However, a randomised trial found modified-release nicotinamide at 1.2 g/m^2 daily (to a maximum of 3 g daily) to be ineffective in preventing the onset of diabetes mellitus in first-degree relatives of patients with the disease.[3] Nicotinic acid can also raise high-density lipoprotein (HDL)-cholesterol concentrations (see below);[4,5] changes in glucose tolerance were mild enough for the drug to be considered as an alternative to statins and fibrates in diabetic patients.

1. Elliott RB, Chase HP. Prevention or delay of type 1 (insulin-dependent) diabetes mellitus in children using nicotinamide. *Diabetologia* 1991; **34:** 362–5.
2. Pozzilli P, *et al.* Meta-analysis of nicotinamide treatment in patients with recent-onset IDDM. *Diabetes Care* 1996; **19:** 1357–63.
3. European Nicotinamide Diabetes Intervention Trial Group. European Nicotinamide Diabetes Intervention Trial (ENDIT): a randomised controlled trial of intervention before the onset of type I diabetes. *Lancet* 2004; **363:** 925–31.
4. Elam MB, *et al.* Effect of niacin on lipid and lipoprotein levels and glycemic control in patients with diabetes and peripheral arterial disease: the ADMIT study: a randomized trial. *JAMA* 2000; **284:** 1263–70.
5. Grundy SM, *et al.* Efficacy, safety, and tolerability of once-daily niacin for the treatment of dyslipidemia associated with type 2 diabetes: results of the assessment of diabetes control and evaluation of the efficacy of Niaspan trial. *Arch Intern Med* 2002; **162:** 1568–76.

Hyperlipidaemias. The first-line treatment for hyperlipidaemias remains dietary and lifestyle modification; where this fails, drug therapy may be considered (p.1169). Nicotinic acid is reported to have a favourable effect on blood-lipid profiles, raising high-density lipoprotein (HDL)-cholesterol and lowering low-density lipoprotein (LDL)-cholesterol.[1-3] Nicotinic acid is used particularly in familial hypertriglyceridaemia, or in familial combined hyperlipidaemia when both triglyceride and cholesterol concentrations are similarly elevated. Nicotinic acid was less effective than lovastatin at reducing LDL-cholesterol in patients with primary hypercholesterolaemia, but more effective at increasing HDL-cholesterol; lovastatin was better tolerated.[4] A combination of nicotinic acid with lovastatin was found to be comparable to atorvastatin and more effective than simvastatin in reducing LDL-cholesterol, and more effective than either atorvastatin or simvastatin in increasing HDL-cholesterol, in a study of patients with dyslipidaemia.[5] Some have recommended that nicotinic acid be substituted for a statin to lower LDL-cholesterol when patients cannot tolerate a statin.[2] Combination therapy is recommended when the reduction in LDL-cholesterol is insufficient with statin monotherapy,[2,6] or when raising HDL-cholesterol would be beneficial,[7-9] as in patients with type 2 diabetes mellitus, or the metabolic syndrome.[8] The risk of muscle toxicity with this combination is not considered to be significantly different to that with statin monotherapy.[7]

1. McKenney JM, *et al.* A comparison of the efficacy and toxic effects of sustained- vs immediate-release niacin in hypercholesterolemic patients. *JAMA* 1994; **271:** 672–7.
2. McKenney J. Niacin for dyslipidemia: considerations in product selection. *Am J Health-Syst Pharm* 2003; **60:** 995–1005.
3. McCormack PL, Keating GM. Prolonged-release nicotinic acid: a review of its use in the treatment of dyslipidaemia. *Drugs* 2005; **65:** 2719–40.
4. Illingworth DR, *et al.* Comparative effects of lovastatin and niacin in primary hypercholesterolemia: a prospective trial. *Arch Intern Med* 1994; **154:** 1586–95.
5. Bays HE, *et al.* Comparison of once-daily, Niacin extended-release/lovastatin with standard doses of atorvastatin and simvastatin (The Advicor Versus Other Cholesterol-Modulating Agents Trial Evaluation [ADVOCATE]). *Am J Cardiol* 2003; **91:** 667–72.
6. Miller M. Niacin as a component of combination therapy for dyslipidemia. *Mayo Clin Proc* 2003; **78:** 735–42.
7. McKenney J. New perspectives on the use of niacin in the treatment of lipid disorders. *Arch Intern Med* 2004; **164:** 697–705.
8. Chapman MJ, *et al.* Raising high-density lipoprotein cholesterol with reduction of cardiovascular risk: the role of nicotinic acid—a position paper developed by the European Consensus Panel on HDL-C. *Curr Med Res Opin* 2004; **20:** 1253–68.
9. Yim BT, Chong PH. Niacin-ER and lovastatin treatment of hypercholesterolemia and mixed dyslipidemia. *Ann Pharmacother* 2003; **37:** 106–15.

Pemphigus. Oral treatment with nicotinamide and a tetracycline[1-6] has controlled lesions in pemphigus and pemphigoid (p.1582), including persistent pemphigoid gestationis,[5] and ocular cicatricial pemphigoid.[6]

1. Sawai T, *et al.* Pemphigus vegetans with oesophageal involvement: successful treatment with minocycline and nicotinamide. *Br J Dermatol* 1995; **132:** 668–70.
2. Kolbach DN, *et al.* Bullous pemphigoid successfully controlled by tetracycline and nicotinamide. *Br J Dermatol* 1995; **133:** 88–90.
3. Reiche L, *et al.* Combination therapy with nicotinamide and tetracyclines for cicatricial pemphigoid: further support for its efficacy. *Clin Exp Dermatol* 1998; **23:** 254–7.
4. Goon ATJ, *et al.* Tetracycline and nicotinamide for the treatment of bullous pemphigoid: our experience in Singapore. *Singapore Med J* 2000; **41:** 327–30.
5. Amato L, *et al.* Successful treatment with doxycycline and nicotinamide of two cases of persistent pemphigoid gestationis. *J Dermatol Treat* 2002; **13:** 143–6.
6. Dragan L, *et al.* Tetracycline and niacinamide: treatment alternatives in ocular cicatricial pemphigoid. *Cutis* 1999; **63:** 181–3.

Preparations

BP 2008: Nicotinamide Tablets; Nicotinic Acid Tablets; Vitamins B and C Injection;
BPC 1973: Compound Vitamin B Tablets; Strong Compound Vitamin B Tablets;
USP 31: Niacin Injection; Niacin Tablets; Niacinamide Injection; Niacinamide Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: NB-3; Niaspan; Nicozinc; ***Austria:*** Direktan; Nicovitol; ***Belg.:*** Ucemine PP; ***Braz.:*** Papuless; ***Canad.:*** Niaspan; ***Chile:*** Cotina; Niacex; Niaspan; Vectidan†; ***Fin.:*** Niaspan; ***Fr.:*** Niaspan; Nicobion; ***Ger.:*** Niaspan; Nicobion; ***Hong Kong:*** Niaspan; ***India:*** Nialip; ***Indon.:*** Niacef; Niaspan; ***Irl.:*** Niaspan; Nicam; ***Mex.:*** Hipocol; Nacro; Pepevit; ***Neth.:*** Niaspan; ***Philipp.:*** Niaspan; ***Port.:*** Niaspan; ***Singapore:*** Niaspan; ***Swed.:*** Niaspan; Nicangin; ***Thai.:*** Nicotabs; ***UK:*** Freederm; Niaspan; Nicam; ***USA:*** Endur-acin; Niaspan; Nicotinex†; Slo-Niacin; ***Venez.:*** Niaspan.

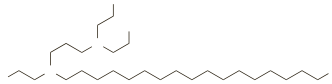
Multi-ingredient: ***Arg.:*** Antikatarata†; Centella Asiatica Compuesta; IP-6; Nicozinc; Parenciasˆ; ***Austral.:*** Bioglan Cirflo†; Chilblain Formula†; Gingo A†; Procholˆ; Silybum Complex†; ***Austria:*** Beneuran Vit B-Komplex†; Diligan; Pertrombon; Spasmocor; ***Belg.:*** Trihistalex; ***Braz.:*** Gaba†; Nicopaverina B6†; Nicopaverina†; ***Canad.:*** PML Crono†; ***Chile:*** Cicapost; Perfungol; Ureadin Forte; Ureadin Rx PS; Ureadin Rx RD; ***Fin.:*** Neurovitan; Vertipam; ***Fr.:*** TTD-B -B ; Vita-Dermacide; ***Ger.:*** Eukalisan N; Hepagrisevit Forte-N†; MerSolˆ; Petehaˆ; Telbibur Nˆ; ***Hung.:*** Paniverin; ***India:*** Diligan; Hepa-Merz; Nutrozyme; Sioneuron; Unienzyme; ***Indon.:*** Biocholes; Cereton; Kitoles; Sotens; ***Irl.:*** Effaclar Al; ***Israel:*** Babyzim; ***Ital.:*** Emazian B12†; Emoantitossina†; Emopon; Epargriseovit; Fisioreve; Folepar B12; Fosforilasi; Neuroftalˆ; Novostatin; Solvobil; Vit-Porphyrinˆ; ***Mon.:*** Monasens; ***Philipp.:*** Jetepar; ***Pol.:*** Dernilan; ***Port.:*** Diligan†; Ureadin Forte; ***Rus.:*** Lidevine (Лидевин); Oftan Catachrom (Офтан Катахром); ***S.Afr.:*** Cosaldonˆ; ***Singapore:*** Erase; ***Spain:*** Depurativo Richelet; Euzymina Lisina I; Euzymina Lisina II; Vitaphakol; ***Swed.:*** Theranylˆ; ***Thai.:*** B-100 Complex; ***Turk.:*** Epargriseovit; ***UK:*** Crampex; Quiet Life; S.P.H.P.; ***USA:*** Advicor; Simcor.

Olaflur *(BAN, USAN, rINN)*

Amine Fluoride 297; GA-297; Olaflurum; SKF-38095. 2,2′-(3-[*N*-(2-Hydroxyethyl)octadecylamino]propylimino)diethanol dihydrofluoride.

Олафлур

$C_{27}H_{60}F_2N_2O_3$ = 498.8.
CAS — 6818-37-7.
ATC — A01AA03.
ATC Vet — QA01AA03.



Profile
Olaflur is used as a source of fluoride (see Sodium Fluoride, p.1962) in the prevention of dental caries. For a report of stomatitis considered to be due to olaflur, see Hypersensitivity, under Sodium Fluoride, p.1963.

Preparations

Proprietary Preparations (details are given in Part 3)
Fr.: Elmexˆ; ***Israel:*** Elmexˆ; ***Pol.:*** Fluormex; ***Port.:*** Elmex.

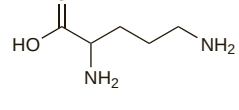
Multi-ingredient: ***Austria:*** Elmex; ***Belg.:*** Elmex; ***Cz.:*** Elmex; ***Fin.:*** Elmex; ***Fr.:*** Elmex Sensitive†; Elmexˆ; Meridolˆ; ***Ger.:*** Elmex; Lawefluor Nˆ; Multifluorid; ***Hung.:*** Elmex; ***Israel:*** Elmex; Meridol; ***Ital.:*** Elmex; ***Neth.:*** Elmex; ***Pol.:*** Fluormex; ***Switz.:*** Elmex; Paro aux fluorures d'amines Gelee.

Ornithine *(rINN)*

α,δ-Diaminovaleric Acid; Orn; L-Ornithine; Ornithinum; Ornitina. L-2,5-Diaminovaleric acid.

Орнитин

$C_5H_{12}N_2O_2$ = 132.2.
CAS — 70-26-8.



Pharmacopoeias. *Ger.* includes Ornithine Aspartate and Ornithine Hydrochloride.

Profile
Ornithine is an aliphatic non-essential amino acid. It is used as a dietary supplement.

The aspartate, hydrochloride, and oxoglurate (ornithine ketoglutarate, see also Parenteral and Enteral Nutrition under Glutamic Acid, p.1947) have been used in various indications including the treatment of hyperammonaemia (p.1929) and hepatic encephalopathy (p.1697).

◊ References.

1. Rapport L, Lockwood B. Ornithine ketoglutarate. *Pharm J* 2001; **266:** 688–90.
2. Coudray-Lucas C, *et al.* Ornithine alpha-ketoglutarate improves wound healing in severe burn patients: a prospective randomized double-blind trial versus isonitrogenous controls. *Crit Care Med* 2000; **28:** 1772–6.
3. Kircheis G, *et al.* Clinical efficacy of L-ornithine-L-aspartate in the management of hepatic encephalopathy. *Metab Brain Dis* 2002; **17:** 453–62.
4. Blonde-Cynober F, *et al.* Use of ornithine alpha-ketoglutarate in clinical nutrition of elderly patients. *Nutrition* 2003; **19:** 73–5.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Cere; Hepa; Ornicetil; ***Chile:*** Hepa-Merzˆ; ***Cz.:*** Hepa-Merzˆ; ***Fr.:*** Cetornan; Ornicetil; ***Ger.:*** Hepa-Merz; Hepa-Merz KT; Hepa-Vibolex; ***Hong Kong:*** Hepa-Merz; ***Hung.:*** Hepa-Merz; ***India:*** Hepa-Merz; ***Indon.:*** Hepa-Merz; Hevtin; ***Ital.:*** Ornicetilˆ; Ornil; Ornil KGF; ***Mex.:*** Hepa-Merz; ***Philipp.:*** Hepa-Merz; ***Pol.:*** Hepatil.

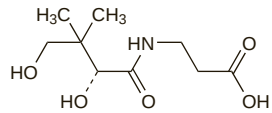
Multi-ingredient: ***Braz.:*** Ornihepatˆ; Ornitargin; ***Fr.:*** Epuramˆ; Ornitaine; ***Ger.:*** Polilevo Nˆ; ***India:*** Biohepˆ; Hepa-Merz; ***Ital.:*** Ipoazotal Complex; Ipoazotalˆ; Polilevoˆ; Somatron; ***Pol.:*** Hepa-Merz.

Pantothenic Acid *(BAN)*

Pantoténico, ácido; Vitamin B_5. (+)-(*R*)-3-(2,4-Dihydroxy-3,3-dimethylbutyramido)propionic acid.

Пантотеновая Кислота; Витамин B5

$C_9H_{17}NO_5$ = 219.2.
CAS — 79-83-4 (D-pantothenic acid); 599-54-2 (DL-pantothenic acid).
ATC — A11HA31; D03AX04.
ATC Vet — QA11HA31; QD03AX04.



(D-pantothenic acid)

Calcium Pantothenate *(BANM, rINN)*

Calcii pantothenas; Calcium, pantothénate de; Dextro Calcium Pantothenate; Kalcio pantotenatas; Kalciumpantotenat; Kalciumpantotenát; Kalsiumpantotenaatti; Pantotenato de calcio; Pantothenan vápenatý; Pantothénate de Calcium; Wapnia pantotenian.

Кальция Пантотенат

$(C_9H_{16}NO_5)_2Ca$ = 476.5.
CAS — 137-08-6 (calcium D-pantothenate); 6381-63-1 (calcium DL-pantothenate);.
ATC — A11HA31; D03AX04.
ATC Vet — QA11HA31; QD03AX04.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn*, *US*, and *Viet.* *US* also has a monograph for Racemic Calcium Pantothenate. *Ger.* also includes Sodium Pantothenate.

Ph. Eur. 6.2 (Calcium Pantothenate). A white or almost white, slightly hygroscopic powder. Freely soluble in water; slightly soluble in alcohol. A 5% solution has a pH of 6.8 to 8.0. Store in airtight containers.

USP 31 (Calcium Pantothenate). The calcium salt of the dextrorotatory isomer of pantothenic acid. A white, odourless, slightly hygroscopic powder. Soluble 1 in 3 of water; practically insoluble in alcohol, in chloroform, and in ether; soluble in glycerol. Store in airtight containers.

USP 31 (Racemic Calcium Pantothenate). A mixture of the calcium salts of the dextrorotatory and laevorotatory isomers of pantothenic acid. The physiological activity of Racemic Calcium Pantothenate is about one-half that of Calcium Pantothenate. A white, slightly hygroscopic powder, having a faint characteristic odour. Freely soluble in water; practically insoluble in alcohol, in chloroform, and in ether; soluble in glycerol. Its solutions are neutral or alkaline to litmus. Store in airtight containers.

Adverse Effects
Pantothenic acid is reported to be generally non-toxic.

Eosinophilia. A report of life-threatening eosinophilic pleuropericarditis associated with the use of biotin and pantothenic acid.[1] Symptoms resolved on stopping the vitamins.

1. Debourdeau PM, *et al.* Life-threatening eosinophilic pleuropericardial effusion related to vitamins B and H. *Ann Pharmacother* 2001; **35:** 424–6.

Pharmacokinetics
Pantothenic acid is readily absorbed from the gastrointestinal tract after oral doses. It is widely distributed in the body tissues and appears in breast milk. About 70% of pantothenic acid is excreted unchanged in the urine and about 30% in the faeces.

Human Requirements
Pantothenic acid is widely distributed in foods. Meat, legumes, and whole grain cereals are particularly rich sources; other good sources include eggs, milk, vegetables, and fruits.

UK and US recommended dietary intake. In the UK neither a reference nutrient intake (RNI) nor an estimated average requirement (EAR) has been set (see p.1925) for pantothenic acid although an intake of 3 to 7 mg daily for adults was believed

to be adequate.[1] Similarly, in the USA a recommended dietary allowance has not been published but an adequate intake for adults was believed to be 5 mg daily, increased to 6 mg in pregnancy and 7 mg during lactation.[2]

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. Standing Committee on the Scientific Evaluation of Dietary Reference Intakes of the Food and Nutrition Board. *Dietary Reference Intakes for thiamin, riboflavin, niacin, vitamin B , folate, vitamin B , pantothenic acid, biotin, and choline*. Washington, DC: National Academy Press, 2000. Also available at: http://www.nap.edu/openbook.php?isbn=0309065542 (accessed 21/07/08)

Uses and Administration

Pantothenic acid is traditionally considered to be a vitamin B substance. It is a component of coenzyme A which is essential in the metabolism of carbohydrate, fat, and protein.

Deficiency of pantothenic acid is unlikely in man because of its widespread distribution in food.

Pantothenic acid has no accepted therapeutic uses in human medicine, though it has been given by mouth as a nutritional supplement, often as the calcium salt and usually with other vitamins of the B group.

Preparations

USP 31: Calcium Pantothenate Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Cidermex; ***Austral.:*** Pantonate; ***Ger.:*** Kerato Biciron; ***Mex.:*** Span Plex; ***Rus.:*** Zorex (Зорекс); ***Switz.:*** Pantothen.

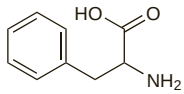
Multi-ingredient: ***Arg.:*** Bifena; Cellskinlab Hydragel B5; Culuflex H; Guarana Diates; Megaplus; Valeriana Relax Diates; ***Austral.:*** Bioglan Zn-A-C; Hair and Skin Formula†; ***Austria:*** Lemuval; ***Belg.:*** Sili-Met-San; ***Braz.:*** Gaba†; Pantevit; Varizol†; ***Chile:*** Foltene Research Anticaspa; Hydrating B5 Gel; Modane; ***Fr.:*** Modane; ***Ger.:*** Azupanthenol†; Carotin; Pantovigar N; Potsilo N; Regepithel; ***Hong Kong:*** Regepithel†; ***India:*** Sioneuron; ***Indon.:*** Proimbus; ***Ital.:*** Esaglut†; Nuleron; Silisan; Vitecaf; ***Malaysia:*** Vitamin C-500 YSP; ***Mex.:*** Espaven; Modaton; ***Spain:*** Calcio 20 Complex; Hubergrip†; Lacerdermol; Lupidon; Pantenil; Pulmofasa; Tri Hachemina; ***Switz.:*** Cortifluid N; Decasept N; Sili-Met-San†.

Phenylalanine *(USAN, rINN)*

α-Aminohydrocinnamic Acid; F; Fenilalanin; Fenilalanina; Fenilalaninas; Fenylalanin; Fenyloalanina; Fenyylialaniini; Phe; Phénylalanine; L-Phenylalanine; Phenylalaninum. L-2-Amino-3-phenylpropionic acid.

Фенилаланин

$C_9H_{11}NO_2$ = 165.2.
CAS — 63-91-2.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn*, and *US*.
Ph. Eur. 6.2 (Phenylalanine). A white or almost white, crystalline powder, or shiny, white flakes. Sparingly soluble in water; very slightly soluble in alcohol. It dissolves in dilute mineral acids and in dilute solutions of alkali hydroxides. Protect from light.
USP 31 (Phenylalanine). White, odourless crystals. Sparingly soluble in water; very slightly soluble in alcohol, in methyl alcohol, and in dilute mineral acids. pH of a 1% solution in water is between 5.4 and 6.0.

Profile

Phenylalanine is an aromatic amino acid that is an essential constituent of the diet. It is used as a dietary supplement.

Phenylalanine intake should be restricted in patients with phenylketonuria (see Amino Acid Metabolic Disorders, p.1922).

Vitiligo. There is no totally effective treatment for vitiligo (localised hypopigmentation, p.1582). Oral or topical photochemotherapy with psoralens is generally considered to be the best available treatment, but experimental therapy includes UVA phototherapy with phenylalanine. Use of phenylalanine in oral doses of up to 100 mg/kg with UVA/sunlight led to beneficial results in more than 90% of 200 patients with vitiligo.[1] Greatest benefit was noted in early disease, but prolonged use still induced repigmentation in long-standing cases. Repigmentation occurred mainly in areas rich in follicles. Such therapy is contraindicated in phenylketonuria and in pregnancy.

Similarly a further open study reported responses in 94 of 149 patients receiving 50 to 100 mg/kg daily of phenylalanine plus twice weekly UVA treatment.[2] However, only 22% of responders had repigmentation in more than 60% of the affected area. Higher doses did not seem to be more effective than 50 mg/kg daily. Another group reported on 6 years of experience of treatment of vitiligo using 50 or 100 mg/kg daily of phenylalanine, with application of 10% phenylalanine gel and daily sun exposure.[3] Although not ideal, they considered the treatment useful, especially for its ability to rapidly repigment the face. The same group performed an open study, adding topical 0.025% clobetasol propionate, and ultraviolet exposure during autumn and winter; 65.5% of patients achieved 100% repigmentation on the face.[4]

1. Cormane RH, *et al.* Treatment of vitiligo with -phenylalanine and light. *Br J Dermatol* 1986; **115:** 587.
2. Siddiqui AH, *et al.* L-Phenylalanine and UVA irradiation in the treatment of vitiligo. *Dermatology* 1994; **188:** 215–18.
3. Camacho F, Mazuecos J. Treatment of vitiligo with oral and topical phenylalanine: 6 years of experience. *Arch Dermatol* 1999; **135:** 216–17.
4. Camacho F, Mazuecos J. Oral and topical L-phenylalanine, clobetasol propionate, and UVA/sunlight - a new study for the treatment of vitiligo. *J Drugs Dermatol* 2002; **2:** 127–31.

Preparations

Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Arg.:*** KLB6 Fruit Diet; ***Fr.:*** Revitalose.

Polysaccharide-Iron Complex

Polisacárido hierro, complejo.

Profile

Polysaccharide-iron complex is used as a source of iron (p.1949) for iron-deficiency anaemia (p.1951). It is given orally in doses containing the equivalent of up to 300 mg of iron daily.

Preparations

Proprietary Preparations (details are given in Part 3)
Belg.: Ferricure; ***Chile:*** Niferex†; ***Hong Kong:*** Niferex; ***Norw.:*** Niferex; ***Pol.:*** Venofer; ***UK:*** Niferex; ***USA:*** Fe-Tinic; Ferrex; Ferrex Plus; Hytinic†; Niferex; Nu-Iron†; Poly-Iron.

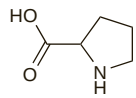
Multi-ingredient: ***USA:*** Fe-Tinic Forte; Ferrex Forte; Ferrex Forte Plus†; Ferrex PC; Hemocyte-F; Niferex Forte; Nu-Iron V; Poly-Iron Forte; Tandem.

Proline *(USAN, rINN)*

P; Pro; Proliini; Prolin; Prolina; Prolinas; L-Proline; Prolinum. L-Pyrrolidine-2-carboxylic acid.

Пролин

$C_5H_9NO_2$ = 115.1.
CAS — 147-85-3.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), and *US*.
Ph. Eur. 6.2 (Proline). A white or almost white, crystalline powder or colourless crystals. Very soluble in water; freely soluble in alcohol. Protect from light.
USP 31 (Proline). White, odourless crystals. Freely soluble in water and in dehydrated alcohol; insoluble in butyl alcohol, in ether, and in isopropyl alcohol.

Profile

Proline is a cyclic non-essential amino acid. It is used as a dietary supplement.

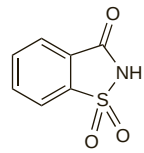
Preparations

Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Port.:*** Creme Laser Hidrante.

Saccharin

Benzoic Acid Sulphimide; Benzoic Sulfimide; Benzosulphimide; E954; Gluside; Sacarina; Saccarina; Saccharine; Saccharinum; Sacharin; Sacharinas; Sacharyna; Sackarin; Sakkariini; *o*-Sulfobenzimide; Szacharin; Zaharina. 1,2-Benzisothiazolin-3-one 1,1-dioxide.

$C_7H_5NO_3S$ = 183.2.
CAS — 81-07-2.



Pharmacopoeias. In *Eur.* (see p.vii) and *Jpn*. Also in *USNF*.
Ph. Eur. 6.2 (Saccharin). A white or almost white, crystalline powder or colourless crystals. Slightly soluble in cold water; sparingly soluble in boiling water and in alcohol. It dissolves in dilute solutions of alkali hydroxides and carbonates. A saturated solution, prepared without heating, is acid to litmus.
USNF 26 (Saccharin). White crystals or white, crystalline powder. Is odourless or has a faint, aromatic odour. In dilute solutions, it is intensely sweet. Soluble 1 in 290 of water, 1 in 25 of boiling water, and 1 in 31 of alcohol; slightly soluble in chloroform and in ether; is readily dissolved by dilute solutions of ammonia, by solutions of alkali hydroxides, and by solutions of alkali carbonates with the evolution of carbon dioxide. Its solutions are acid to litmus.

Saccharin Calcium

Calcium Benzosulphimide; Calcium Saccharin; E954; Sacarina cálcica; Saccharine calcique; Saccharinum calcicum.

$C_{14}H_8CaN_2O_6S_2,3H_2O$ = 467.5.
CAS — 6485-34-3 (anhydrous saccharin calcium); 6381-91-5 (hydrated saccharin calcium).

Pharmacopoeias. In *US*.
USP 31 (Saccharin Calcium). White crystals or white, crystalline powder. Is odourless, or has a faint, aromatic odour, and has an intensely sweet taste, even in dilute solutions. Its dilute solution is about 300 times as sweet as sucrose. Soluble 1 in 2.6 of water and 1 in 4.7 of alcohol.

Saccharin Potassium

E954; Potassium Benzosulphimide; Potassium Saccharin.

$C_7H_5NO_3SK$ = 222.3.
CAS — 10332-51-1.

Saccharin Sodium

E954; Sacarina sódica; Saccharin Sod.; Saccharine sodique; Saccharinnatrium; Saccharinum natricum; Saccharoidum Natricum; Sacharin sodná sůl; Sacharino natrio druska; Sacharyna sodowa; Sackarinnatrium; Sakkariininatrium; Sodium Benzosulphimide; Sodium Saccharin; Soluble Gluside; Soluble Saccharin; Szacharinnátrium.

$C_7H_4NNaO_3S$ = 205.2.
CAS — 128-44-9 (anhydrous saccharin sodium); 6155-57-3 (saccharin sodium dihydrate).

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, and *US*. Some pharmacopoeias specify the dihydrate but it may contain a variable quantity of water as a result of efflorescence.
Ph. Eur. 6.2 (Saccharin Sodium). A white or almost white, crystalline powder or colourless crystals. It may contain a variable quantity of water. Efflorescent in dry air. Freely soluble in water; sparingly soluble in alcohol. Store in airtight containers.
USP 31 (Saccharin Sodium). White crystals or white, crystalline powder. Is odourless, or has a faint, aromatic odour, and has an intensely sweet taste, even in dilute solutions. Its dilute solution is about 300 times as sweet as sucrose. When in powdered form, it usually contains about one-third the theoretical amount of water of hydration as a result of efflorescence. Soluble 1 in 1.5 of water and 1 in 50 of alcohol.

Adverse Effects

There have been rare reports of hypersensitivity and photosensitivity reactions with saccharin.

Saccharin-associated bladder tumours in *rats* given high doses have been the cause of much concern and investigation. However, it is now generally accepted that these findings are not relevant to the use of saccharin as a sweetener in man.

Effects on the liver. Elevated liver enzyme values in an elderly woman followed use of two different medications sweetened with saccharin sodium.[1] Findings resolved on stopping all preparations containing saccharin, and recurred on rechallenge with a small amount of saccharin sodium.

1. Negro F, *et al.* Hepatotoxicity of saccharin. *N Engl J Med* 1994; **331:** 134–5.

Pharmacokinetics

Saccharin is readily absorbed from the gastrointestinal tract. It is almost all excreted unchanged in the urine within 24 to 48 hours.

Uses and Administration

Saccharin and its salts are intense sweeteners, a dilute solution having about 300 times the sweetening power of sucrose. They are used in pharmaceuticals and in foods and beverages and are heat stable. They have no food value. The salts are more often used than saccharin itself as they are considered to be more palatable.

Preparations

USP 31: Saccharin Sodium Oral Solution; Saccharin Sodium Tablets.

Proprietary Preparations (details are given in Part 3)
Chile: Dul-Suc; Sukar-Sin; ***Fr.:*** Sucredulcor†; ***NZ:*** Sactabs; ***Turk.:*** Hermesetas; ***Venez.:*** Hermesetas.

Multi-ingredient: ***Arg.:*** Chuker; Rondo; Semble; Sucaryl; Suimel; ***Austral.:*** Sucaryl; ***Braz.:*** Finn Cristal; ***Chile:*** Sucaryl†; Sukar-Sin; ***Fr.:*** Sucaryl; ***Israel:*** Sucrin; ***Ital.:*** Diet Sucaryl; ***NZ:*** Sucaryl; ***Port.:*** Dulceril†; ***Rus.:*** Zuckli (Цюкли); ***Turk.:*** Dolce.

Safflower Oil

Aceite de alazor; Aceite de cártamo; Carthame (huile de) raffinée; Carthami oleum raffinatum; Dygminų aliejus, rafinuotas; Saffloriolja, raffinerad; Safloriöljy, puhdistettu; Světlicový olej čištěný.

Pharmacopoeias. In *Eur.* (see p.vii) and *US*.
Chin., *Eur.* (see p.vii), and *Jpn* include Safflower, the flower of *Carthamus tinctorius*.
Ph. Eur. 6.2 (Safflower Flower; Carthami Flos). Dried flower of