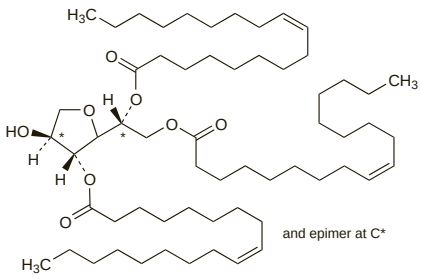
Sorbitan Trioleate *(BAN, USAN, rINN)*

Sorbitaanitrioleaatti; Sorbitan, trioléate de; Sorbitani trioleas; Sorbitano trioleatas; Sorbitantrioleat; Sorbitan-trioleát; Szorbitán-trioleát; Trioleato de sorbitán.

Сорбитана Триолеат

$C_{60}H_{108}O_8$ (approximate).

CAS — 26266-58-0.



Pharmacopoeias. In *Eur.* (see p.vii). Also in *USNF.*

Ph. Eur. 6.2 (Sorbitan Trioleate). A mixture usually obtained by esterification of 1 mole of sorbitol and its mono- and di-anhydrides per 3 moles of oleic acid. A suitable antoxidant may be added. A pale yellow, light yellowish or brown solid which becomes a brownish-yellow, viscous, oily liquid at about 25°. Relative density about 0.98. Practically insoluble but dispersible in water; slightly soluble in alcohol; soluble in fatty oils. Protect from light.

USNF 26 (Sorbitan Trioleate). A tri-ester of sorbitol and its mono- and di-anhydrides with oleic acid. A yellow to amber-coloured, oily liquid. Insoluble in water, in ethylene glycol, and in propylene glycol; soluble in alcohol, in isopropyl alcohol, in methyl alcohol, in maize oil, in cottonseed oil, and in liquid paraffin. Store in airtight containers.

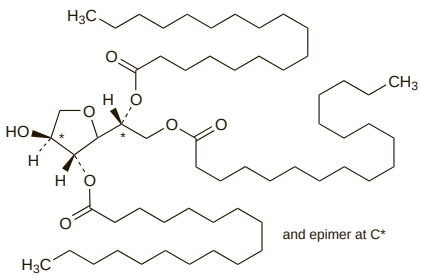
Sorbitan Tristearate *(BAN, USAN, rINN)*

E492; Sorbitan, Tristéarate de; Sorbitani Tristearas; Triestearato de sorbitán.

Сорбитана Тристеарат

$C_{60}H_{114}O_8$ (approximate).

CAS — 26658-19-5.



Description. A mixture of the partial tri-esters of sorbitol and its mono- and di-anhydrides with stearic acid.

Adverse Effects

There have been occasional reports of hypersensitive skin reactions after the topical application of creams containing sorbitan esters.

Hypersensitivity. References.

1. Finn OA, Forsyth A. Contact dermatitis due to sorbitan monolaurate. *Contact Dermatitis* 1975; **1:** 318.
2. Hannuksela M, *et al.* Allergy to ingredients of vehicles. *Contact Dermatitis* 1976; **2:** 105–10.
3. Austad J. Allergic contact dermatitis to sorbitan monooleate (Span 80). *Contact Dermatitis* 1982; **8:** 426–7.
4. Boyle J, Kennedy CTC. Contact urticaria and dermatitis to Alphaderm. *Contact Dermatitis* 1984; **10:** 178.
5. Hardy MP, Maibach HI. Contact urticaria syndrome from sorbitan sesquioleate in a corticosteroid ointment. *Contact Dermatitis* 1995; **32:** 114.
6. Wakelin SH, *et al.* Sorbitan mono-oleate: a potential allergen in paste bandages. *Contact Dermatitis* 1996; **35:** 377.
7. de Waard-van der Spek FB, *et al.* Allergic contact dermatitis to sorbitan sesquioleate in Adaptic wound dressing. *Contact Dermatitis* 2007; **57:** 54–6.

Uses

Sorbitan esters are lipophilic nonionic surfactants that are used as emulsifying agents in the preparation of emulsions, creams, and ointments for pharmaceutical and cosmetic use. When used alone they produce stable water-in-oil emulsions but they are frequently used with a polysorbate in varying proportions to produce water-in-oil or oil-in-water emulsions or creams with a variety of different textures and consistencies. Sorbitan esters are also used as emulsifiers and stabilisers in food.

Sucrose Esters

E473 (sucrose esters of fatty acids); Sacarosa, ésteres de; Sacchari monopalmitas (sucrose monoplamitate); Sacchari monostearas (sucrose monostearate); Saccharose, monopalmitate de (sucrose monoplamitate); Saccharose, monostéarate de (sucrose monostearate); Sucroésteres.

Эфиры Сахарозы

Pharmacopoeias. *Eur.* (p.vii) includes Sucrose Monopalmitate and Sucrose Stearate.

Ph. Eur. 6.2 (Sucrose Monopalmitate). A mixture of sucrose monoesters, mainly sucrose monopalmitate, obtained by transesterification of palmitic acid methyl esters of vegetable origin with sucrose. It contains 55.0% monoesters, a maximum 40.0% diesters, and a maximum of 20.0% for the sum of triesters and polyesters. A white or almost white, unctuous powder. Very slightly soluble in water; sparingly soluble in alcohol. Protect from humidity.

Ph. Eur. 6.2 (Sucrose Stearate). A mixture of sucrose esters, mainly sucrose stearate, obtained by transesterification of stearic acid methyl esters of vegetable origin with sucrose. Sucrose stearate type I contains a minimum 50.0% monoesters, a maximum 40.0% diesters, and a maximum of 25.0% for the sum of triesters and polyesters. Sucrose stearate type II contains 20.0 to 45.0% monoesters, 30.0 to 40.0% diesters, and a maximum of 30.0% for the sum of triesters and polyesters. A white or almost white, unctuous powder. Very slightly soluble in water; sparingly soluble in alcohol. Protect from humidity.

Profile

Sucrose esters are nonionic compounds with surface-active properties produced by esterification of 1 or more hydroxyl groups in sucrose with a fatty acid such as stearic or palmitic acid. Commercial sucrose esters are mixtures of the mono-, di-, and tri-esters of palmitic and stearic acids with sucrose; various grades are available. Sucrose esters are used as dispersing, emulsifying, and stabilising agents in food and cosmetic preparations.

Tyloxapol *(BAN, USAN, rINN)*

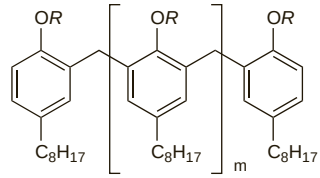
Superinone; Tiloxapol; Tyloksapoli; Tyloxapolum.

Тилоксапол

CAS — 25301-02-4.

ATC — R05CA01.

ATC Vet — QR05CA01.



R = $(CH_2CH_2O)_nOH$
n = 8-10
m < 6

Pharmacopoeias. In *US.*

USP 31 (Tyloxapol). A polymer of 4-(1,1,3,3-tetramethylbutyl)phenol with ethylene oxide and formaldehyde. A viscous amber liquid, sometimes slightly turbid, with a slight aromatic odour. Slowly but freely miscible with water; soluble in chloroform, in glacial acetic acid, in carbon disulfide, in carbon tetrachloride, in toluene, and in benzene. A 5% solution has a pH of 4.0 to 7.0. Tyloxapol should not be allowed to come into contact with metals. Store in airtight containers.

Adverse Effects

Slight inflammation of the eyelids has been reported after prolonged use of aqueous inhalations of tyloxapol. It has been reported that occasional febrile reactions may occur.

Uses and Administration

Tyloxapol is a nonionic surfactant of the alkyl aryl polyether alcohol type. It is used in solutions for cleansing contact lenses and artificial eyes. Aqueous solutions have been used for inhalation as a mucolytic for tenacious bronchopulmonary secretions. Tyloxapol has also been used as a vehicle for aerosol medication and for antibacterials given in irrigation solutions for pyogenic bone or joint infections.

Preparations

Proprietary Preparations (details are given in Part 3)

Austria: Tacholiquin; ***Canad.:*** Enuclene; ***Ger.:*** Enuclen†; Tacholiquin; ***NZ:*** Enuclene; ***USA:*** Enuclene.

Multi-ingredient: ***Austral.:*** Blink-N-Clean.

30. Khaw K-T, *et al.* Relation between plasma ascorbic acid and mortality in men and women in EPIC-Norfolk prospective study: a prospective population study. *Lancet* 2001; **357:** 657–63.
31. Ingraham BA, *et al.* Molecular basis of the potential of vitamin D to prevent cancer. *Curr Med Res Opin* 2008; **24:** 139–49.
32. Bairati I, *et al.* A randomized trial of antioxidant vitamins to prevent second primary cancers in head and neck cancer patients. *J Natl Cancer Inst* 2005; **97:** 481–8.
33. Heinonen OP, *et al.* Prostate cancer and supplementation with α-tocopherol and β-carotene: incidence and mortality in a controlled trial. *J Natl Cancer Inst* 1998; **90:** 440–6.
34. Giovannucci E, *et al.* Multivitamin use, folate, and colon cancer in women in the Nurses' Health Study. *Ann Intern Med* 1998; **129:** 517–24.
35. Willett WC. Diet and cancer: one view at the start of the millennium. *Cancer Epidemiol Biomarkers Prev* 2001; **10:** 3–8.
36. Zhang S, *et al.* A prospective study of folate intake and the risk of breast cancer. *JAMA* 1999; **281:** 1632–7.
37. US Preventive Services Task Force. Routine vitamin supplementation to prevent cancer and cardiovascular disease: recommendations and rationale. *Ann Intern Med* 2003; **139:** 51–5.

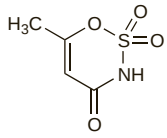
Acesulfame Potassium *(BANM, rINNM)*

Acesulfam draselná sůl; Acesulfam potasowy; Acesulfame K; Acésulfame potassique; Acesulfamkalium; Acesulfamo kalio druska; Acesulfamo potásico; Acesulfamum kalicum; Aceszulfámkálium; Asesulfaamikalium; E950; H73-3293; H-733293; Hoe-095K; Kalii Acesulfamum. 6-Methyl-1,2,3-oxathiazin-4(3*H*)-one 2,2-dioxide potassium.

Калия Ацесульфам

$C_4H_4KNO_4S$ = 201.2.

CAS — 55589-62-3.



(acesulfame)

Pharmacopoeias. In *Eur.* (see p.vii). Also in *USNF.*

Ph. Eur. 6.2 (Acesulfame Potassium). A white or almost white, crystalline powder or colourless crystals. Soluble in water; very slightly soluble in alcohol and in acetone.

USNF 26 (Acesulfame Potassium). A white, crystalline powder or colourless crystals. Soluble in water; very slightly soluble in alcohol and in acetone. Protect from light.

Profile

Acesulfame potassium is an intense sweetener about 200 times as sweet as sucrose. It is used in beverages, cosmetics, pharmaceuticals, and foods and does not appear to be affected by cooking.

Preparations

Proprietary Preparations (details are given in Part 3)

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

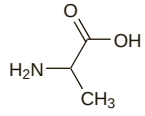
Alanine *(USAN, rINN)*

A; Ala; Alaniini; Alanin; Alanina; Alaninas; L-Alanine; Alaninum; NSC-206315. L-2-Aminopropionic acid.

Аланин

$C_3H_7NO_2$ = 89.09.

CAS — 56-41-7.



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

Ph. Eur. 6.2 (Alanine). A white or almost white crystalline powder or colourless crystals. Freely soluble in water; very slightly soluble in alcohol. Protect from light.

USP 31 (Alanine). White, odourless, crystals or crystalline powder. Freely soluble in water; slightly soluble in 80% alcohol; insoluble in ether. pH of a 5% solution in water is between 5.5 and 7.0. Store in airtight containers.

Profile

Alanine is an aliphatic non-essential amino acid. It is used as a dietary supplement. The dipeptide *N*(2)-L-alanyl-L-glutamine is used similarly.

Hypoglycaemia. References to the investigational use of alanine in the management of insulin-induced hypoglycaemia.[1-4]

1. Wiethop BV, Cryer PE. Glycemic actions of alanine and terbutaline in IDDM. *Diabetes Care* 1993; **16:** 1124–30.
2. Wiethop BV, Cryer PE. Alanine and terbutaline in treatment of hypoglycemia in IDDM. *Diabetes Care* 1993; **16:** 1131–6.
3. Saleh TY, Cryer PE. Alanine and terbutaline in the prevention of nocturnal hypoglycemia in IDDM. *Diabetes Care* 1997; **20:** 1231–6.
4. Evans ML, *et al.* Alanine infusion during hypoglycaemia partly supports cognitive performance in healthy human subjects. *Diabet Med* 2004; **21:** 440–6.

Preparations

Proprietary Preparations (details are given in Part 3)

Fr.: Abufene; ***Singapore:*** Abufene.

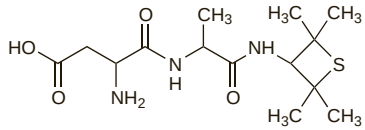
Multi-ingredient: ***Arg.:*** Normoprost Compuesto; ***Ital.:*** Chetonex; ***Spain:*** Tebetane Compuesto.

Alitame *(USAN)*

CP-54802. (3*S*)-Amino-*N*-{(1*R*)-1-[(2,2,4,4-tetramethyl-3-thietanyl) carbamoyl] ethyl} succinamic acid hydrate.

$C_{14}H_{25}N_3O_4S.2/H_2O$ = 376.5.

CAS — 80863-62-3 (anhydrous alitame); 99016-42-9 (alitame hydrate).



(anhydrous alitame)

Profile

Alitame is an intense sweetener used in foods. It is about 2000 times sweeter than sucrose.

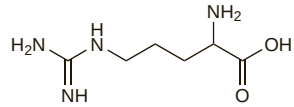
Arginine *(rINN)*

Arg; Arginiini; Arginin; Arginina; Argininas; L-Arginine; Argininum; R. L-2-Amino-5-guanidinovaleric acid.

Аргинин

$C_6H_{14}N_4O_2$ = 174.2.

CAS — 74-79-3.



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

Ph. Eur. 6.2 (Arginine). A white or almost white crystalline powder, or colourless crystals. Freely soluble in water; very slightly soluble in alcohol. Protect from light.

USP 31 (Arginine). White, practically odourless crystals. Freely soluble in water; sparingly soluble in alcohol; insoluble in ether.

Arginine Aspartate

Arginiiniaspartaatti; Arginina, aspartato de; Argininaspartat; Arginin-aspartát; Arginine, aspartate d'; Arginini aspartas; Arginino aspartatas; Asparginínum. (2*S*)-2-Amino-5-guanidinopentanoic acid (2*S*)-2-aminobutanedioate.

$C_{10}H_{21}N_5O_6$ = 307.3.

CAS — 7675-83-4.

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

Ph. Eur. 6.2 (Arginine Aspartate). White or almost white granules or powder. Very soluble in water, practically insoluble in alcohol and in dichloromethane.

Arginine Glutamate *(BAN, USAN, rINNM)*

Arginine, Glutamate d'; Arginini Glutamas; Glutamato de arginina. L-Arginine L-glutamate.

Аргинина Глутамат

$C_6H_{14}N_4O_2.C_5H_9NO_4$ = 321.3.

CAS — 4320-30-3.

ATC — A05BA01.

ATC Vet — QA05BA01.

Arginine Hydrochloride *(USAN, rINNM)*

Argininihydrokloridi; Arginine, chlorhydrate d'; L-Arginine Monohydrochloride; Arginin-hidroklorid; Arginin-hydrochlorid; Arginhydroklorid; Arginini hydrochloridum; Arginino hidrochloridas; Hidrocloruro de arginina.

Аргинина Гидрохлорид

$C_6H_{14}N_4O_2.HCl$ = 210.7.

CAS — 1119-34-2.

ATC — B05XB01.

ATC Vet — QB05XB01.

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

Ph. Eur. 6.2 (Arginine Hydrochloride). A white or almost white crystalline powder, or colourless crystals. Freely soluble in water; very slightly soluble in alcohol. Protect from light.

USP 31 (Arginine Hydrochloride). White, practically odourless, crystals or crystalline powder. Freely soluble in water.

Adverse Effects and Precautions

Nausea, vomiting, flushing, headache, numbness, and local venous irritation may occur if arginine solutions are infused too rapidly. Elevated plasma-potassium concentrations have been reported in uraemic patients and arginine should therefore be used with caution in patients with renal disease or anuria. Arginine hydrochloride should be given cautiously to patients with electrolyte disturbances as its high chloride content could lead to the development of hyperchloraemic acidosis.

Extravasation. Full-thickness skin necrosis has been reported[1,2] after extravasation of a 10% solution of arginine hydrochloride. Both osmotic and local hyperkalaemic effects have been proposed as a mechanism for the injury.[1]

1. Bowlby HA, Elanjian SI. Necrosis caused by extravasation of arginine hydrochloride. *Ann Pharmacother* 1992; **26:** 263–4.
2. Salameh Y, Shoufani A. Full-thickness skin necrosis after arginine extravasation—a case report and review of literature. *J Pediatr Surg* 2004; **39:** E9–E11.

Hyperkalaemia. Two alcoholic patients with severe liver disease and moderate renal insufficiency developed severe hyperkalaemia when given arginine hydrochloride and one died.[1] Both patients had received a total of 300 mg of spironolactone some time before arginine hydrochloride, but the contribution of spironolactone to the hyperkalaemia was not known. In a study to investigate the mechanism of metabolic changes due to arginine, plasma-potassium concentrations were found to be significantly higher in diabetic subjects than those for normal subjects, leading the authors to suppose that while arginine-induced hyperkalaemia may be promoted by low insulin blood levels, it could not be attributed to glucagon, pH changes, or aldosterone inhibition.[2]

In another fatal case due to an overdose of arginine,[3] a 21-month-old girl developed an acute metabolic acidosis with transient but severe hyponatraemia, and irreversible brain death; no hyperkalaemia was observed. Unlike the previously reported case, the patient had normal renal function, and the authors supposed the absence of hyperkalaemia to be due to a rapid increase in renal potassium excretion.

1. Bushinsky DA, Gennari FJ. Life-threatening hyperkalemia induced by arginine. *Ann Intern Med* 1978; **89:** 632–4.
2. Massara F, *et al.* The risk of pronounced hyperkalaemia after arginine infusion in the diabetic subject. *Diabete Metab* 1981; **7:** 149–53.
3. Gerard JM, Luisiri A. A fatal overdose of arginine hydrochloride. *J Toxicol Clin Toxicol* 1997; **35:** 621–5.

Hypersensitivity. There are 2 reports of anaphylactic reactions shortly after the start of infusions of arginine 5 or 10% given to test growth-hormone output.[1,2] Anaphylaxis to arginine was considered to be a very rare event and only one other apparent allergic reaction had been reported to the manufacturers.

1. Tiwary CM, *et al.* Anaphylactic reaction to arginine infusion. *N Engl J Med* 1973; **288:** 218.
2. Resnick DJ, *et al.* Case report of an anaphylactoid reaction to arginine. *Ann Allergy Asthma Immunol* 2002; **88:** 67–8.

Myocardial infarction. A placebo-controlled trial investigated whether the addition of arginine to standard therapy after myocardial infarction would decrease vascular stiffness and improve left ventricular function. The study was stopped early due to an increased number of deaths in the arginine group. The authors commented that, while the results could be due to chance, nevertheless arginine should not be given to patients after a myocardial infarction.[1]

1. Schulman SP, *et al.* -Arginine therapy in acute myocardial infarction: the Vascular Interaction with Age in Myocardial Infarction (VINTAGE MI) randomized clinical trial. *JAMA* 2006; **295:** 58–64.

Uses and Administration

Arginine is a basic amino acid that is essential for infant growth. It is used as a dietary supplement.

Arginine stimulates the release of growth hormone by the pituitary gland and may be used instead of, or in addition to, other tests such as insulin-induced hypoglycaemia, for the evaluation of growth disorders; false-positive and false-negative results are relatively common and evaluation therefore should not be made on the basis of a single arginine test. It is used as a 10% solution of the hydrochloride in usual doses of 30 g by intravenous infusion given over 30 minutes; children should be given 500 mg/kg.