Ph. Eur. 6.2 (Asparagine Monohydrate). A white or almost white, crystalline powder or colourless crystals. Slightly soluble in water; practically insoluble in alcohol and in dichloromethane. A 2% solution in water has a pH of 4.0 to 6.0.
USNF 26 (Asparagine). It is anhydrous or contains one molecule of water of hydration. A white, crystalline powder or white crystals. Soluble in water; practically insoluble in alcohol and in ether. Its solutions are acid to litmus. Protect from light.

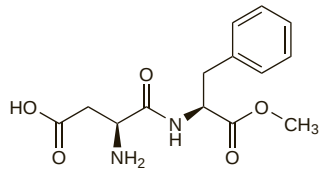
Profile
Asparagine is a non-essential amino acid.

Preparations
Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Ital.:*** Acutil Fosforo; Neuralfa; Tiofort; ***Spain:*** Agudil.

Aspartame *(BAN, USAN, rINN)*

APM; Aspartaami; Aspartam; Aspartamas; Aspartamo; Aspartamum; Aszpartám; E951; SC-18862. Methyl *N*-L-α-aspartyl-L-phenylalaninate; 3-Amino-*N*-(α-methoxycarbonylphenethyl)succinamic acid; *N*-L-α-aspartyl-L-phenylalanine, 1-methyl ester.

Аспартам
$C_{14}H_{18}N_2O_5$ = 294.3.
CAS — 22839-47-0.



Pharmacopoeias. In *Chin.* and *Eur.* (see p.vii). Also in *USNF.*
Ph. Eur. 6.2 (Aspartame). A white or almost white, slightly hygroscopic, crystalline powder. Sparingly or slightly soluble in water and in alcohol; practically insoluble in dichloromethane and in *n*-hexane. Store in airtight containers.
USNF 26 (Aspartame). White, odourless, crystalline powder having a sweet taste. Sparingly soluble in water; slightly soluble in alcohol. pH of a 0.8% solution in water is about 5.

Stability. In the presence of moisture aspartame hydrolyses to form aspartylphenylalanine and a diketopiperazine derivative, with a resulting loss of sweetness.

Adverse Effects and Precautions
Excessive use of aspartame should be avoided by patients with phenylketonuria since one of its metabolic products is phenylalanine. Aspartame's sweetness is lost during prolonged cooking.

Adverse effects. The safety and adverse effects of aspartame as a pharmaceutical excipient have been reviewed.[1,2]

Aspartame is hydrolysed in the gastrointestinal tract to methyl alcohol, aspartic acid, and phenylalanine. However, even with extraordinary consumption, methyl alcohol toxicity stemming from aspartame use is extremely unlikely. Aspartate concentrations in blood do not rise significantly after a very large dose (50 to 100 mg/kg) and therefore toxicity related to aspartate is also not expected to occur. Despite the similarity of aspartate to glutamate, studies in glutamate-sensitive persons have shown that they are not affected by aspartame consumption. Plasma concentrations of phenylalanine are also unlikely to be markedly elevated after modest consumption of aspartame by healthy persons but persons with phenylketonuria should avoid or limit their use of aspartame.

A number of adverse effects have been reported[1,2] after the use of aspartame, either as spontaneously recorded complaints from consumers or as published case reports in the medical literature. Most frequently reported problems have been headache, neuropsychiatric or behavioural symptoms, seizures, gastrointestinal symptoms, and hypersensitivity or dermatological symptoms. Available data do not provide evidence for serious widespread health consequences attendant upon the use of aspartame but it would appear that certain individuals may have an unusual sensitivity to the product. A safety review[3] by the European Commission Scientific Committee on Food (ECSCF) concluded that no causal link could be established between the consumption of aspartame and the occurrence of epilepsy or seizures, or cognition, mood and behaviour; this included individuals considered sensitive to aspartame.

Studies have confirmed aspartame's lack of effect on children's behaviour or cognitive function.[4,5]

An increased incidence of brain cancer was postulated to be related to aspartame use in one report;[6] however, the FDA[7] and the ECSCF[3] maintained that the available evidence did not support an association. Multiple malignancies have been reported[8] in *rats* given doses lower than the current acceptable daily intake of 40 or 50 mg/kg. The European Food Safety Authority assessed this study and concluded,[9] on the basis of all current available evidence, that the increased incidence of cancers in the *rats* was unrelated to aspartame treatment, and that there was no need to further review the safety of aspartame, nor to revise the established acceptable daily intake for aspartame of 40 mg/kg.

1. Golightly LK, *et al.* Pharmaceutical excipients: adverse effects associated with 'inactive' ingredients in drug products (part II). *Med Toxicol* 1988; **3:** 209–40.
2. American Academy of Pediatrics. "Inactive" ingredients in pharmaceutical products: update. *Pediatrics* 1997; **99:** 268–78.
3. European Commission Health and Consumer Protection Directorate-General. Opinion of the Scientific Committee on Food: update on the safety of aspartame (expressed on 4 December 2002). Available at: http://europa.eu.int/comm/food/fs/sc/scf/out155_en.pdf (accessed 08/11/05)
4. Shaywitz BA, *et al.* Aspartame, behavior, and cognitive function in children with attention deficit disorder. *Pediatrics* 1994; **93:** 70–5.
5. Wolraich ML, *et al.* Effects of diets high in sucrose or aspartame on the behavior and cognitive performance of children. *N Engl J Med* 1994; **330:** 301–7.
6. Olney JW, *et al.* Increasing brain tumor rates: is there a link to aspartame? *J Neuropathol Exp Neurol* 1996; **55:** 1115–23.
7. Anonymous. Aspartame: no apparent link with brain tumours. *WHO Drug Inf* 1997; **11:** 18–19.
8. Soffritti M, *et al.* First experimental demonstration of the multipotential carcinogenic effects of aspartame administered in the feed to Sprague-Dawley rats. *Environ Health Perspect* 2006; **114:** 379–85.
9. European Food Safety Authority. Opinion of the Scientific Panel on food additives, flavourings, processing aids and materials in contact with food (AFC) on a request from the Commission related to a new long-term carcinogenicity study on aspartame. *EFSA J* 2006; **356** 1–44. Available at: http://www.efsa.europa.eu/EFSA/Scientific_Opinion/afc_op_ej356_aspartame_en1,2.pdf (accessed 03/03/08)

Breast feeding. Aspartame 50 mg/kg given orally to healthy women resulted in small but significant increases in breast milk aspartate, phenylalanine, and tyrosine concentrations.[1] However, it was noted that these levels were similar to postprandial milk samples and were unlikely to impact upon total amounts of amino acids ingested by the infant. Furthermore, the dose of aspartame given in the study was considerably higher than the projected intake of about 7.5 to 8.5 mg/kg daily, assuming all sucrose intake were replaced by aspartame, and no aspartame abuse. Nonetheless, the American Academy of Pediatrics[2] considers that caution is required when aspartame is ingested by mothers where either the mother or breast-fed infant has phenylketonuria.

1. Stegink LD, *et al.* Plasma, erythrocyte and human milk levels of free amino acids in lactating women administered aspartame or lactose. *J Nutr* 1979; **109:** 2173–81.
2. American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. *Pediatrics* 2001; **108:** 776–89. Correction. *ibid.*; 1029. Also available at: http://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776 (accessed 19/11/04)

Pharmacokinetics
Aspartame is hydrolysed in the gastrointestinal tract to its 3 primary constituents, methyl alcohol, aspartic acid, and phenylalanine.

Uses
Aspartame is an intense sweetening agent about 180 to 200 times as sweet as sucrose. It is used in foods, beverages, and pharmaceuticals. Each g provides about 17 kJ (4 kcal).

Sickle-cell disease. There is some preliminary evidence that aspartame may have beneficial effects in sickle-cell disease.[1]

1. Manion CV, *et al.* Aspartame effect in sickle cell anemia. *Clin Pharmacol Ther* 2001; **69:** 346–55.

Preparations
Proprietary Preparations (details are given in Part 3)
Arg.: Nutrasweet†; Slap; ***Braz.:*** Dietacil; Dietamina†; Doce Vida†; Finn; ***Canad.:*** Equal; ***Chile:*** Marco Sweett†; Modellsweet†; Naturalist; Originalsweet; Ridersweet†; Valsweet; ***India:*** Lo-Kal†; Low-Cal†; ***Ital.:*** Aspartina; Futura; Suaviter; ***NZ:*** Equal; ***Port.:*** Dolcevita†; ***Rus.:*** Sugarfree (Шугафри); ***Thai.:*** Equal†; Espar; ***Turk.:*** Aspartil; Canderel; Demi Canderel; Diyet Tat; Hermesetas Gold; Nutra-Tat; Sanpa; ***Venez.:*** Dolsiprim†; Dulcolite†; Dulcosil; Edul; Equal†; Hermesetas Gold.

Multi-ingredient: ***Arg.:*** Chuker; Equalsweet; Genser Sweet; Rondo Sweet; Semble; Sucaryl; ***Chile:*** Marco Sweet Light; Nutrasweet†; ***UK:*** Sweet 'n Low; ***Venez.:*** Hermesetas Gold; Sweet 'n' Low†.

Aspartame Acesulfame

L-Phenylalanine, L-α-aspartyl-2-methyl ester, compound with 6-methyl-1,2,3-oxathiazin-4(3*H*)-one 2,2-dioxide (1:1).
$C_{18}H_{23}O_9N_3S$ = 457.5.
CAS — 106372-55-8.

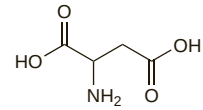
Pharmacopoeias. In *USNF.*
USNF 26 (Aspartame Acesulfame). White, odourless, crystalline powder. Slightly soluble in water and in alcohol. It contains not less than 63.0% and not more than 66.0% of aspartame, calculated on the dried basis, and not less than 34.0% and not more than 37.0% of acesulfame, calculated as the acid form on the dried basis.

Profile
Aspartame acesulfame is a compound of aspartame (see above) and acesulfame (see p.1928), and is used similarly in foods. It is an intense sweetener about 350 times as sweet as sucrose.

Aspartic Acid *(USAN, rINN)*

Acide aspartique; Ácido aspártico; Acidum asparticum; Asp; Asparagiinihappo; Asparaginsyra; L-Aspartic Acid; Asparto rūgštis; Aszparaginsav; D; Kwas asparaginowy; Kyselina asparagová. L-Aminosuccinic acid.

Аспарагиновая Кислота
$C_4H_7NO_4$ = 133.1.
CAS — 56-84-8.



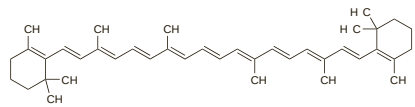
Pharmacopoeias. In *Chin., Eur.* (see p.vii), *Jpn,* and *US.*
Ph. Eur. 6.2 (Aspartic Acid). A white or almost white crystalline powder, or colourless crystals. Slightly soluble in water; practically insoluble in alcohol. It dissolves in dilute solutions of alkali hydroxides and in dilute mineral acids. Protect from light.
USP 31 (Aspartic Acid). A white or almost white crystalline powder, or colourless crystals. Slightly soluble in water; practically insoluble in alcohol and in ether; soluble in dilute solutions of alkali hydroxides and in dilute mineral acids. Protect from light.

Profile
Aspartic acid is a non-essential amino acid. It is used as a dietary supplement.

Betacarotene *(BAN, rINN)*

all-*trans*-β-Carotene; Beetakaroteeni; Beta Carotene *(USAN)*; Bétacarotène; Betacaroteno; Betacarotenum; Betakaroten; Betakarotenas; Bétakarotin; E160(a); Provitamin A. β,β-Carotene; (*all-E*)-1,1′-(3,7,12,16-Tetramethyl-1,3,5,7,9,11,13,15,17-octadecanonaene-1,18-diyl)bis[2,6,6-trimethylcyclohexene].

Бетакаротен
$C_{40}H_{56}$ = 536.9.
CAS — 7235-40-7.
ATC — A11CA02; D02BB01.
ATC Vet — QA11CA02; QA11HA90; QD02BB01.



Description. Carotene exists in 3 isomeric forms, all of which are converted to some extent into vitamin A in the livers of man and *animals*. Of the 3 isomers of carotene, the *beta* compound is more active than the *alpha-* or *gamma*-isomers. The vitamin A activity of plants is due to the presence of *alpha-*, *beta-*, and *gamma*-carotenes and to kryptoxanthine; that of *animal* tissues is due to both vitamin A and carotene, while fish-liver oils contain vitamin A but no carotene.

Pharmacopoeias. In *Eur.* (see p.vii) and *US.*
Ph. Eur. 6.2 (Betacarotene). A brown-red or brownish-red crystalline powder. Practically insoluble in water and in dehydrated alcohol; slightly soluble in cyclohexane. It is sensitive to air, heat and light, especially in solution. Store in airtight containers at a temperature not exceeding 25°. Protect from light.
USP 31 (Beta Carotene). Red or reddish-brown to violet-brown crystals or crystalline powder. Insoluble in water, in acids, and in alkalis; practically insoluble in alcohol and in methyl alcohol; soluble in carbon disulfide, in chloroform, and in benzene; sparingly soluble in ether, in petroleum spirit, and in vegetable oils. Store in airtight containers. Protect from light.

Units
Vitamin A activity in foods is expressed in terms of retinol equivalents: 6 micrograms of betacarotene represents 1 retinol equivalent (or 10 of the former International units for provitamin A—see p.1971).

Adverse Effects and Precautions
Loose stools may occasionally occur during treatment with betacarotene and the skin may assume a slightly yellow discoloration. Bruising, dizziness, and arthralgia have been reported rarely.

Excessive intake of betacarotene does not result in hypervitaminosis A (see Pharmacokinetics, below).

Carcinogenicity. For reference to studies finding an increased incidence of lung cancers in individuals given betacarotene sup-

plements to protect against malignancy, see under Prophylaxis of Malignant Neoplasms, p.1927.

Effects on mortality. A systematic review of the effect of antoxidant supplements on mortality in randomised primary and secondary prevention studies found that betacarotene, used either singly or with other antoxidants, significantly increased all-cause mortality.[1] In another review and meta-analysis, betacarotene supplementation showed a trend towards increased cancer mortality.[2]

1. 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).
2. Bardia A, *et al.* Efficacy of antioxidant supplementation in reducing primary cancer incidence and mortality: systematic review and meta-analysis. *Mayo Clin Proc* 2008; **83:** 23–34.

Effects on the skin. Yellow pigmentation of the skin may result from an unusually high consumption of carrots or other source of carotene,[1] or from a defect in the enzyme that normally metabolises betacarotene to vitamin A.[2] Hypercarotenaemia can be distinguished from jaundice by the fact that the sclerae retain their normal white colour. Pigmentation occurs first on the palms and soles and may extend to the nasolabial folds. Although it has been stated that the condition is harmless as the body converts carotene to retinol only as required,[1] others consider that long-standing hypercarotenaemia can have clinical sequelae:[2] neutropenia[3] and amenorrhoea[4] have been reported to be associated with the condition.

1. Sharman IM. Hypercarotenaemia. *BMJ* 1985; **290:** 95.
2. Vaughan Jones SA, Black MM. Metabolic carotenaemia. *Br J Dermatol* 1994; **131:** 145.
3. Shoenfeld Y, *et al.* Neutropenia induced by hypercarotenaemia. *Lancet* 1982; **i:** 1245.
4. Kemmann E, *et al.* Amenorrhoea associated with carotenemia. *JAMA* 1983; **249:** 926–9.

Pharmacokinetics

Gastrointestinal absorption of betacarotene depends on the presence of bile and is increased by dietary fat. About 20 to 60% of betacarotene is metabolised to retinol in the intestinal wall, and a small amount is converted to vitamin A in the liver. The proportion of betacarotene converted to vitamin A decreases as the intake of betacarotene increases, and high doses of betacarotene do not lead to abnormally high serum concentrations of vitamin A. Unchanged betacarotene is distributed to various tissues including fat, the adrenal glands, and ovaries.

◊ References.

1. Wang X-D. Review: absorption and metabolism of β-carotene. *J Am Coll Nutr* 1994; **13:** 314–25.

Human Requirements

Carotenes, of which betacarotene has the highest activity, are major dietary sources of vitamin A—see p.1972.

UK and US recommended dietary intake. There is currently no UK dietary reference value (see p.1925) for betacarotene, and in the USA recommended dietary allowances or dietary reference intakes (see p.1925) have not been set. However, the Expert Group on Vitamins and Minerals[1] has established a safe upper level (SUL) for betacarotene of 7 mg daily, or about 0.11 mg/kg daily for a 60-kg adult.

1. 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 06/01/06)

Uses and Administration

Betacarotene is a carotenoid precursor of vitamin A (p.1971). In the *treatment* of vitamin A deficiency, vitamin A is preferred to betacarotene. However, betacarotene has been used for the *prevention* of vitamin A deficiency at a dose of 6 to 15 mg daily for adults and 3 to 6 mg daily for children.

Betacarotene may be given by mouth to reduce the severity of photosensitivity reactions in patients with erythropoietic protoporphyria (see also Porphyria, below). Doses are in the range of 30 to 300 mg daily for adults and 30 to 150 mg daily for children, depending upon severity; they may be taken as either single daily doses or divided doses but should preferably be taken with meals. The protection offered by betacarotene is not total and generally 2 to 6 weeks of treatment resulting in a yellow coloration of palms and soles is necessary before patients should attempt to increase their exposure to sunlight.

Betacarotene and other carotenoids (alphacarotene and gammacarotene) are used as colouring agents for foods and medicinal products.

Betacarotene has antoxidant activity and has been studied for its possible protective benefit in a number of disorders (but see Effects on Mortality, above).

Age-related macular degeneration. A study in patients with age-related macular degeneration (p.785) indicated that the risk of developing this disorder (a leading cause of irreversible blindness among elderly persons) was markedly decreased amongst those with the highest dietary carotenoid intake;[1] in particular, lutein and zeaxanthin, or green leafy vegetables (which contain high concentrations of these carotenoids) were associated with a lower risk. Increasing the dietary intake of these carotenoids may be of benefit in reducing the development of this disorder. Despite this, systematic reviews found no evidence that antoxidant vitamin and mineral supplementation would either prevent[2,3] or delay the onset of macular degeneration. However, one study[4] has shown modest benefit from vitamin C, vitamin E, betacarotene, and zinc supplementation in those with moderate to severe signs of the disease. A systematic review to assess the effects of antoxidant vitamin or mineral supplementation on the progression of age-related macular degeneration included this study, and noted that the generalisability of these findings to other populations (with differing nutritional status) was unknown. Long-term harm from supplementation could not be ruled out.[5]

1. Seddon JM, *et al.* Dietary carotenoids, vitamins A, C, and E, and advanced age-related macular degeneration. *JAMA* 1994; **272:** 1413–20.
2. Evans JR, Henshaw K. Antioxidant vitamin and mineral supplements for preventing age-related macular degeneration. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2008 (accessed 11/03/08).
3. Chong EW-T, *et al.* Dietary antioxidants and primary prevention of age related macular degeneration: systematic review and meta-analysis. *BMJ* 2007; **335:** 755–9.
4. Age-Related Eye Disease Study Research Group. A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E, beta carotene, and zinc for age-related macular degeneration and vision loss: AREDS report no.8. *Arch Ophthalmol* 2001; **119:** 1417–36.
5. Evans JR. Antioxidant vitamin and mineral supplements for slowing the progression of age-related macular degeneration. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2006 (accessed 11/03/08).

Deficiency states. A study in Senegalese children with vitamin A deficiency found that supplementation with betacarotene (in a single dose equivalent to 200 000 units of vitamin A) was as effective as a single 200 000 unit dose of vitamin A palmitate in reversing ocular changes.[1] Since betacarotene is less toxic than vitamin A itself it would have some advantages for supplementation, either as an oral supplement or by encouraging the consumption of carotenoid-rich fruit and vegetables. A study in anaemic Indonesian women found that a supplement containing betacarotene with iron, vitamin C, and folate improved vitamin A status, whereas an additional daily portion of dark-green leafy vegetables containing a similar amount of betacarotene did not.[2] However, others contended that consumption of food sources of carotenoids were effective in improving vitamin A status in deficiency states,[3,4] and that it might not be appropriate to extrapolate these findings in adults (not necessarily deficient in vitamin A) to vitamin A deficient children.[3,5] WHO policy was to promote dietary adjustment wherever vitamin A deficiency was endemic.[5] Despite further studies confirming improved vitamin A status among those given foods high in betacarotene,[6,7] a review[8] considered the bioavailability of betacarotene from plant foods to be low, and questioned the retinol equivalency determined by WHO (see Units, above). Another study[9] found that increasing dietary fat consumption and eliminating helminthic infection further increased serum retinol concentrations in children given food high in betacarotene.

For a trial reporting improved vitamin A status with betacarotene plus zinc compared with betacarotene or zinc alone, and the suggestion that zinc may have a role in the conversion of betacarotene to retinol, see Vitamin A Deficiency, under Zinc, p.2001.

For further discussion of vitamin A deficiency and the value of supplementation in various disease states, see under Vitamin A Substances, p.1973.

1. Carlier C, *et al.* A randomised controlled trial to test equivalence between retinyl palmitate and β carotene for vitamin A deficiency. *BMJ* 1993; **307:** 1106–10.
2. de Pee S, *et al.* Lack of improvement in vitamin A status with increased consumption of dark-green leafy vegetables. *Lancet* 1995; **346:** 75–81.
3. Reddy V. Vitamin A status and dark green leafy vegetables. *Lancet* 1995; **346:** 1634–5.
4. Underwood BA. Vitamin A status and dark green leafy vegetables. *Lancet* 1995; **346:** 1635.
5. WHO. Vitamin A status: is dietary replacement practicable. *WHO Drug Inf* 1995; **9:** 141.
6. Ncube TN, *et al.* Supplementing lactating women with puréed papaya and grated carrots improved vitamin A status in a placebo-controlled trial. *J Nutr* 2001; **131:** 1497–1502.
7. Vuong LT, *et al.* Plasma β-carotene and retinol concentrations of children increase after a 30-d supplementation with the fruit Momordica cochinchinensis (gac). *Am J Clin Nutr* 2002; **75:** 872–9.
8. West CE, *et al.* Consequences of revised estimates of carotenoid bioefficacy for dietary control of vitamin A deficiency in developing countries. *J Nutr* 2002; **132** (suppl): 2920S–2926S.
9. Jalal F, *et al.* Serum retinol concentrations in children are affected by food sources of β-carotene, fat intake, and anthelmintic drug treatment. *Am J Clin Nutr* 1998; **68:** 623–9.

Ischaemic heart disease. There are results from epidemiological studies suggesting the potential benefits of dietary betacarotene in preventing ischaemic heart disease, particularly in smokers; however, randomised placebo-controlled studies of betacarotene supplements have returned negative results, as discussed on p.1926.

Malignant neoplasms. Some evidence from epidemiological studies suggested that higher dietary intakes of carotenoids and especially betacarotene had a protective effect against cancer. Consequently several randomised placebo-controlled trials examining the use of betacarotene supplements in the primary or secondary prevention of malignancy were instigated. However, the results of studies so far published have generally been disappointing. Moreover, some results suggest that supplementation with betacarotene may actually be harmful (see Prophylaxis of Malignant Neoplasms, p.1927 and Effects on Mortality, above).

Porphyria. Despite a lack of robust evidence, betacarotene is the most widely used systemic drug for the management of erythropoietic protoporphyria,[1,2] a non-acute porphyria characterised by cutaneous photosensitivity (p.1448). It has been given with canthaxanthin to reduce the skin discoloration caused by betacarotene alone.

1. Todd DJ. Erythropoietic protoporphyria. *Br J Dermatol* 1994; **131:** 751–66.
2. Todd DJ. Therapeutic options for erythropoietic protoporphyria. *Br J Dermatol* 2000; **142:** 826.

Preparations

USP 31: Beta Carotene Capsules.

Proprietary Preparations (details are given in Part 3)
Arg.: B-Caroteno; ***Austria:*** Carotaben; ***Braz.:*** Vitcaroten†; Vitizin Beta; Zirvit Beta; ***Cz.:*** Carotaben; ***Ger.:*** Carotaben; Carotana†; Carotinora; ***Ital.:*** Tannisol; ***Switz.:*** Carotaben; ***Turk.:*** Carovit; ***UK:*** Biocarotine.

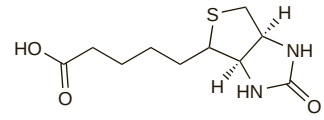
Multi-ingredient: ***Arg.:*** Bronsul; Natubrown; Sigmasol; Sol Bronce Vital; ***Austral.:*** Antioxidant Forte Tablets; Antioxidant Tablets; Beta A-C; Eye Health Herbal Plus Formula 4; Lifesystem Herbal Plus Formula 5 Eye Relief†; Lifesystem Herbal Plus Formula 8 Echinacea†; Odourless Garlic†; ***Austria:*** Oleovit A; Oleovit A + D; ***Braz.:*** Purpuralin†; ***Chile:*** Unitone; ***Fr.:*** Difrarel; Phytolongbronze; Phytosolaire; ***Ger.:*** Carotin; ***Hong Kong:*** Purpuralin†; Sanjukei Panax Ginseng; ***India:*** Rovigon†; ***Indon.:*** Bioretin; Lesifit; Matase; Matovit; Nu-Derm Sunblock; Retivit; ***Ital.:*** Agedin Plus; Angstrom Viso; Ecamannan; Keratolip; Levudin†; Mirtilene; Solecin; Tannidin Plus; ***Mex.:*** Unitone; ***Neth.:*** Difrarel; ***Philipp.:*** Pynocare 40 Actisome; ***Pol.:*** Biovision; ***Port.:*** Rilastil Dermo Solar; ***Rus.:*** Strix (Стрикс); ***Spain:*** Aceite Acalorico; Mirtilus; ***Switz.:*** Visaline; ***Turk.:*** Dervanol; ***Venez.:*** Unitone†.

Biotin *(rINN)*

Biotiini; Biotina; Biotinas; Biotine; Biotinum; Coenzyme R; Vitamin H. *cis*-5-(Hexahydro-2-oxo-1*H*-thieno[3,4-*d*]imidazol-4-yl)valeric acid.

Биотин

$C_{10}H_{16}N_2O_3S$ = 244.3.
CAS — 58-85-5.
ATC — A11HA05.
ATC Vet — QA11HA05.



Pharmacopoeias. In *Eur.* (see p.vii) and *US.*

Ph. Eur. 6.2 (Biotin). A white or almost white, crystalline powder or colourless crystals. Very slightly soluble in water and in alcohol; practically insoluble in acetone. It dissolves in dilute solutions of alkali hydroxides. Protect from light.

USP 31 (Biotin). A practically white crystalline powder. Very slightly soluble in water and in alcohol; insoluble in other common organic solvents. Store in airtight containers.

Profile

Biotin is traditionally considered to be a vitamin B substance. It is an essential coenzyme in fat metabolism and in other carboxylation reactions. Biotin deficiency may result in the urinary excretion of organic acids and changes in skin and hair. Deficiency of biotin is very unlikely in man because of its widespread distribution in food. Egg-yolk and offal are especially good sources. Biotin deficiency has been reported however during long-term parenteral nutrition and in patients with biotinidase deficiency, an inherited metabolic disorder. For dosage in biotinidase or isolated carboxylase deficiency see below. A combination of biotin and chromium tripicolinate (p.1934) has been promoted as an adjunct for the management of diabetes mellitus.

Biotin combines with avidin, a glycoprotein present in raw egg-white, to form an inactive compound.