caltrol; ***Irl.:*** Calcijex†; One-Alpha; Rocaltrol; Silkis; Zemplar; ***Israel:*** Alpha D3; Calcijex; One-Alpha; ***Ital.:*** Alpha D3; Atiten; Calcijex; Dediol; Deril; Dibase; Didrogyl; Difix; Diseon; Diserinal; Geniad; Ostelin; Ostidil-D3; Rocaltrol; Sefal; Silkis; Tridelta; Trikal; Zemplar; ***Jpn:*** Alfarol; Hornel; Onealfa; Oxarol; Rocaltrol; ***Malaysia:*** Calcijex; Fairy ADE; One-Alpha; Osteocap; Rocaltrol; Roical; Zemplar; ***Mex.:*** Alfad; Altrical; Altrol; Calciofem; Geldex; Lemytriol; Rocaltrol; Silkis; Tirocal; Zemplar; Zygium; ***Neth.:*** Calcijex; Devaron; Dihydral; Etalpha; Rocaltrol; Silkis; Zemplar; ***Norw.:*** AFI-D ; Calcijex; Etalpha; Rocaltrol; Silkis; Zemplar; ***NZ:*** CalD; One-Alpha; Rocaltrol; ***Philipp.:*** Bon-One; Osteomeg; Rocaltrol; Silkis; ***Pol.:*** Alfadiol; Calcijex; Devikap; Devisol; Juvit D ; Kalcytriol; Rocaltrol; Silkis; Vigantol; Vigantoletten; ***Port.:*** Calcijex; Dedrogyl; Etalpha; Rocaltrol; Silkis; Vigantol; Zemplar; ***Rus.:*** Alpha D3 (Альфа Д3-тев); Aquadetrim (Аквадетрим); Etalpha (Этальфа); Osteotriol (Остеотриол)†; Tachystin (Тахистин); Vigantol (Вигантол); ***S.Afr.:*** AT 10; One-Alpha; Rocaltrol; ***Singapore:*** Alpha D3; Bon-One; Bongreen†; Calcijex; One-Alpha; Rocaltrol†; Roical; Silkis; Zemplar; ***Spain:*** Calcijex; Etalpha; Hidroferol; Oseofort; Rocaltrol; Silkis; Zemplar; ***Swed.:*** Calcijex; Devitre†; Dygratyl; Etalpha; Rocaltrol; Zemplar; ***Switz.:*** AT 10; Bocatriol†; Calcijex; Rocaltrol; Silkis; Vi-De ; Zemplar; ***Thai.:*** Alpha D3; Bon-One; Calcit; Decostriol; Meditrol; One-Alpha; OsteoD; Rocaltrol; ***Turk.:*** Alpha D3; Calcijex; Devit-3; One-Alpha; Osteo-D; Rocaltrol; ***UK:*** AT 10; Calcijex; One-Alpha; Rocaltrol; Silkis; Zemplar; ***USA:*** Calciferol; Calcijex; Calderol; Delta-D; DHT; Drisdol; Hectorol; Hytakerol†; Maximum D3; Rocaltrol; Zemplar; ***Venez.:*** Alpha D3; Rocaltrol; Silkis; Zemplar.

**Multi-ingredient:** ***Arg.:*** A-D-C; AD Shock; Adermicina; Anartrit; Atomoderma A-D; Calcimax D3; Calcimax Magnesio; Calcio Cit; Calcio Masticable; Calcional D3; Calcium D†; Calnier-D; Caltrate + D; Cavirox; Cavirox Cit; Citramar D; Dermosan; Dr Selby; Femorel Max; Fosamax Plus; Full Calcio; Glossderm†; Magnesio Incaico; Ostram D3; Regenesis Max; Regucal D; Ribastamin Duo; Sinamida Cicatrizante†; Snella; Taxus; Ultracalcium D3; Vitapelen†; ***Austral.:*** Bio Magnesium; Caltrate + Vitamin D; Caltrate Plus; FAB Tri-Cal; Fosamax Plus; Prosteo†; Soy Forte with Black Cohosh†; ***Austria:*** Cacit mit Vitamin D ; Cal-D-or; Cal-D-Vita; Cal-De; Calcichew D ; Calcimagon-D3; Calcipot D ; Calcisan D; Calcium Plus; Calcium-D-Sandoz; Kombi-Kalz; Maxi-Kalz Vit D3; Oleovit A + D; Ruticalzon; ***Belg.:*** Cacit Vitamine D ; D-Vital; Fosavance; Newderm†; Sandoz Ca-D; Steovit D3; Topcal D3†; ***Braz.:*** AD-Til; ADE 2 (Adedois); Adecal; Adederme; Adeforte; Aderogil D3; Alendil Calcio D; Babymed; Calcifix B12; Calcifix Irradiado; Calcinol Complexo; Calcium D3; Calde; Caltrate + D; Caltrate + M; Caridem†; Dermalisan; Dermoden; Gaduol†; Glossaliv; Hipoderme; Hipodermon; Hipodex; Hipoglos; Maxicalc-D; Miocalven D; Multiderme; Natecal D†; Os-Cal + D; Ossocal-D; OsteoNutri; Pronenen; Reposcal D; Sensibaby; Solemil†; Suavederm; Vitadesan; ***Canad.:*** A & D; A & D Ointment†; Antiseptic Skin Cream†; Cal D; Calburst†; Calcia; Calcite D; Calcium D; Calcium Magnesium Plus†; Caltrate Plus; Caltrate Select; Caltrate with Vitamin D; Mega Cal Calcium†; Neo Cal D; Nu Cal D; Nutrol A D; Os-Cal D; Viactiv; ***Chile:*** Aplical-D†; Brexon†; Cadevit; Calcefor D; Calcigran; Calcigran D; Calcimax D3; Calcio Day D†; Calcio Nil Forte†; Calciovit Puro; Calcium Forte D; Calcium-Sandoz + D; Calcium-Sandoz Forte D; Calcivorin D; Caldar-D; Caldeval; Caprimida D; Caprimida D Balance; Crevet Calcio + D3 + C; Dermaglos Plus†; Dical-D†; Elcal-D; Kaplus-D; Levucal D; Macrocal-D; Natecal D; Nenegloss; Oseofort; Osteocaps; Ostram D3; Pediaderm†; Platsul A; Pomada Vitaminica; Povin; Sanidecal-D; Sanoderm; Trical-D; ***Cz.:*** Adrovance; Calcichew D ; Caltrate Plus; Fosavance; Ideos; Infadolan; Kombi-Kalz; Osteocare; Vita-Calc†; Vitacalcin D†; ***Denm.:*** Calcichew D ; CaviD; Ideos†; ***Fin.:*** Calcichew D ; D-Calsor; Fosavance; Ideos; Kalcipos-D; Ostram-Vit D †; ***Fr.:*** Actonelcombi; Adrovance; Arthrolib; Cacit Vitamine D ; Calcidose Vitamine D; Calciforte Vitamin D ; Calciprat D ; Calcos Vitamine D ; Calperos D ; Caltrate Vitamine D ; Eptavit; Estrofort; Fixical Vitamine D ; Fluosterol; Fosavance; Frubiose Vitamine D†; Ideos; Metocalcium; Osseans D3; Osteocal D3; Ostram Vitamine D ; Zymaduo; ***Ger.:*** CalciAPS D3; Calcigen D; Calcilac KT; Calcimagon-D3; Calcimed D ; Calcium D ; Calcium Verla D; Calcium-D-Sandoz†; Calcium-dura Vit D ; Calcium-Sandoz D Osteo; Calcivit D; calcivitase†; D-Fluoretten; Fluor-Vigantoletten; Fosavance; Frubiase Calcium forte 500; Ideos; Ossofortin D; Ossofortin forte; Ossofortin Plus; Ossofortin†; Ossplusvit D ; Ossplusvit S†; Osteoplus; Ostocavid; Remicalcin + D ; Sandocal-D; Strafortin†; Zymafluor D; ***Gr.:*** Adrovance; Aquasol A+D; Cal+D; Calcidina; Calcioral D3; Calcium-D-Sandoz; Cald 3-Therapy; Caldesil; Calvidin; D-Calcium; Decal; Dioflam; Flavobion-C; Fosavance; Ideos; Natecal D3; Taminol; Videcalcio; ***Hong Kong:*** Calcichew D †; Calcioday-D; Calperos D ; Caltrate + D; Caltrate + Soy; Caltrate Plus; Citracal + D; Doctor's Choice Fortified Bone Support; Flavettes Cal D3; Fosamax Plus; Mega-Cal with Vit D; Os-Cal + D; Osteocare; ***Hung.:*** Actonel Trio; Calcichew D ; Calcisedron-D; Calcium-D-Sandoz; Calcivid; Caldea†; Fosavance; Ideos; Neogranormon; Osteocare; Vitacalc†; ***India:*** Alfacip Plus; Anemidox; Aristrol Forte†; Cafe-Kit†; Cal-Aid; Calcigen; Calcinol; Calcom; Calfa-Plus; Calmix†; Cipcal; Cipcal M; Incad; Kalzana; Kemicetine Antiozena; Logical; Macalvit; Milical; Milical-XP†; Minroset-C; Omilcal; Ossivite; Ostebon; Osteobon; Osteobon-M; Ostocalcium; Ostocalcium B-12; Sandocal with Vit D ; Sharkomalt; Sharkovit; Sigmacalvit; Styptocid; Trical-D; ***Indon.:*** Cal-95; Calc-Os; Calcidin; Calosbon; Calporosis D; Calsical; Cavit D3; CDR Fortos; Day-Cal; Dumocalcin Plus; Epocaldi; Fosamax Plus; Hi-Bone; Hical; Jointfit; Licokalk Plus; Menoxa; Osfit; Ossovit; Osteocal Plus; Osteocare; Osteopor; Scott's E Vita; Steopor; Vitacal-D; ***Irl.:*** Bio-Calcium + D ; Bio-Calcium + D + K; Calcichew D ; Calvidin; Chocovite; Decal; Fosavance; Ideos; Osteofos D3; ***Israel:*** Aquitol†; Baby A + D; Calcichew D ; Calcium Citrate; Caltrate + Vit D; Oleovit A + D †; Vitamidyne A and D; ***Ital.:*** AD Pabyrn; Adisterolo; Biocalcium D3; Cacit Vitamina D3; Cadtre; Calcicold3; Calcidon; Calciozim†; Calcium-D3-Sandoz; Calciumcafe; Calisvit; Calma D3; CalplusD3; Caltrate; Carbo D3; Cartago; Dicalcium†; Ditrevit; Ditrost; Effercal D3; Eurocal D3; Fitogen; Fosavance; Foscald3; Granoleina†; Ideos; Kalaz D3; Metocal Vitamina D; Natecal; Orotre; Osteofos D3; Ostram D ; Tonacal D3; Urtotre; ***Malaysia:*** Adult Citrex Cal-Mag-D3; Bio-Enhanced Calcium Plus; Calcioday-D†; Caltrate + D; Caltrate Plus; Citracal + D†; Dumocalcin†; Effcal; Fosamax Plus; Junior Citrex Cal-Mag-D3; Milical; Os-Cal + D†; Revital Calcium D3; Vitacal + D†; ***Mex.:*** Adekals; Adekon; Adekon C; Adeloren†; Adibal; Alfem; Aquasol AD; Caltrate + D; Caltrate + M; Caltrate + S; Caltrec†; Capent; Dical; Fosamax Plus; Minerbon; Os-Cal + D; Osteocalcio; Osteomin D; Posture D; Sandoz Calcium + D; Sutin†; Valmetrol-3; Vidamil; Vitalorange; ***Neth.:*** CaD; Calci-Chew D3; Calisvit; Halitran; Ideos; Sandoz Ca-D; ***Norw.:*** Calcigran; Ideos; Nycoplus Calcigran; ***NZ:*** Fosamax Plus; ***Philipp.:*** Agre-Calvit; Calciday; Caltrate Plus; Calvit; Esvical; Fosavance; Her Soy Plus; Osteo-4; Osteo-D; Osteocare; Vandol; ***Pol.:*** Alantavit; Calcium 500D; Caldetrin; Caltrate + Witamina D; Caltrate Plus; Ideos; Orocal D ; Ostowap D ; Tranvit; Vicalvit D; ***Port.:*** Bidiam; Cacit; Calcigenol; Calcior-D; Calcitab D; Calcium 600†; Calcium D; Calcium-D-Sandoz; Caltrate Plus Mastigavel†; Caltrate Plus†; Decalcit; Densical D; Dermabut; Fosavance; Ideos; Natecal D; Ostram D3†; Osvical; ***Rus.:*** Calcemin (Кальцемин); Calcemin Advance (Кальцемин Адванс); Calcium-D3 Nycomed (Кальций-Д3 Никомед); Ideos (Идеос); Natecal D (Натекаль Д ); Vectrum Calcium (Вектрум Кальций); ***S.Afr.:*** Phytopause BSF; Vandol†; ***Singapore:*** BoneCare; Cal-D3†; Calcioday-D†; Calcium-D; Caltrate + Soy; Caltrate + Vit D; Caltrate Plus; Cavit-D3; Citracal + D; Dumocalcin; Effcal; Fosamax Plus; Glucocal; Os-Cal + D; Vitacal; Vitacal + D; ***Spain:*** Adiod; Biominol A D; Calcial D; Calcio 20 Complex; Calcio 20 Fuerte; Calcio D; Calcium-Sandoz Forte D; Caosina D; Carbocal D; Cicatral; Cimascal D; Creacal†; Disnal; Fosavance; Grietalgen; Grietalgen Hidrocort†; Ibercal D; Ideos; Mastical D; Maxbon; Mencalisvit; Metafisol; Mitosyl; Natecal D; Osteomerck; Ostine; Osvical D; Redoxon Calcivit; Tepox Cal D; Trabex; Veriscal D; ***Swed.:*** AD-vitamin; Cal-D-Vita; Calcichew D ; Ideos; Kalcipos-D; ***Switz.:*** Cal-De†; Calcimagon-D3; Calcium D Sauter; Calcium-Sandoz D3; Calcivit; Calperos D ; Decalcit; Malvedrin; Osteocal D3; Phytopharma Calcium; Riccovitan†; ***Thai.:*** Bio-Calcium + D3 + K; Cal-D-Vita; Calcalcin; Calcioday-D†; Calcium D; Caldoxon; Caltab W/Vitamin D; Caltrate + D; Caltrate Plus; Calvin Plus; Combi-Cal†; Effcal; Fortica; Ostone-B12; Prima-Cal Plus Vit D; ***Turk.:*** Balya; Cal-D-Vita; Calcidine; Calcimax D3; Calcium-D-Sandoz; Caltrate; D-Flor; Folic Plus; Fosfokalsiyum; Kalsifluor; Nature Made Oyster Shell Calcium; Osteocare; ***UK:*** Actonel Combi; Adcal-D ; Cacit D3; Calceos; Calcichew D ; Calcium and Ergocalciferol Tablets; Calfovit D3; Caltrate Plus; Crampex; Fosavance; Haliborange Calcium Plus Vitamin D; Natecal D3; Osteo-Life; Osteocare; S.P.H.P.; ***USA:*** A and D Medicated; Calcarb with Vitamin D; Calcet; Calcium 600 + D; Calel-D; Caltrate + Iron & Vitamin D; Caltrate + Vitamin D; Caltrate Plus; Calvite P & D; Citracal + D; Citracal Creamy Bites†; Citracal Plus with Magnesium; Clocream; Desert Pure Calcium; Diaper Guard; Fosamax Plus; Fosteum; Lobana Derm-Aide; Lobana Peri-Garde; Os-Cal + D; Oyster Calcium with Vitamin D; Paladin; Posture-D; ***Venez.:*** A-D-Vit; Adaderm; Adenar; Brocalcio D3; Cal.Cell; Calcibon D; Calcibon D Magnesio; Calcibon D Soya; Calcibon Natal; Calcinor D; Calcio Ostelin; Calciofar D; Calciogenol; Calcion D Plus; Calcitrex D3; Calpal D†; Caltrate + D; Citracal D; Dicalcico†; Hipoglos†; Ideos; Kidcal; Maltocalcine; Oscal D; Vandol; Viteno†.

## Vitamin E Substances

Vitamina E.

*ATC — A11HA03.*

*ATC Vet — QA11HA03.*

NOTE. The food additive number E306 is used for tocopherols.

Vitamin E is a generic term applied to a large number of natural or synthetic compounds. The most important substances are the **tocopherols** of which **alpha tocopherols** are the most active and widely distributed in nature; other naturally occurring tocopherols include beta, gamma, and delta tocopherols, but these are not used in therapeutics. The other group of compounds with vitamin E activity are the tocotrienols.

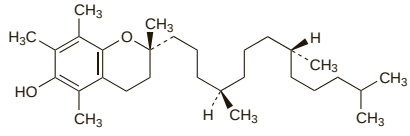
Alpha tocopherols occur naturally in the *d* optical isomer form, which is more active than the synthetic racemic *dl* form; for further details concerning the comparative activities of the different forms and isomers of vitamin E compounds, see under Units, below.

### *d*-Alpha Tocopherol

*d*-Alfa Tokoferol; (+)-Alpha-Tocopherol; *RRR*-alpha-Tocophérol; *RRR*-alpha-Tocopherolum; Natural Alpha Tocopherol; Natural α-Tocopherol; RRR-α-Tocopherolum; RRR-α-Tokoferol; D-α-Tocoferol; *RRR*-α-Tocopherol; *d*-α-Tocopherol; *RRR*-α-tocopherolum; *RRR*-α-tokoferol; *RRR*-α-Tokoferoli; *RRR*-α-Tokoferolis. (+)-2,5,7,8-Tetramethyl-2-(4,8,12-trimethyltridecyl)chroman-6-ol.

$C_{29}H_{50}O_2$ = 430.7.

*CAS — 59-02-9.*



**Pharmacopoeias.** In *Eur.* (see p.vii). *US* allows it under the title Vitamin E.

**Ph. Eur. 6.2** (*RRR*-α-Tocopherol; *RRR*-Alpha-Tocopherol BP 2008). A clear, colourless, or yellowish-brown viscous oily liquid. Practically insoluble in water; freely soluble in dehydrated alcohol, in acetone, in dichloromethane, and in fatty oils. Store under an inert gas in airtight containers. Protect from light.

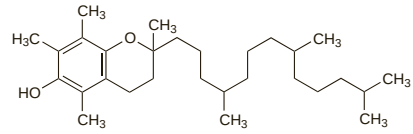
**USP 31** (Vitamin E). A clear, yellow, or greenish-yellow, practically odourless, viscous oil. It is unstable to air and light, particularly in alkaline media. Insoluble in water; soluble in alcohol; miscible with acetone, with chloroform, with ether, and with vegetable oils. Store under an inert gas in airtight containers. Protect from light.

### *dl*-Alpha Tocopherol

all-rac-α-Tokoferol; all-*rac*-α-Tocopherol; Alpha Tocopherol; (±)-Alpha-Tocopherol; E307; int-rac-α-Tocopherolum; int-*rac*-α-Tocopherol; Synthetic Alpha Tocopherol; Synthetic α-Tocopherol; DL-α-Tocoferol; Tocoferolum Alfa; α-Tocopherol; *dl*-α-Tocopherol; α-Tocopherolum; α-Tokoferol; Tokoferol-alfa; tout-*rac*-α-Tocophérol; Visų racematų α-Tokoferolis. (±)-2,5,7,8-Tetramethyl-2-(4,8,12-trimethyltridecyl)chroman-6-ol.

$C_{29}H_{50}O_2$ = 430.7.

*CAS — 10191-41-0.*



**Pharmacopoeias.** In *Eur.* (see p.vii) and *Jpn. US* allows it under the title Vitamin E.

**Ph. Eur. 6.2** (all-*rac*-α-Tocopherol; all-*rac*-Alpha Tocopherol BP 2008). A clear, colourless or yellowish-brown viscous oily liquid. Practically insoluble in water; freely soluble in dehydrated alcohol, in acetone, in dichloromethane, and in fatty oils. Store under an inert gas. Protect from light.

**USP 31** (Vitamin E). A clear, yellow, or greenish-yellow, practically odourless, viscous oil. It is unstable to air and light, particularly in alkaline media. Insoluble in water; soluble in alcohol; miscible with acetone, with chloroform, with ether, and with vegetable oils. Store under an inert gas in airtight containers. Protect from light.

### *d*-Alpha Tocoferil Acetate

*d*-Alpha Tocopheryl Acetate; (+)-Alpha-Tocopherol Acetate; (+)-Alpha-Tocopheryl Acetate; *RRR*-alpha-Tocophéryle, acétate de; *RRR*-alpha-Tocopherylis acetas; RRR-α-Tocopherylis acetas; RRR-α-Tokoferylu octan; D-α-Tocoferilo, acetato de; Tocoferoli Alfa *RRR* Acetas; *RRR*-α-Tocopheroli Acetas; *d*-α-Tocopheryl Acetate; *RRR*-α-Tocopheryl Acetate; *RRR*-α-Tocopherylis Acetas; *RRR*-α-Tokoferilio acetatas; *RRR*-α-Tokoferol-acetát; Tokoferol-acetát alfa *RRR*; Tokoferol-alfa-*RRR*-acetát; *RRR*-α-Tokoferylacetat; *RRR*-α-Tokoferyyliasetaatti. (+)-α-Tocopherol acetate.

$C_{31}H_{52}O_3$ = 472.7.

*CAS — 58-95-7.*

**Pharmacopoeias.** In *Eur.* (see p.vii). *US* allows it under the title Vitamin E.

**Ph. Eur. 6.2** (*RRR*-α-Tocopheryl Acetate; *RRR*-Alpha-Tocopheryl Acetate BP 2008). A clear, colourless or slightly greenish-yellow, viscous oily liquid. Practically insoluble in water; soluble in alcohol; freely soluble in dehydrated alcohol, in acetone, and in fatty oils. Protect from light.

**USP 31** (Vitamin E). A clear, yellow, or greenish-yellow, practically odourless, viscous oil. It may solidify in the cold. It is stable to air and light, but unstable to alkali. Insoluble in water; soluble in alcohol; miscible with acetone, with chloroform, with ether, and with vegetable oils. Store in airtight containers. Protect from light.

### *dl*-Alpha Tocoferil Acetate

*dl*-Alfa Tokoferil Asetat; all-rac-α-Tokoferylu octan; all-*rac*-α-Tocopheryl Acetate; Alpha Tocopheryl Acetate; *dl*-Alpha Tocopheryl Acetate; (±)-Alpha-Tocopherol acetate; int-rac-α-Tocopherylis acetas; int-*rac*-α-Tocopherylis Acetas; DL-α-Tocoferilo, acetato de; Tocoferoli Alfa Acetas; α-Tocopherol Acetate; α-Tocopheroli Acetas; *dl*-α-Tocopheryl Acetate; Tokoferol alfa-acetát; Tokoferolu octan; tout-*rac*-α-Tocophéryle, acétate de; Visų racematų α-Tokoferilio acetatas. (±)-α-Tocopherol acetate.

$C_{31}H_{52}O_3$ = 472.7.

*CAS — 7695-91-2; 52225-20-4.*

**Pharmacopoeias.** In *Chin., Eur.* (see p.vii), and *Jpn. US* allows it under the title Vitamin E.

*Eur.* also has a monograph for the concentrated powdered form.

**Ph. Eur. 6.2** (all-*rac*-α-Tocopheryl Acetate; all-*rac*-Alpha Tocopheryl Acetate BP 2008). A clear, colourless or slightly greenish-yellow, viscous, oily liquid. Practically insoluble in water; freely soluble in dehydrated alcohol, in acetone, and in fatty oils. Protect from light.

**Ph. Eur. 6.2** (α-Tocopheryl Acetate Concentrate (Powder Form); α-Tocopherylis Acetatis Pulvis; Alpha Tocopheryl Acetate Concentrate (Powder Form) BP 2008). It is prepared either by finely dispersing *dl*-alpha tocoferil acetate in a suitable carrier (e.g. gelatin, acacia, carbohydrates, lactoproteins, or a mixture of these) or by adsorbing *dl*-alpha tocoferil acetate on to silicic acid. The concentrate contains not less than 25% of *dl*-alpha tocoferil acetate. Almost white, yellowish, or light-brown small particles. Depending on the formulation, the powder may be practically insoluble in water or may swell or form a dispersion. Store in well-filled airtight containers. Protect from light.

**USP 31** (Vitamin E). A clear, yellow, or greenish-yellow, practically odourless, viscous oil. It is stable to air and light, but unstable to alkali. Insoluble in water; soluble in alcohol; miscible with acetone, with chloroform, with ether, and with vegetable oils. Store in airtight containers. Protect from light.

### *d*-Alpha Tocoferil Acid Succinate

*d*-Alpha Tocopheryl Acid Succinate; *d*-Alpha-Tocopherol acid succinate; *RRR*-alpha-Tocophéryle, hydrogénosuccinate de; *RRR*-alpha-Tocopherylis hydrogenosuccinas; D-α-Tocoferilo, succinato ácido; Tocoferoli Alfa *RRR* Hydrogenosuccinas; *RRR*-α-Tocoferoli Hydrogenosuccinas; *d*-α-Tocopheryl Acid Succinate; *RRR*-α-Tocopheryl Hydrogen Succinate; *RRR*-α-Tocopherylis Hydrogenosuccinas; *RRR*-α-Tokoferilio-vandenilio sukcinatas; Tokoferol-alfa-*RRR*-hydrogen-sukcinát; *RRR*-α-Tokoferol-hidrogén-szukcinát; *RRR*-α-Tokoferylvätesuccinat; *RRR*-α-Tokoferyylivetysuksinaatti. (+)-α-Tocopherol hydrogen succinate.

$C_{33}H_{54}O_5$ = 530.8.

*CAS — 4345-03-3.*

**Pharmacopoeias.** In *Eur.* (see p.vii). *US* allows it under the title Vitamin E.

*US* also includes Vitamin E Polyethylene Glycol Succinate, a mixture formed by the esterification of *d*-alpha tocoferil acid succinate with a macrogol.

**Ph. Eur. 6.2** (*RRR*-α-Tocopheryl Hydrogen Succinate; *RRR*-Alpha Tocopheryl Hydrogen Succinate BP 2008). A white or almost white crystalline powder. Practically insoluble in water; soluble in dehydrated alcohol and in acetone; very soluble in dichloromethane. Protect from light.

**USP 31** (Vitamin E). A white, practically odourless, powder. M.p. about 75°; it is unstable when held molten. It is stable to air and light, but unstable to alkali. Insoluble in water; soluble in alcohol, in acetone, in ether, and in vegetable oils; very soluble in chloroform; slightly soluble in alkaline solution. Store in airtight containers. Protect from light.

### *dl*-Alpha Tocoferil Acid Succinate

*dl*-Alpha Tocopheryl Acid Succinate; Alpha Tocopheryl Hydrogen Succinate; DL-alpha-Tocophéryle, hydrogénosuccinate de; DL-alpha-Tocopherylis hydrogenosuccinas; DL-α-Tocoferilo, succinato ácido; Tocoferoli Alfa Hydrogenosuccinas; DL-α-Tocopheroli Hydrogenosuccinas; *dl*-α-Tocopheryl Acid Succinate; DL-α-Tocopheryl Hydrogen Succinate; DL-α-tocopherylis Hydrogenosuccinas; DL-α-Tokoferilio-vandenilio sukcinatas; Tokoferol-alfa hydrogen sukcinát; DL-α-tokoferol-hidrogén-szukcinát; DL-α-Tokoferylvätesuccinat; DL-α-Tokoferyylivetysuksinaatti. (±)-α-Tocopherol hydrogen succinate.

$C_{33}H_{54}O_5$ = 530.8.

*CAS — 17407-37-3.*

**Pharmacopoeias.** In *Eur.* (see p.vii). *US* allows it under the title Vitamin E.

**Ph. Eur. 6.2** (DL-α-Tocopheryl Hydrogen Succinate; Alpha Tocopheryl Hydrogen Succinate BP 2008). A white or almost white, crystalline powder. Practically insoluble in water; soluble in dehydrated alcohol and in acetone; very soluble in dichloromethane. Protect from light.

**USP 31** (Vitamin E). A white, practically odourless, powder. M.p. about 70°; it is unstable when held molten. It is stable to air and light, but unstable to alkali. Insoluble in water; soluble in alcohol, in acetone, in ether, and in vegetable oils; very soluble in chloroform; slightly soluble in alkaline solution. Store in airtight containers. Protect from light.

## Units

Though the potency of preparations of vitamin E is still sometimes expressed in units, the International Standard for vitamin E was discontinued in 1956. The International Unit was the activity contained in 1 mg of a standard preparation of *dl*-alpha-tocoferil acetate. Past editions of the USP have stated that in expressing vitamin E activity of tocopherol products, the following equivalents of 1 mg were to be used:

- *d*-alpha tocopherol, 1.49 units
- *dl*-alpha tocopherol, 1.1 units
- *d*-alpha tocoferil acetate, 1.36 units
- *dl*-alpha tocoferil acetate, 1 unit
- *d*-alpha tocoferil acid succinate, 1.21 units
- *dl*-alpha tocoferil acid succinate, 0.89 unit.

For dietary purposes, vitamin-E activity may now be expressed in terms of alpha tocopherol equivalents (α-TEs). One α-TE is the activity contained in:

- 1 mg of *d*-alpha tocopherol (natural alpha tocopherol; *RRR*-α-tocopherol)
- 1.4 mg *dl*-alpha tocopherol
- 1.1 mg *d*-alpha tocoferil acetate
- 1.5 mg *dl*-alpha tocoferil acetate
- 1.2 mg *d*-alpha tocoferil acid succinate
- 1.7 mg *dl*-alpha tocoferil acid succinate.

## Adverse Effects and Precautions

Vitamin E is usually well tolerated. Large doses may cause diarrhoea, abdominal pain, and other gastrointestinal disturbances, and have also been reported to cause blurred vision, dizziness, fatigue and weakness. Contact dermatitis has occurred after topical application.

Large doses of vitamin E have been reported to increase bleeding tendency in vitamin-K deficient patients such as those taking oral anticoagulants. However, it has also been suggested that it may increase the risk of thrombosis in some patients, such as those taking oestrogens. The clinical significance of these effects is not known.

A higher incidence of necrotising enterocolitis has been noted in premature infants weighing less than 1.5 kg treated with vitamin E.

**Carcinogenicity.** For mention of an *increased* incidence of second primary cancers and reduced cancer-free survival in patients with head and neck cancer receiving vitamin E (and betacarotene initially), see Prophylaxis of Malignant Neoplasms, p.1927.

**Effects on mortality.** While some studies of antoxidants, including vitamin E, have suggested beneficial effects on the progression of cardiovascular disease and cancer, other studies (including large randomised studies such as the Women's Health Study[1]) have shown little or no effect.[2] Vitamin E may even cause an increased risk of heart failure, or incidence of cancer (see Prophylaxis of Ischaemic Heart Disease, p.1926, and Prophylaxis of Malignant Neoplasms, p.1927). A meta-analysis[3] and a systematic review[4] of vitamin E supplementation found no benefit in terms of mortality. Another meta-analysis[5] found no effect for vitamin E supplementation on all-cause mortality overall. However, in dose-response analysis, high-dosage vitamin E (greater than 400 units daily) showed a significantly increased risk; there was some suggestion of a decreased risk with low doses (less than 400 units daily); all-cause mortality progressively increased for doses greater than 150 units daily. (Such an effect was not seen in the Women's Health Study, in which participants received 600 units on alternate days.) Some have commented[6] that the meta-analysis may not have isolated the effects of vitamin E, since in many of the trials studied, other nutritional supplements had been given, including betacarotene, itself possibly associated with an increased risk of death; however, the use of high-dose vitamin E was considered unjustified. A systematic review of antoxidant supplementation found that vitamin E, either singly or with other antoxidants, increased mortality.[7] A large cohort study in a population aged 65 years or older, after adjustment for age and sex, found that there was no association between vitamin E use and mortality. However, mortality was increased in vitamin E users who had a history of cardiovascular disease, or who were taking nitrates, warfarin, and diuretics. There was a consistent trend towards reduced mortality in vitamin E users without cardiovascular disease or taking these drugs. The authors concluded that vitamin E should be used with caution in those with cardiovascular disease, and that further investigation of the potential interaction between vitamin E and particular drugs was warranted.[8]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2. Brown BG, Crowley J. Is there any hope for vitamin E? *JAMA* 2005; **293:** 1387–90.
3. Vivekananthan DP, *et al.* Use of antioxidant vitamins for the prevention of cardiovascular disease: meta-analysis of randomised trials. *Lancet* 2003; **361:** 2017–23.
4. Shekelle PG, *et al.* Effect of supplemental vitamin E for the prevention and treatment of cardiovascular disease. *J Gen Intern Med* 2004; **19:** 380–9.
5. Miller ER, *et al.* Meta-analysis: high-dosage vitamin E supplementation may increase all-cause mortality. *Ann Intern Med* 2005; **142:** 37–46.
6. Greenberg ER. Vitamin E supplements: good in theory, but is the theory good? *Ann Intern Med* 2005; **142:** 75–6.
7. Bjelakovic G, *et al.* Antioxidant supplements for prevention of mortality in healthy participants and patients with various diseases. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2008 (accessed 18/06/08).
8. Hayden KM, *et al.* Cache County Investigators. Risk of mortality with vitamin E supplements: the Cache County study. *Am J Med* 2007; **120:** 180–4.


**Neonatal toxicity.** For a review and discussion of liver and kidney toxicity in premature neonates associated with an intravenous preparation of vitamin E (E-Ferol) and attributed to the inclusion of polysorbates, see Effects in Infants, p.1919.

## Interactions

Various drugs may interfere with the absorption of vitamin E including colestyramine, colestipol, and orlistat. High doses of vitamin E may increase the effects of oral anticoagulants.

## Pharmacokinetics

Absorption of vitamin E from the gastrointestinal tract is dependent on the presence of bile and on normal pancreatic function. The amount of vitamin E absorbed varies widely between about 20% and 80% and appears to decrease as the dose is increased. It enters the blood via the chylomicrons in the lymph and is bound to beta lipoproteins. It is widely distributed to all tissues, and stored in adipose tissue. Some vitamin E is metabolised in the liver to glucuronides of tocopheronic acid and its γ-lactone. Some is excreted in the urine, but most of a dose is slowly excreted in the bile. Vitamin E appears in breast milk but is poorly transferred across the placenta.

## Human Requirements

The daily requirement of vitamin E has not been clearly defined but is probably about 3 to 12 mg of *d*-alpha tocopherol or the equivalent of other vitamin E substances. Requirements increase with increased dietary amounts of polyunsaturated fatty acids. There appears to be no evidence that supplements are required in subjects on balanced diets.

Vitamin E is widely distributed in food. The richest sources are vegetable oils especially wheat-germ oil (p.2415), sunflower oil, and cottonseed oil; cereals and nuts are also good sources. Significant losses of vitamin E from food may occur during cooking and storage.

**UK and US recommended dietary intake.** In the UK neither a reference nutrient intake (RNI—see p.1925) nor an estimated average requirement (EAR) has been set for vitamin E although daily intakes of 4 mg and 3 mg α-tocopherol equivalents (see under Units, above) were considered adequate for men and women, respectively.[1] The Expert Group on Vitamins and Minerals[2] have established a safe upper level (SUL) for vitamin E of 800 units or 540 mg of *d*-alpha tocopherol daily.

In the USA the recommended dietary allowance for adults is 15 mg daily of alpha tocopherol, and the tolerable upper intake level is 1000 mg daily.[3]


1. DoH. Dietary reference values for food energy and nutrients for the United Kingdom: report of the panel on dietary reference values of the committee on medical aspects of food policy. *Report on health and social subjects 41.* London: HMSO, 1991.
2. Expert Group on Vitamins and Minerals. Safe Upper Levels for vitamins and minerals (May 2003). Available at: http://www.food.gov.uk/multimedia/pdfs/vitmin2003.pdf (accessed 09/01/06)
3. Standing Committee on the Scientific Evaluation of Dietary Reference Intakes of the Food and Nutrition Board. *Dietary Reference Intakes for vitamin C, vitamin E, selenium, and carotenoids.* Washington DC: National Academy Press, 2000. Also available at: http://www.nap.edu/openbook.php?isbn=0309069351 (accessed 21/07/08)


## Uses and Administration

Vitamin E, a fat-soluble vitamin, prevents the oxidation of polyunsaturated fatty acids. It reacts with free radicals, which are the cause of oxidative damage to cell membranes, without the formation of another free radical in the process.

Vitamin E deficiency is rare but develops when the dietary intake is inadequate. In children with cystic fibrosis or biliary atresia, malabsorption of fat may lead to a vitamin E deficiency; deficiency may also occur in children with abnormalities of lipid transport, as in abetalipoproteinaemia. Low vitamin E concentrations are also found in premature, very low birth-weight infants. In previously healthy adults malabsorption and low intake of vitamin E must continue for a number of years before signs of deficiency appear. The major signs of vitamin E deficiency are the development of myopathic and neurological disorders.

Vitamin E is used in the treatment and prevention of vitamin E deficiency. It is usually given orally, generally the preferred route, but has also been given by intramuscular or intravenous routes. It may be given as *d*- or *dl*-alpha tocopherol or as the respective acetates or acid succinates.

Recommended doses vary, in part because of differences in the activity of different preparations; however, a daily dose of several times the recommended dietary allowance (RDA), or around 40 to 50 mg of *d*-alpha tocopherol, has been suggested for deficiency syndromes; somewhat higher daily doses have been given