Sodium Starch Glycolate

Carboxyméthylamidon sodique; Carboxymethylamylum natricum; Glicolato sódico de almidón; Karboksymetyloskrobia sodowa; Karboximetilkeményítő-nátrium; Karboxymethylškrob sodná sůl; Natriumstärkelseglykolat; Natriumtärkkelysglykolaatti; Sodium Carboxymethyl Starch; Sodium Starch Glycollate; Starch Sodium Glycolate.

CAS — 9063-38-1.

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

Ph. Eur. 6.2 (Sodium Starch Glycolate (Type A); Carboxymethylamylum Natricum A). The sodium salt of a cross-linked partly *O*-carboxymethylated potato starch. It contains 2.8 to 4.2% of sodium, calculated with reference to the substance washed with alcohol (80%) and dried. A fine, white or almost white, very hygroscopic, free-flowing powder. It forms a translucent suspension in water; practically insoluble in dichloromethane. pH of a 3.33% dispersion in water is 5.5 to 7.5. Store in airtight containers. Protect from light.

Ph. Eur. 6.2 (Sodium Starch Glycolate (Type B); Carboxymethylamylum Natricum B). The sodium salt of a cross-linked partly *O*-carboxymethylated potato starch. It contains 2.0 to 3.4% of sodium, calculated with reference to the substance washed with alcohol (80%) and dried. A fine, white or almost white, very hygroscopic, free-flowing powder. It forms a translucent suspension in water; practically insoluble in dichloromethane. pH of a 3.33% dispersion in water is 3.0 to 5.0. Store in airtight containers. Protect from light.

Ph. Eur. 6.2 (Sodium Starch Glycolate (Type C); Carboxymethylamylum Natricum C). The sodium salt of a cross-linked by physical dehydration, partly *O*-carboxymethylated starch. It contains 2.8 to 5.0% of sodium, calculated with reference to the substance washed with alcohol (80%) and dried. A fine, white or almost white, very hygroscopic, free-flowing powder. It forms a translucent gel-like product in water; practically insoluble in dichloromethane. pH of a 3.33% gel in water is 5.5 to 7.5. Store in airtight containers. Protect from light.

USNF 26 (Sodium Starch Glycolate). The sodium salt of a carboxymethyl ether of starch or of a cross-linked carboxymethyl ether of starch. It may contain not more than 7.0% of sodium chloride. The sodium content is 2.8 to 4.2% (Type A) or 2.0 to 3.4% (Type B). pH of a 1 g in 30 mL suspension in water is between 5.5 and 7.5 (Type A) or between 3.0 and 5.0 (Type B).

A white, odourless, relatively free-flowing powder available in several different viscosity grades. A 2% dispersion in cold water settles, on standing, in the form of a highly hydrated layer. Protect from wide variations in temperature and humidity which may cause caking.

Uses

Sodium starch glycolate is used as a disintegrating agent in tablet manufacture.

Tragacanth

Dragant; E413; Goma Alcatira; Goma de tragacanto; Gomme adragante; Gum Dragon; Gum Tragacanth; Trag.; Tragacanta; Tragacantha; Tragacanto; Tragakanta; Tragakantas; Tragant; Tragantti.

CAS — 9000-65-1.

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

Ph. Eur. 6.2 (Tragacanth). The air-hardened gummy exudation flowing naturally or obtained by incision from the trunk and branches of *Astragalus gummifer* and some other species of *Astragalus* (Leguminosae) from western Asia. It occurs as thin, flattened, ribbon-like, white or pale yellow, translucent, horny strips. When reduced to a powder it forms a mucilaginous gel with about ten times its weight of water. Protect from light.

USNF 26 (Tragacanth). The dried gummy exudation from *Astragalus gummifer* or other Asiatic species of *Astragalus* (Leguminosae). It occurs as odourless, flattened, lamellated, frequently curved fragments or straight or spirally twisted linear pieces. It is white to weak yellow, translucent, and horny in texture. Powdered tragacanth is white to yellowish-white.

Adverse Effects

Hypersensitivity reactions, sometimes severe, have occurred rarely after the ingestion of products containing tragacanth. Contact dermatitis has been reported following the external use of tragacanth.

Uses

Tragacanth forms viscous solutions or gels with water, depending on the concentration. It is used in pharmaceutical manufacturing as a suspending agent and as an emulsifying agent. In dispensing aqueous preparations of tragacanth, the powdered tragacanth is first dispersed in a wetting agent, such as alcohol, to prevent agglomeration on the addition of water.

Tragacanth is also used for similar purposes in the food industry.

Xanthan Gum

Corn Sugar Gum; E415; Goma de xantána; Gomme xanthane; Ksantaanikumi; Ksantano lipai; Polysaccharide B 1459; Xantán gumi; Xantangummi; Xantham Gum; Xanthani gummi; Xanthanová klovatina.

CAS — 11138-66-2.

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

Ph. Eur. 6.2 (Xanthan Gum). A gum produced by fermentation of a carbohydrate with *Xanthomonas campestris* and purified. It is the sodium, potassium, or calcium salt of a high-molecular-weight polysaccharide containing D-glucose, mannose, and glucuronic acid. It also contains not less than 1.5% of pyruvic acid, calculated with reference to the dried substance. A white or yellowish-white, free-flowing powder. Soluble in water giving a highly viscous solution; practically insoluble in organic solvents. A 1% solution in water has a pH of 6.0 to 8.0.

USNF 26 (Xanthan Gum). A high-molecular-weight polysaccharide gum produced by a pure-culture fermentation of a carbohydrate with *Xanthomonas campestris* and purified. It contains D-glucose, D-mannose, and D-glucuronic acid. It is prepared as the sodium, potassium, or calcium salt. A cream-coloured powder. Soluble in hot or cold water. Its solutions are neutral to litmus.

Uses

Xanthan gum is used in pharmaceutical manufacturing as a suspending, stabilising, thickening, and emulsifying agent. It is also used similarly in the food industry.

◊ Suspensions of crushed tablets or insoluble powders made with xanthan gum were reported to be preferable to those made with tragacanth.[1]

The stability was generally good and only a small number of drugs had been found to be incompatible (amitriptyline, tamoxifen, and verapamil).[1] For extemporaneous dispensing, a 1% solution of xanthan gum with hydroxybenzoate, prepared in advance, was diluted to 0.5% with water when preparing the suspension.

Xanthan gum was found to be a suitable suspending vehicle for delivering antispasmodics topically along the length of the oesophagus in patients with oesophageal spasm.[2] Coagulation of the gum had been observed when it was used for suspensions of certain film-coated tablets.

1. Anonymous. "Extremely useful" new suspending agent. *Pharm J* 1986; **237:** 665.
2. Evans BK, Fenton-May V. Keltrol. *Pharm J* 1986; **237:** 736–7.

Preparations

USNF 26: Xanthan Gum Solution.

Proprietary Preparations (details are given in Part 3)
Ger.: Ronfnyl; ***Malaysia:*** Ronfnyl†; ***Switz.:*** TenderWet†.

Multi-ingredient: ***Ital.:*** Resource Gelificata.

Obesity

Obesity results from an imbalance between energy intake and energy expenditure and increases the risk of cardiovascular disease, diabetes mellitus, gallstones, respiratory disease, osteoarthritis, and some forms of cancer. The prevalence of obesity is increasing especially in developed countries. Obesity may be defined in terms of the body-mass index (BMI), which is the weight (kg) divided by the square of the height (m^2):

- BMI 25.0 to 29.9: overweight
- BMI 30.0 to 34.9: obese, moderate risk of co-morbidity
- BMI 35.0 to 39.9: obese, severe risk of co-morbidity
- BMI 40.0 or more: obese, very severe risk of co-morbidity

Weight loss appears to improve control of diabetes mellitus and hypertension, and to reduce cardiovascular risk factors but long-term benefits are difficult to assess as weight is often regained.

Initial management involves dietary modification and includes calorie restriction and changes in the dietary proportions of fat, protein, and carbohydrates. Physical activity should also be increased and excess alcohol avoided. These measures should be followed for at least 3 months. If there has then been less than 10% reduction in weight and the BMI is still above 30, drug treatment may be considered. For patients with associated risk factors such as diabetes mellitus, ischaemic heart disease, hyperlipidaemias, hypertension, or sleep apnoea, drugs may be considered when the BMI is 27 or 28. Combination drug therapy is not recommended. Drugs should be given initially for 12 weeks. If weight loss is less than 5% then they should be considered a failure and stopped. If weight loss is more than 5% they may be continued and the patient monitored at monthly intervals. Treatment should be stopped once the BMI falls below 30 (or 27/28 as appropriate, see above), or if weight is regained, or there is any suspicion of toxicity.

Many drugs are capable of reducing appetite and have been used as such in the treatment of obesity. Both centrally acting (appetite suppressant, anorectic) drugs and those with a local action on the gastrointestinal tract have been used. However, toxicity has been a major problem with centrally acting drugs and very few are still in current use.

Appetite suppressants can be divided into two main groups: central stimulants that act on central catecholamine pathways and drugs acting on central serotonin pathways. Stimulants such as the amfetamines and phenmetrazine are no longer recommended because of their addictive potential. Other stimulants that have been used include diethylpropion, phentermine, mazindol, and phenylpropanolamine but they are also no longer recommended. The serotonergic drugs dexfenfluramine and fenfluramine were formerly used in long-term therapy (up to 1 year) but have both been associated with valvular heart defects and have generally been withdrawn worldwide. There have also been reports of valvular heart defects in patients receiving combinations of anorectics. UK and US guidelines therefore emphasise the centrally acting serotonin and noradrenaline reuptake inhibitor sibutramine, and the gastric lipase inhibitor orlistat, as appropriate choices for the drug treatment of obesity, in combination with diet and exercise. Rimonabant, a cannabinoid type-1 receptor antagonist, is also used as an adjunct in the treatment of obesity (although it was not mentioned in the guidelines). A systematic review of long-term studies (1 year or more) found orlistat, rimonabant, and sibutramine to be modestly effective in reducing weight; however, further studies, particularly on safety, are warranted.

Many other drugs have been tried, including fluoxetine, which has met with some success, and ephedrine with caffeine. The antiepileptics topiramate and zonisamide have also been investigated. Bulk-forming drugs such as methylcellulose and sterculia have been used in an attempt to control appetite by the local effect they might exert when they swell in the gastrointestinal tract, but there is little evidence of efficacy. Nondigestible fat substitutes such as sucrose polyesters have been promoted by the food industry, as part of a strategy to reduce fat and calories in the diet to aid body-weight control.

The control of appetite and the mechanisms of obesity are under investigation. A gene, called the ob-gene, and its protein product, leptin, have been identified and appear to be involved in regulation of food intake.

References.

1. Epstein LH, *et al.* Treatment of pediatric obesity. *Pediatrics* 1998; **101:** 554–70.
2. Kolanowski J. A risk-benefit assessment of anti-obesity drugs. *Drug Safety* 1999; **20:** 119–31.
3. Carek PJ, Dickerson LM. Current concepts in the pharmacological management of obesity. *Drugs* 1999; **57:** 883–904.
4. Collazo-Clavell ML. Safe and effective management of the obese patient. *Mayo Clin Proc* 1999; **74:** 1255–60.
5. Egger G, *et al.* The effectiveness of popular, non-prescription weight loss supplements. *Med J Aust* 1999; **171:** 604–8.
6. WHO. Obesity: preventing and managing the global epidemic. *WHO Tech Rep Ser 894* 2000. Available at: http://libdoc.who.int/trs/WHO_TRS_894.pdf (accessed 11/08/08)
7. National Heart, Lung, and Blood Institute. The practical guide: identification, evaluation, and treatment of overweight and obesity in adults (October 2000). Available at: http://www.nhlbi.nih.gov/guidelines/obesity/practgde.htm (accessed 15/06/05)
8. Glazer G. Long-term pharmacotherapy of obesity 2000: a review of efficacy and safety. *Arch Intern Med* 2001; **161:** 1814–24.
9. ASHP Commission on Therapeutics. ASHP therapeutic position statement on the safe use of pharmacotherapy for obesity management in adults (approved April 23, 2001). *Am J Health-Syst Pharm* 2001; **58:** 1645–55.
10. Yanovski SZ, Yanovski JA. Obesity. *N Engl J Med* 2002; **346:** 591–602.
11. Hitchcock Noël P, Pugh JA. Management of overweight and obese adults. *BMJ* 2002; **325:** 757–61.
12. Fernández-López JA, *et al.* Pharmacological approaches for the treatment of obesity. *Drugs* 2002; **62:** 915–44.
13. Royal College of Physicians of London. *Anti-obesity drugs: guidance on appropriate prescribing and management*. Salisbury: Royal College of Physicians of London, 2003.
14. McTigue KM, *et al.* Screening and interventions for obesity in adults: summary of the evidence for the U.S. Preventive Services Task Force. *Ann Intern Med* 2003; **139:** 933–49.
15. Kopelman PG, Grace C. New thoughts on managing obesity. *Gut* 2004; **53:** 1044–53.
16. Snow V, *et al.* Pharmacologic and surgical management of obesity in primary care: a clinical practice guideline from the American College of Physicians. *Ann Intern Med* 2005; **142:** 525–31.
17. Li Z, *et al.* Meta-analysis: pharmacologic treatment of obesity. *Ann Intern Med* 2005; **142:** 532–46.
18. Ioannides-Demos LL, *et al.* Pharmacotherapy for obesity. *Drugs* 2005; **65:** 1391–1418.
19. Haslam DW, James WPT. Obesity. *Lancet* 2005; **366:** 1197–1209.
20. Wadden TA, *et al.* Randomized trial of lifestyle modification and pharmacotherapy for obesity. *N Engl J Med* 2005; **353:** 2111–20.
21. Daniels SR, *et al.* Overweight in children and adolescents: pathophysiology, consequences, prevention, and treatment. *Circulation* 2005; **111:** 1999–2012.
22. Speiser PW, *et al.* Obesity Consensus Working Group. Childhood obesity. *J Clin Endocrinol Metab* 2005; **90:** 1871–87.
23. NICE. Obesity: guidance on the prevention, identification, assessment and management of overweight and obesity in adults and children (issued December 2006). Available at: http://www.nice.org.uk/nicemedia/pdf/word/CG43NICEGuideline.doc (accessed 21/05/08)
24. Thompson WG, *et al.* Treatment of obesity. *Mayo Clin Proc* 2007; **82:** 93–101.
25. Freemark M. Pharmacotherapy of childhood obesity: an evidence-based, conceptual approach. *Diabetes Care* 2007; **30:** 395–402.
26. Rucker D, *et al.* Long term pharmacotherapy for obesity and overweight: updated meta-analysis. Abridged version: *BMJ* 2007; **335:** 1194–9. Full version: http://www.bmj.com/cgi/reprint/335/7631/1194 (accessed 21/05/08)
27. Barlow SE. Expert Committee. Expert committee recommendations regarding the prevention, assessment, and treatment of child and adolescent overweight and obesity: summary report. *Pediatrics* 2007; **120** (suppl 4): S164–S192.

Prader-Willi syndrome

Compulsive eating and a voracious appetite are two of the many clinical features of Prader-Willi syndrome, a congenital disorder characterised by infantile hypotonia, hypogonadism, and facial dysmorphism, with subsequent development of abnormalities of behaviour and intellect.[1,2] Supervision and restricted access to food are the mainstay in preventing obesity, but are commonly not sufficient. Fluoxetine may decrease food intake in some patients. It has also been tried for associated self-mutilatory behaviour (skin picking) with variable results.[3,4] Growth hormone may be of benefit in increasing associated short stature and decreasing percentage body fat,[5-11] but close surveillance of glucose homoeostasis is advisable and there have been reports of fatalities in patients with severe obesity or risk factors for respiratory impairment or obstruction.[12] Anorectics have been ineffective.[2]

1. Donaldson MDC, *et al.* The Prader-Willi syndrome. *Arch Dis Child* 1994; **70:** 58–63.
2. Couper RTL, Couper JJ. Prader-Willi syndrome. *Lancet* 2000; **356:** 673–5.
3. Warnock JK, Kestenbaum T. Pharmacologic treatment of severe skin-picking behaviors in Prader-Willi syndrome. *Arch Dermatol* 1992; **128:** 1623–5.
4. Schepis C, *et al.* Failure of fluoxetine to modify the skin-picking behaviour of Prader-Willi syndrome. *Australas J Dermatol* 1998; **39:** 57–60.
5. Lindgren AC, *et al.* Five years of growth hormone treatment in children with Prader-Willi syndrome. *Acta Paediatr Suppl* 1999; **433:** 109–11.
6. Myers SE, *et al.* Physical effects of growth hormone treatment in children with Prader-Willi syndrome. *Acta Paediatr Suppl* 1999; **433:** 112–14.
7. Burman P, *et al.* Endocrine dysfunction in Prader-Willi syndrome: a review with special reference to GH. *Endocr Rev* 2001; **22:** 787–99.
8. Paterson WF, Donaldson MDC. Growth hormone therapy in the Prader-Willi syndrome. *Arch Dis Child* 2003; **88:** 283–5.
9. Eiholzer U, *et al.* Growth hormone and body composition in children younger than 2 years with Prader-Willi syndrome. *J Pediatr* 2004; **144:** 753–8.
10. Carrel AL, *et al.* Growth hormone improves mobility and body composition in infants and toddlers with Prader-Willi syndrome. *J Pediatr* 2004; **145:** 744–9.
11. Mogul HR, *et al.* Growth hormone treatment of adults with Prader-Willi syndrome and growth hormone deficiency improves lean body mass, fractional body fat, and serum triiodothyronine without glucose impairment: results from the United States multicenter trial. *J Clin Endocrinol Metab* 2008; **93:** 1238–45.
12. Stafler P, Wallis C. Prader-Willi syndrome: who can have growth hormone? *Arch Dis Child* 2008; **93:** 341–5.

Adrafinil *(rINN)* ⊗

Adrafinilo; Adrafinilum; CRL-40028. 2-[(Diphenylmethyl)sulfinyl]acetohydroxamic acid.

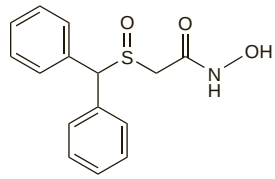
Адрафинил

$C_{15}H_{15}NO_3S$ = 289.3.

CAS — 63547-13-7.

ATC — N06BX17.

ATC Vet — QN06BX17.



Profile

Adrafinil is a central stimulant and alpha$_1$-adrenergic agonist chemically related to modafinil (p.2160). It is given orally for mental function impairment in the elderly in doses of 600 mg to 1.2 g daily.

Preparations

Proprietary Preparations (details are given in Part 3)
Fr.: Olmifon.

Almitrine Dimesilate *(BANM, rINNM)*

Almitrine Bismesylate; Almitrine, Dimésilate d'; Almitrine Dimesylate; Almitrine Mesylate *(USAN)*; Almitrini Dimesilas; Dimesilato de almitrina; S-2620 (almitrine or almitrine dimesilate). *NN'*-Diallyl-6-[4-(4,4'-difluorobenzhydryl)piperazin-1-yl]-1,3,5-triazine-2,4-diyldiamine bis(methanesulphonate).

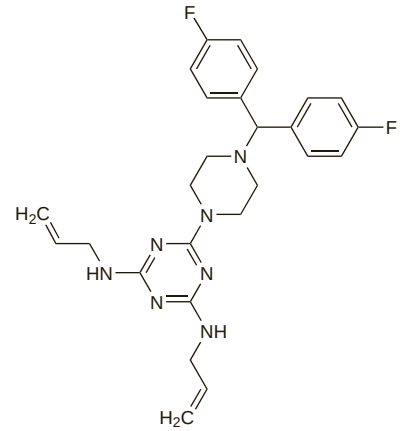
Альмитрина Димезилат

$C_{26}H_{29}F_2N_7,2CH_4SO_3$ = 669.8.

CAS — 27469-53-0 (almitrine); 29608-49-9 (almitrine dimesilate).

ATC — R07AB07.

ATC Vet — QR07AB07.



(almitrine)

Pharmacopoeias. In *Chin.*

Profile

Almitrine dimesilate has been used as a respiratory stimulant in acute respiratory failure associated with conditions such as chronic obstructive pulmonary disease. Usual oral doses range from 50 to 100 mg daily and treatment may be intermittent. Up to 3 mg/kg has been given daily by intravenous infusion in 2 or 3 divided doses, each dose being infused over 2 hours. It is also available in a compound preparation with raubasine for mental function impairment in the elderly.