oral liquids	Variable
Solvent in topical products	60–90

8 Description

In the BP 2009, the term 'ethanol' used without other qualification refers to ethanol containing ⩾99.5% v/v of C_2H_6O. The term 'alcohol', without other qualification, refers to ethanol 95.1–96.9% v/v. Where other strengths are intended, the term 'alcohol' or 'ethanol' is used, followed by the statement of the strength.

In the PhEur 6.0, anhydrous ethanol contains not less than 99.5% v/v of C_2H_6O at 20°C. The term ethanol (96%) is used to describe the material containing water and 95.1–96.9% v/v of C_2H_6O at 20°C.

In the USP 32, the term 'dehydrated alcohol' refers to ethanol ⩾99.5% v/v. The term 'alcohol' without other qualification refers to ethanol 94.9–96.0% v/v.

In the JP XV, ethanol (alcohol) contains 95.1–96.9% v/v (by specific gravity) of C_2H_6O at 15°C.

In the *Handbook of Pharmaceutical Excipients*, the term 'alcohol' is used for either ethanol 95% v/v or ethanol 96% v/v.

Alcohol is a clear, colorless, mobile, and volatile liquid with a slight, characteristic odor and burning taste.

See also Section 17.

9 Pharmacopeial Specifications

See Table II. *See also* Sections 17 and 18.

Table II: Pharmacopeial specifications for alcohol.

Test	JP XV	PhEur 6.0	USP 32
Identification	+	+	+
Characters	—	+	—
Specific gravity	0.809–0.816	0.805–0.812	0.812–0.816
Acidity or alkalinity	+	+	+
Clarity and color of solution	+	+	+
Nonvolatile residue	⩽2.5 mg	⩽25 ppm	⩽2.5 mg
Volatile impurities	+	+	+
Absorbance	+	+	+
at 240 nm	⩽0.40	⩽0.40	⩽0.40
at 250–260 nm	⩽0.30	⩽0.30	⩽0.30
at 270–340 nm	⩽0.10	⩽0.10	⩽0.10
Assay	95.1–96.9%	95.1–96.9%	92.3–93.8% by weight 94.9–96.0% by volume

10 Typical Properties

Antimicrobial activity Ethanol is bactericidal in aqueous mixtures at concentrations between 60% and 95% v/v; the optimum concentration is generally considered to be 70% v/v. Antimicrobial activity is enhanced in the presence of edetic acid or edetate salts.[1] Ethanol is inactivated in the presence of nonionic surfactants and is ineffective against bacterial spores.

Boiling point 78.15°C

Flammability Readily flammable, burning with a blue, smokeless flame.

Flash point 14°C (closed cup)

NIR spectra *see* Figures 1 and 2.

Solubility Miscible with chloroform, ether, glycerin, and water (with rise of temperature and contraction of volume).

Specific gravity 0.8119–0.8139 at 20°C

Note The above typical properties are for alcohol (ethanol 95% or 96% v/v). *See* Section 17 for typical properties of dehydrated alcohol.

11 Stability and Storage Conditions

Aqueous ethanol solutions may be sterilized by autoclaving or by filtration and should be stored in airtight containers, in a cool place.

12 Incompatibilities

In acidic conditions, ethanol solutions may react vigorously with oxidizing materials. Mixtures with alkali may darken in color owing to a reaction with residual amounts of aldehyde. Organic

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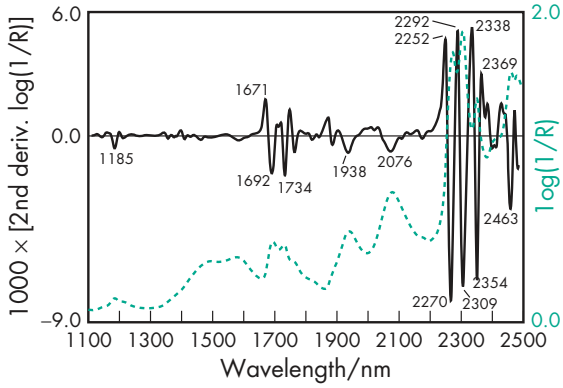

Figure 1: Near-infrared spectrum of alcohol (96%) measured by transflectance (1 mm path-length).

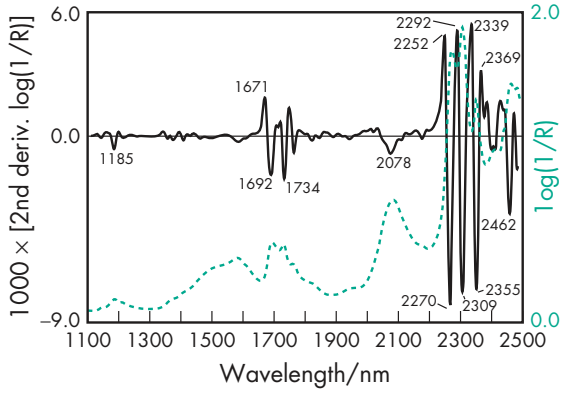

Figure 2: Near-infrared spectrum of alcohol (absolute) measured by transflectance (1 mm path-length).

salts or acacia may be precipitated from aqueous solutions or dispersions. Ethanol solutions are also incompatible with aluminum containers and may interact with some drugs.

13 Method of Manufacture

Ethanol is manufactured by the controlled enzymatic fermentation of starch, sugar, or other carbohydrates. A fermented liquid is produced containing about 15% ethanol; ethanol 95% v/v is then obtained by fractional distillation. Ethanol may also be prepared by a number of synthetic methods.

14 Safety

Ethanol and aqueous ethanol solutions are widely used in a variety of pharmaceutical formulations and cosmetics. It is also consumed in alcoholic beverages.

Ethanol is rapidly absorbed from the gastrointestinal tract and the vapor may be absorbed through the lungs; it is metabolized, mainly in the liver, to acetaldehyde, which is further oxidized to acetate.

Ethanol is a central nervous system depressant and ingestion of low to moderate quantities can lead to symptoms of intoxication including muscle incoordination, visual impairment, slurred speech, etc. Ingestion of higher concentrations may cause depression of medullary action, lethargy, amnesia, hypothermia, hypoglycemia, stupor, coma, respiratory depression, and cardiovascular collapse. The lethal human blood-alcohol concentration is generally estimated to be 400–500 mg/100 mL.

Although symptoms of ethanol intoxication are usually encountered following deliberate consumption of ethanol-containing beverages, many pharmaceutical products contain ethanol as a solvent, which, if ingested in sufficiently large quantities, may cause adverse symptoms of intoxication. In the USA, the maximum quantity of alcohol included in OTC medicines is 10% v/v for products labeled for use by people of 12 years of age and older, 5% v/v for products intended for use by children aged 6–12 years of age, and 0.5% v/v for products for use by children under 6 years of age.[14]

Parenteral products containing up to 50% of alcohol (ethanol 95 or 96% v/v) have been formulated. However, such concentrations can produce pain on intramuscular injection and lower concentrations such as 5–10% v/v are preferred. Subcutaneous injection of alcohol (ethanol 95% v/v) similarly causes considerable pain followed by anesthesia. If injections are made close to nerves, neuritis and nerve degeneration may occur. This effect is used therapeutically to cause anesthesia in cases of severe pain, although the practice of using alcohol in nerve blocks is controversial. Doses of 1 mL of absolute alcohol have been used for this purpose.[15]

Preparations containing more than 50% v/v alcohol may cause skin irritation when applied topically.

LD_{50} (mouse, IP): 0.93 g/kg[16]
LD_{50} (mouse, IV): 1.97 g/kg
LD_{50} (mouse, oral): 3.45 g/kg
LD_{50} (mouse, SC): 8.29 g/kg
LD_{50} (rat, IP): 3.75 g/kg
LD_{50} (rat, IV): 1.44 g/kg
LD_{50} (rat, oral): 7.06 g/kg

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. Ethanol and aqueous ethanol solutions should be handled in a well-ventilated environment. In the UK, the long-term 8-hour TWA workplace exposure limit for ethanol is 1920 mg/m^3 (1000 ppm).[17] Ethanol may be irritant to the eyes and mucous membranes, and eye protection and gloves are recommended. Ethanol is flammable and should be heated with care. Fixed storage tanks should be electrically grounded to avoid ignition from electrostatic discharges when ethanol is transferred.

16 Regulatory Status

Included in the FDA Inactive Ingredients Database (dental preparations; inhalations; IM, IV, and SC injections; nasal and ophthalmic preparations; oral capsules, solutions, suspensions, syrups, and tablets; rectal, topical, and transdermal preparations). Included in the Canadian List of Acceptable Non-medicinal Ingredients. Included in nonparenteral and parenteral medicines licensed in the UK.

17 Related Substances

Dehydrated alcohol; denatured alcohol; dilute alcohol; isopropyl alcohol.

Dehydrated alcohol

Synonyms Absolute alcohol; anhydrous ethanol; ethanol.
Autoignition temperature 365°C
Boiling point 78.5°C
Explosive limits 3.5–19.0% v/v in air
Flash point 12°C (closed cup)
Melting point −112°C
Moisture content Absorbs water rapidly from the air.
Refractive index n_D^{20} = 1.361
Specific gravity 0.7904–0.7935 at 20°C
Surface tension 22.75 mN/m at 20°C (ethanol/vapor)
Vapor density (relative) 1.59 (air = 1)

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Vapor pressure 5.8 Pa at 20°C
Viscosity (dynamic) 1.22 mPa s (1.22 cP) at 20°C
Comments Dehydrated alcohol is ethanol ⩾99.5% v/v. *See* Section 8. Dehydrated alcohol is one of the materials that have been selected for harmonization by the Pharmacopeial Discussion Group. For further information see the General Information Chapter <1196> in the USP32–NF27, the General Chapter 5.8 in PhEur 6.0, along with the 'State of Work' document on the PhEur EDQM website, and also the General Information Chapter 8 in the JP XV.

Denatured alcohol

Synonyms Industrial methylated spirit; surgical spirit.
Comments Denatured alcohol is alcohol intended for external use only. It has been rendered unfit for human consumption by the addition of a denaturing agent such as methanol or methyl isobutyl ketone.

Dilute alcohol

Synonyms Dilute ethanol.
Specific gravity *see* Table III.

Table III: Specific gravity of alcohol.

Strength of alcohol (% v/v)	Specific gravity at 20°C
90	0.8289–0.8319
80	0.8599–0.8621
70	0.8860–0.8883
60	0.9103–0.9114
50	0.9314–0.9326
45	0.9407–0.9417
25	0.9694–0.9703
20	0.9748–0.9759

Comments The term 'dilute alcohol' refers to a mixture of ethanol and water of stated concentration. The USP32–NF27 lists diluted alcohol. The BP 2009 lists eight strengths of dilute alcohol (dilute ethanol) containing 90%, 80%, 70%, 60%, 50%, 45%, 25%, and 20% v/v respectively of ethanol.

18 Comments

Alcohol is one of the materials that have been selected for harmonization by the Pharmacopeial Discussion Group. For further information see the General Information Chapter <1196> in the USP32–NF27, the General Chapter 5.8 in PhEur 6.0, along with the 'State of Work' document on the PhEur EDQM website, and also the General Information Chapter 8 in the JP XV.

Possession and use of nondenatured alcohols are usually subject to close control by excise authorities.

A specification for alcohol is contained in the Food Chemicals Codex (FCC).[18]

The EINECS number for alcohol is 200-578-6. The PubChem Compound ID (CID) for alcohol is 702.

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21 Author

ME Quinn.

22 Date of Revision

5 February 2009.

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21 Authors

SA Shah, D Thassu.

22 Date of Revision

12 February 2009.

Alpha Tocopherol

1 Nonproprietary Names

BP: *RRR*-Alpha-Tocopherol

JP: Tocopherol

PhEur: *RRR*-α-Tocopherol

USP: Vitamin E

See also Sections 3, 9, and 17.

2 Synonyms

Copherol F1300; (±)-3,4-dihydro-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)-2*H*-1-benzopyran-6-ol; E307; *RRR*-α-tocopherolum; 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 centers, 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.

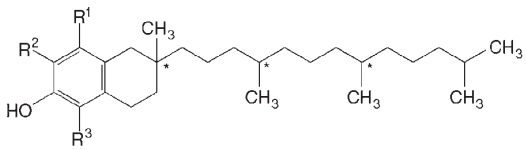
Similar considerations apply to beta, delta, and gamma tocopherol and tocopherol esters.

See Section 17 for further information.

4 Empirical Formula and Molecular Weight

$C_{29}H_{50}O_2$ 430.72

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 centers.

6 Functional Category

Antioxidant; therapeutic agent.

7 Applications in Pharmaceutical Formulation or Technology

Alpha tocopherol is primarily recognized as a source of vitamin E, and the commercially available materials and specifications reflect this purpose. While alpha tocopherol also exhibits antioxidant properties, the beta, delta, and gamma tocopherols are considered to be more effective as antioxidants.

Alpha-tocopherol is a highly lipophilic compound, and is an excellent solvent for many poorly soluble drugs.[1–4] Of widespread regulatory acceptability, tocopherols are of value in oil- or fat-based pharmaceutical products and are normally used in the concentration range 0.001–0.05% v/v. There is frequently an optimum concentration; thus the autoxidation of linoleic acid and methyl linolenate is reduced at low concentrations of alpha tocopherol, and is accelerated by higher concentrations. Antioxidant effectiveness can be increased by the addition of oil-soluble synergists such as lecithin and ascorbyl palmitate.[4]

Alpha tocopherol may be used as an efficient plasticizer.[5] It has been used in the development of deformable liposomes as topical formulations.[6]

d-Alpha-tocopherol has also been used as a non-ionic surfactant in oral and injectable formulations.[3]

8 Description

Alpha tocopherol is a natural product. The PhEur 6.0 describes alpha-tocopherol as a clear, colorless or yellowish-brown, viscous, oily liquid. *See also* Section 17.

9 Pharmacopeial Specifications

See Table I.

Table I: Pharmacopeial specifications for alpha tocopherol.

Test	JP XV	PhEur 6.0	USP 32
Identification	+	+	+
Characters	—	+	—
Acidity	—	—	+
Optical rotation	—	+0.05° to +0.10°	+
Heavy metals	≤20 ppm	—	—
Related substances	—	+	—
Absorbance at 292 nm	+	—	—
Refractive index	71.0–76.0	—	—
Specific gravity	1.503–1.507	—	—
Clarity and color of solution	0.947–0.955	—	—
Assay	+	—	—
	96.0–102.0%	94.5–102.0%	96.0–102.0%

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Note that the USP 32 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 6.0 describes alpha tocopherol and alpha tocopheryl acetate in separate monographs.

The diversity of the tocopherols described in the various pharmacopeial monographs makes the comparison of specifications more complicated; *see* Section 17.

10 Typical Properties

Boiling point 235°C
Density 0.947–0.951 g/cm^3
Flash point 240°C
Ignition point 340°C
Refractive index n_D^{20} = 1.503–1.507
Solubility Practically insoluble in water; freely soluble in acetone, ethanol, ether, and vegetable oils.

11 Stability and Storage Conditions

Tocopherols are oxidized slowly 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 17.

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.[7]

13 Method of Manufacture

Naturally occurring tocopherols are obtained by the extraction or molecular distillation of steam distillates of vegetable oils; for example, alpha tocopherol occurs in concentrations of 0.1–0.3% in corn, rapeseed, soybean, sunflower, and wheat germ oils.[8] Beta 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.[9]

14 Safety

Tocopherols (vitamin E) occur in many food substances that are consumed as part of the normal diet. The daily nutritional requirement has not been clearly defined but is estimated to be 3.0–20.0 mg. Absorption from the gastrointestinal tract is dependent upon normal pancreatic function and the presence of bile. Tocopherols are widely distributed throughout the body, with some ingested tocopherol metabolized in the liver; excretion of metabolites is via the urine or bile. Individuals with vitamin E deficiency are usually treated by oral administration of tocopherols, although intramuscular and intravenous administration may sometimes be used.

Tocopherols are well tolerated, although excessive oral intake may cause headache, fatigue, weakness, digestive disturbance, and nausea. Prolonged and intensive skin contact may lead to erythema and contact dermatitis.

The use of tocopherols as antioxidants in pharmaceuticals and food products is unlikely to pose any hazard to human health since the daily intake from such uses is small compared with the intake of naturally occurring tocopherols in the diet.

The WHO has set an acceptable daily intake of tocopherol used as an antioxidant at 0.15–2.0 mg/kg body-weight.[10]

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. Gloves and eye protection are recommended.

16 Regulatory Status

GRAS listed. Accepted in Europe as a food additive. Included in the FDA Inactive Ingredients Database (IV injections, powder, lyophilized powder for liposomal suspension; oral capsules, tablets, and topical preparations). Included in the Canadian List of Acceptable Non-medicinal Ingredients. Included in nonparenteral medicines licensed in the UK.

17 Related Substances

d-Alpha tocopherol; *d*-alpha tocopheryl acetate; *dl*-alpha tocopheryl acetate; *d*-alpha tocopheryl acid succinate; *dl*-alpha tocopheryl acid succinate; beta tocopherol; delta tocopherol; gamma tocopherol; tocopherols excipient.

d-Alpha tocopherol

Empirical formula $C_{29}H_{50}O_2$
Molecular weight 430.72
CAS number [59-02-9]
Synonyms Natural alpha tocopherol; (+)-(2*R*,4′*R*,8′*R*)-2,5,7,8-tetramethyl-2-(4′,8′,12′-trimethyltridecyl)-6-chromanol; *d*-α-tocopherol; vitamin E.
Appearance A practically odorless, clear, yellow, or greenish-yellow viscous oil.
Melting point 2.5–3.5°C
Solubility Practically insoluble in water; soluble in ethanol (95%). Miscible with acetone, chloroform, ether, and vegetable oils.
Specific gravity 0.95
Comments *d*-Alpha tocopherol is the naturally occurring form of alpha tocopherol.

d-Alpha tocopheryl acetate

Empirical formula $C_{31}H_{52}O_3$
Molecular weight 472.73
CAS number [58-95-7]
Synonyms (+)-(2*R*,4′*R*,8′*R*)-2,5,7,8-Tetramethyl-2-(4′,8′,12′- trimethyltridecyl)-6-chromanyl acetate; *d*-α-tocopheryl acetate; vitamin E.
Appearance A practically odorless, clear, yellow, or greenish-yellow colored viscous oil that may solidify in the cold.
Melting point 28°C
Solubility Practically insoluble in water; soluble in ethanol (95%). Miscible with acetone, chloroform, ether, and vegetable oils.
Specific rotation $[\alpha]_D^{25}$ = +0.25° (10% w/v solution in chloroform)
Comments Unstable to alkalis.

dl-Alpha tocopheryl acetate

Empirical formula $C_{31}H_{52}O_3$
Molecular weight 472.73
CAS number [7695-91-2]
Synonyms (±)-3,4-Dihydro-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)-2*H*-1-benzopyran-6-ol acetate; (±)-(2*RS*,4′*RS*,8′*RS*)-2,5,7,8-tetramethyl-2-(4′,8′,12′-trimethyltridecyl)-6-chromanyl acetate; (±)-α-tocopherol acetate; α-tocopheroli acetas; all-*rac*-α-tocopheryl acetate; *dl*-α-tocopheryl acetate; vitamin E.
Appearance A practically odorless, clear, yellow, or greenish-yellow viscous oil.
Density 0.953 g/cm^3
Melting point –27.5°C
Refractive index n_D^{20} = 1.4950–1.4972
Solubility Practically insoluble in water; freely soluble in acetone, chloroform, ethanol, ether, and vegetable oils; soluble in ethanol (95%).
Comments Unstable to alkali. However, unlike alpha tocopherol, the acetate is much less susceptible to the effects of air, light, or

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ultraviolet light. Alpha tocopherol acetate concentrate, a powdered form of alpha tocopherol acetate, is described in the PhEur 6.0. The concentrate may be prepared by either dispersing alpha tocopherol acetate in a suitable carrier such as acacia or gelatin, or by adsorbing alpha tocopherol acetate on silicic acid.

d-Alpha tocopheryl acid succinate

Empirical formula $C_{33}H_{54}O_5$
Molecular weight 530.8
CAS number [4345-03-3]
Synonyms (+)-α-Tocopherol hydrogen succinate; *d*-α-tocopheryl acid succinate; vitamin E.
Appearance A practically odorless white powder.
Melting point 76–77°C
Solubility Practically insoluble in water; slightly soluble in alkaline solutions; soluble in acetone, ethanol (95%), ether, and vegetable oils; very soluble in chloroform.
Comments Unstable to alkalis.

dl-Alpha tocopheryl acid succinate

Empirical formula $C_{33}H_{54}O_5$
Molecular weight 530.8
CAS number [17407-37-3]
Synonyms (±)-α-Tocopherol hydrogen succinate; *dl*-α-tocopheryl acid succinate; *dl*-α-tocopherol succinate; vitamin E.
Appearance A practically odorless, white crystalline powder.
Solubility Practically insoluble in water; slightly soluble in alkaline solutions; soluble in acetone, ethanol (95%), ether, and vegetable oils; very soluble in chloroform.
Comments Unstable to alkalis.

Beta tocopherol

Empirical formula $C_{28}H_{48}O_2$
Molecular weight 416.66
CAS number [148-03-8]
Synonyms Cumotocopherol; (±)-3,4-dihydro-2,5,8-trimethyl-2-(4,8,12-trimethyltridecyl)-2*H*-1-β-benzopyran-6-ol; 5,8-dimethyltocol; neotocopherol; *dl*-β-tocopherol; vitamin E; *p*-xylotocopherol.
Appearance A pale yellow-colored viscous oil.
Solubility Practically insoluble in water; freely soluble in acetone, chloroform, ethanol (95%), ether, and vegetable oils.
Specific rotation $[\alpha]_D^{20} = +6.37°$
Comments Less active biologically than alpha tocopherol. Obtained along with alpha tocopherol and gamma tocopherol from natural sources. Beta tocopherol is very stable to heat and alkalis and is slowly oxidized by atmospheric oxygen.

Delta tocopherol

Empirical formula $C_{27}H_{46}O_2$
Molecular weight 402.64
CAS number [119-13-1]
Synonyms (±)-3,4-Dihydro-2,8-dimethyl-2-(4,8,12-trimethyltridecyl)-2*H*-1-benzopyran-6-ol; E309; 8-methyltocol; *dl*-δ-tocopherol; vitamin E.
Appearance A pale yellow-colored viscous oil.
Solubility Practically insoluble in water; freely soluble in acetone, chloroform, ethanol (95%), ether, and vegetable oils.
Comments Occurs naturally as 30% of the tocopherol content of soybean oil. Delta tocopherol is said to be the most potent antioxidant of the tocopherols.

Gamma tocopherol

Empirical formula $C_{28}H_{48}O_2$
Molecular weight 416.66
CAS number [7616-22-0]
Synonyms (±)-3,4-Dihydro-2,7,8-trimethyl-2-(4,8,12-trimethyltridecyl)-2*H*-1-benzopyran-6-ol; 7,8-dimethyltocol; E308; *dl*-γ-tocopherol; vitamin E; *o*-xylotocopherol.
Appearance A pale yellow-colored viscous oil.
Melting point −30°C
Solubility Practically insoluble in water; freely soluble in acetone, chloroform, ethanol (95%), ether, and vegetable oils.
Specific rotation $[\alpha]_D^{20} = -2.4°$ (in ethanol (95%))
Comments Occurs in natural sources along with alpha and beta tocopherol. Gamma tocopherol is biologically less active than alpha tocopherol. Very stable to heat and alkalis; slowly oxidized by atmospheric oxygen and gradually darkens on exposure to light.

Tocopherols excipient

Synonyms *Embanox tocopherol*.
Appearance A pale yellow-colored viscous oil.
Comments Tocopherols excipient is described in the USP32–NF27 as a vegetable oil solution containing not less than 50.0% of total tocopherols, of which not less than 80.0% consists of varying amounts of beta, delta, and gamma tocopherols.

18 Comments

Note that most commercially available tocopherols are used as sources of vitamin E, rather than as antioxidants in pharmaceutical formulations.

Various mixtures of tocopherols, and mixtures of tocopherols with other excipients, are commercially available, and individual manufacturers should be consulted for specific information on their products.

Molecularly imprinted polymers for use in the controlled release of alpha tocopherol in gastrointestinal simulating fluids have been investigated.[11]

The EINECS number for α-tocopherol is 215-798-8. The EINECS number for *d*-α-tocopherol is 200-412-2; and the EINECS number for *dl*-α-tocopherol is 233-466-0. The PubChem Compound ID (CID) for alpha tocopherol includes 14985 and 1548900.

19 Specific References

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22 Date of Revision

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