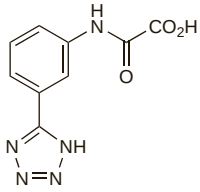
Acitazanolast *(rINN)*

Acitazanolastum; WP-871. 3′-(1*H*-tetrazol-5-yl)oxanilic acid.

Ацитазаноласт

$C_9H_7N_5O_3$ = 233.2.

CAS — 114607-46-4.



Profile

Acitazanolast is a leukotriene inhibitor used as the hydrate in a concentration of 0.1 or 0.3% in eye drops for the treatment of allergic conjunctivitis (p.564).

Preparations

Proprietary Preparations (details are given in Part 3)
Jpn: Zepelin.

Aconite

Acetylbenzoylaconine (aconitine); Aconit.; Aconit napel; Aconite Root; Aconiti Tuber; Acónito; Aconitum napellus; Monkshood Root; Radix Aconiti; Wolfsbane Root. 8-Acetoxy-3,11,18-trihydroxy-16-ethyl-1,6,19-trimethoxy-4-methoxymethylaconitan-10-yl benzoate (aconitine).

$C_{34}H_{47}NO_{11}$ = 645.7 (aconitine).

CAS — 8063-12-5 (aconite); 302-27-2 (aconitine).

NOTE. Wolfsbane is also used as a common name for arnica flower (p.2260).

Description. Aconite consists of the dried tuberous root of *Aconitum napellus* agg. (Ranunculaceae). It contains a number of alkaloids, the main pharmacologically active one being aconitine.

Pharmacopoeias. In *Chin.*

Adverse Effects and Treatment

Aconite has variable effects on the heart leading to heart failure. It also affects the CNS.

Symptoms of aconite poisoning may appear within minutes or up to 2 hours after oral ingestion; in fatal poisoning death usually occurs within 12 hours, although with larger doses it may be instantaneous.

Initial symptoms (and an important diagnostic feature) are tingling sensations of the tongue, mouth, fingers, and toes followed by generalised paraesthesia. Other symptoms include nausea, vomiting, diarrhoea, muscle weakness, skeletal muscle paralysis, and difficult respiration; also sweats, chills and a feeling of intense cold may occur. Respiratory paralysis, hypotension, and cardiac arrhythmias may develop in severe cases.

Although the benefits of gastric decontamination are uncertain, gastric lavage may be tried in patients within one hour of life-threatening oral poisoning; activated charcoal may also be considered. Patients should be observed and monitored, and corrective and supportive treatment given as necessary. Arrhythmias are relatively resistant to treatment, although atropine has been tried for bradycardia.

Poisoning. Reports of poisoning with aconite.

1. Kelly SP. Aconite poisoning. *Med J Aust* 1990; **153:** 499.
2. Tai Y-T, *et al.* Cardiotoxicity after accidental herb-induced aconite poisoning. *Lancet* 1992; **340:** 1254–6.
3. Kolev ST, *et al.* Toxicity following accidental ingestion of Aconitum containing Chinese remedy. *Hum Exp Toxicol* 1996; **15:** 839–42.
4. Mak W, Lau CP. A woman with tetraparesis and missed beats. *Hosp Med* 2000; **61:** 438.
5. Imazio M, *et al.* Malignant ventricular arrhythmias due to Aconitum napellus seeds. *Circulation* 2000; **102:** 2907–8.
6. Chan TYK. Incidence of herb-induced aconitine poisoning in Hong Kong: impact of publicity measures to promote awareness among the herbalists and the public. *Drug Safety* 2002; **25:** 823–8.
7. Lowe L, *et al.* Herbal aconite tea and refractory ventricular tachycardia. *N Engl J Med* 2005; **353:**1532.

Uses and Administration

Aconite liniments have been used in the treatment of neuralgia, sciatica, and rheumatism. Sufficient aconitine may be absorbed through the skin to cause poisoning; liniments should never be applied to wounds or abraded surfaces. Aconite should not be used internally because of its low therapeutic index and variable potency; however it is reported to be a common ingredient in traditional Chinese remedies and is also an ingredient of some cough mixtures.

Homoeopathy. Aconite has been used in homoeopathic medicines.

Preparations

Proprietary Preparations (details are given in Part 3)

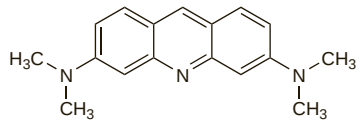
Multi-ingredient: ***Arg.:*** No-Tos Adultos; ***Austria:*** Rheuma; ***Belg.:*** Colimax†; Eucalyptine Pholcodine Le Brun†; Saintbois; ***Braz.:*** Agrimel†; Expectomel; Gotas Nican†; Limao Bravo†; Melagriao; Pectal†; Xarope de Caraguata†; Xarope Peitoral de Ameixa Composto†; Xarope Sao Joao†; ***Chile:*** Gotas Nican†; ***Cz.:*** Homeovox; Pleumolysin; ***Ital.:*** Lactocol; ***Port.:*** Anti-Gripe†; Calmarum†; ***Spain:*** Encialina†.

Acridine Orange

Naranja de acridina. 3,6-Bis(dimethylamino)acridine.

$C_{17}H_{19}N_3$ = 265.4.

CAS — 494-38-2.



Profile

Acridine orange is a dye with antiseptic properties. It has been used as a diagnostic stain in microbiology.

For details of the antiseptic properties of acridine derivatives, see p.1624.

Diagnostic use. Acridine orange has been used for the diagnostic staining of malarial parasites.[1] For the quantitative buffy coat method, acridine orange is used to stain the parasites in a blood sample that is then centrifuged, and the area just below the buffy coat is examined under a fluorescence microscope. It has been described as easier and quicker to use than the standard examination of stained blood films. However, this method is not specific for diagnosis of malarial type, gives only a rough indication of infection intensity, and can give false-positive results. Acridine orange has also been tried for the staining of blood slides.[2-5]

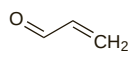
1. Warhurst DC, Williams JE. ACP Broadsheet no 148, July 1996, Laboratory diagnosis of malaria. *J Clin Pathol* 1996; **49:** 533–8.
2. Gay F, *et al.* Direct acridine orange fluorescence examination of blood slides compared to current techniques for malaria diagnosis. *Trans R Soc Trop Med Hyg* 1996; **90:** 516–18.
3. Craig MH, Sharp BL. Comparative evaluation of four techniques for the diagnosis of Plasmodium falciparum infections. *Trans R Soc Trop Med Hyg* 1997; **91:** 279–82.
4. Tarimo DS, *et al.* Appraisal of the acridine orange method for rapid malaria diagnosis at three Tanzanian district hospitals. *East Afr Med J* 1998; **75:** 504–7.
5. Lema OE, *et al.* Comparison of five methods of malaria detection in the outpatient setting. *Am J Trop Med Hyg* 1999; **60:** 177–82.

Acrolein

Acraldehyde; Acrialdehído; Acroleína; Acrylaldehyde; Acrylic Aldehyde. Prop-2-enal.

C_3H_4O = 56.06.

CAS — 107-02-8.



Profile

Acrolein is a volatile, highly flammable liquid at ordinary temperature and pressure. It has various industrial uses, but is also a toxic byproduct of combustion and may be present in exhaust gases, tobacco smoke, and smoke from fires. It is irritant to the skin and may cause skin burns. Ingestion of acrolein produces severe gastrointestinal distress. The vapour causes lachrymation and pulmonary irritation. Inhalation may cause pulmonary oedema and permanent lung damage.

Acrolein is a metabolite of cyclophosphamide (p.702) and may be responsible for the latter's bladder toxicity.

◊ References.

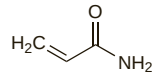
1. WHO. Acrolein. *IPCS Health and Safety Guide 67*. Geneva: WHO, 1991. Available at: http://www.inchem.org/documents/hsg/hsg/hsg067.htm (accessed 23/07/08)
2. WHO. Acrolein. *Environmental Health Criteria 127*. Geneva: WHO, 1992. Available at: http://www.inchem.org/documents/ehc/ehc/ehc127.htm (accessed 23/07/08)
3. Kehrer JP, Biswal SS. The molecular effects of acrolein. *Toxicol Sci* 2000; **57:** 6–15.

Acrylamide

Acrilamida; Akryloamid; Amida acrílica. Propenamide.

C_3H_5NO = 71.08.

CAS — 79-06-1.



Profile

Acrylamide is highly toxic and irritant; it can be absorbed through unbroken skin. Symptoms of poisoning include burning and ulceration of the mouth and throat following ingestion. Excessive sweating is common and other symptoms may include numbness of limbs, paraesthesias, and muscle weakness. CNS effects such as somnolence, confusion, hallucinations, ataxia, tremors, dysarthria, and nystagmus may occur depending on the severity of exposure. Peripheral neuropathies may appear several weeks after severe acute exposure or as a result of chronic exposure. Gastric lavage may be tried in patients within one hour of ingestion; activated charcoal may also be considered. Contamination of eyes and skin should be irrigated and treated as for burns. Patients should be observed and monitored, and corrective and supportive treatment given as necessary.

Acrylamide has various industrial applications, including use as a plasticiser and a waterproof 'chemical grout'.

◊ References.

1. Kesson CM, *et al.* Acrylamide poisoning. *Postgrad Med J* 1977; **53:** 16–17.
2. WHO. Acrylamide *IPCS Health and Safety Guide 45*. Geneva: WHO, 1991. Available at: http://www.inchem.org/documents/hsg/hsg/hsg045.htm (accessed 31/03/06)

Food toxicity. Concerns have been expressed by the Swedish National Food Administration about the level of acrylamide they found in certain cooked foods, particularly those exposed to very high temperatures such as fried foods, and the potential carcinogenic risk. However, it has been acknowledged that, although the results have been replicated in other international laboratories, the total sample size is small and none of the methods being used have so far been validated.[1] One subsequent population-based study failed to find any excess risk or convincing trend of cancer of the bowel, bladder, or kidney in high consumers of foods with a high or moderate acrylamide content.[2] The joint FAO/WHO Expert Committee on Food Additives (JECFA)[3] reviewed data provided by 24 countries on acrylamide in food analysed between 2002 and 2004. Their recommendations were for re-evaluation of the effects of acrylamide on completion of studies of carcinogenicity and neurotoxicity, and that efforts to reduce the concentrations of acrylamide in food should continue.

1. Kapp C. WHO urges more research into acrylamide in food. *Lancet* 2002; **360:** 64.
2. Mucci LA, *et al.* Dietary acrylamide and cancer of the large bowel, kidney, and bladder: absence of an association in a population-based study in Sweden. *Br J Cancer* 2003 **88:** 84–9.
3. FAO/WHO. Evaluation of certain food contaminants: sixty-fourth report of the joint FAO/WHO expert committee on food additives. *WHO Tech Rep Ser 930* 2006. Available at: http://whqlibdoc.who.int/trs/WHO_TRS_930_eng.pdf (accessed 18/07/08)

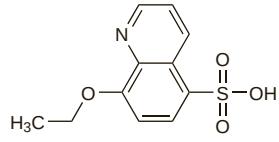
Actinoquinol Sodium *(USAN, rINNM)*

Actinoquinol sódico; Actinoquinol Sodique; Natrii Actinoquinolum; Sodium Etoquinol; Sodium Tequinol. Sodium 8-ethoxy-5-quinolinesulfonate.

Натрий Актинохинол

$C_{11}H_{10}NNaO_4S$ = 275.3.

CAS — 15301-40-3 (actinoquinol); 7246-07-3 (actinoquinol sodium).



(actinoquinol)

Profile

Actinoquinol and actinoquinol sodium are ingredients of eye drop preparations intended to protect the eyes from the effects of light.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Ultra Augenschutz.

Multi-ingredient: ***Fr.:*** Uvicol; ***Ger.:*** durautra; ***Ital.:*** Fotofil.

Ademetionine *(rINN)*

Ademethionine; Ademetioniini; Adémétionin; Ademetionin; Ademetionina; Ademetioninum; *S*-Adenosyl-L-methionine; Methioninyl adenylate; SAMe. (*S*)-5′-[(3-Amino-3-carboxypropyl)methylsulphonio]-5′-deoxyadenosine hydroxide, inner salt.

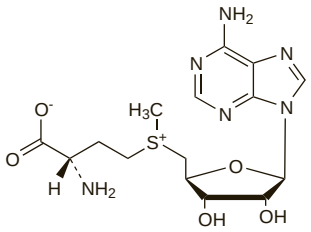
Адеметионин

$C_{15}H_{22}N_6O_5S$ = 398.4.

CAS — 29908-03-0; 485-80-3; 17176-17-9.

ATC — A16AA02.

ATC Vet — QA16AA02.



Profile

Ademetionine is a naturally occurring molecule found in virtually all body tissues and fluids. It acts as a methyl group donor in many transmethylation reactions and therefore is involved in the synthesis or metabolism of a wide range of compounds that maintain normal cell function. Ademetionine sulfate tosilate and ademetionine butanedisulfonate are stable forms of ademetionine that have been used for the treatment of depression (see below), liver disorders, and osteoarthritis.

◊ References.

1. Bottiglieri T, *et al.* The clinical potential of ademetionine (S-adenosylmethionine) in neurological disorders. *Drugs* 1994; **48:** 137–52.
2. Chavez M. SAMe: S-adenosylmethionine. *Am J Health-Syst Pharm* 2000; **57:** 119–23.
3. Fetrow CW, Avila JR. Efficacy of the dietary supplement S-adenosyl-L-methionine. *Ann Pharmacother* 2001; **35:** 1414–25.
4. Bottiglieri T. S-Adenosyl-L-methionine (SAMe): from the bench to the bedside—molecular basis of a pleiotrophic molecule. *Am J Clin Nutr* 2002; **76** (suppl): 1151S–1157S.
5. Gören JL, *et al.* Bioavailability and lack of toxicity of S-adenosyl-L-methionine (SAMe) in humans. *Pharmacotherapy* 2004; **24:** 1501–7.

Depression. Ademetionine has been given orally or parenterally in the management of depression (p.373). It appears to be of similar efficacy to the tricyclic antidepressants but evidence is limited to small, heterogeneous groups of patients studied over short periods of time; additionally many studies have involved parenteral rather than oral therapy.

References.

1. Bressa GM. S-Adenosyl-1-methionine (SAMe) as antidepressant: meta-analysis of clinical studies. *Acta Neurol Scand* 1994; **154** (suppl): 7–14.
2. Anonymous. SAMe for depression. *Med Lett Drugs Ther* 1999; **41:** 107–8.
3. Mischoulon D, Fava M. Role of *S*-adenosyl- -methionine in the treatment of depression: a review of the evidence. *Am J Clin Nutr* 2002; **76:** 1158S–1161S.
4. Papakostas GI, *et al.* S-Adenosyl-methionine in depression: a comprehensive review of the literature. *Curr Psychiatry Rep* 2003; **5:** 460–6.

Liver disorders. Some workers have found that ademetionine produced clinical improvement in patients with **intrahepatic cholestasis**,[1,2] including that associated with pregnancy.[3,4] Pruritus associated with the condition has also been relieved. Other studies,[5,6] however, have not found any benefit.

Ademetionine produced a good or excellent clinical response in patients with **hepatic steatosis**.[7] In a study[8] of patients with **alcoholic liver cirrhosis**, treated with ademetionine for 2 years, there was a trend towards reduced overall mortality or need for liver transplantation, but only in patients with less severe hepatic dysfunction. However, a systematic review[9] of 9 randomised placebo-controlled studies, which included the latter study could not find evidence to support or refute the claim that ademetionine has a beneficial effect in patients with alcoholic liver diseases, and larger high quality randomised placebo-controlled studies are needed.

1. Frezza M, *et al.* Oral S-adenosylmethionine in the symptomatic treatment of intrahepatic cholestasis: a double-blind, placebo-controlled study. *Gastroenterology* 1990; **99:** 211–15.
2. Almasio P, *et al.* Role of S-adenosyl- -methionine in the treatment of intrahepatic cholestasis. *Drugs* 1990; **40** (suppl 3): 111–23.
3. Bonfirraro G, *et al.* S-Adenosyl- -methionine (SAMe)-induced amelioration of intrahepatic cholestasis of pregnancy: results of an open study. *Drug Invest* 1990; **2:** 125–8.
4. Frezza M, *et al.* S-Adenosylmethionine for the treatment of intrahepatic cholestasis of pregnancy: results of a controlled clinical trial. *Hepatogastroenterology* 1990; **37** (suppl 2): 122–5.
5. Ribalta J, *et al.* S-Adenosyl-L-methionine in the treatment of patients with intrahepatic cholestasis of pregnancy: a randomized, double-blind, placebo-controlled study with negative results. *Hepatology* 1991; **13:** 1084–9.
6. Floreani A, *et al.* S-Adenosylmethionine versus ursodeoxycholic acid in the treatment of intrahepatic cholestasis of pregnancy: preliminary results of a controlled trial. *Eur J Obstet Gynecol Reprod Biol* 1996; **67:** 109–13.
7. Caballeria E, Moreno J. Therapeutic effects of S-adenosylmethionine (SAMe) in hepatic steatosis. *Acta Ther* 1990; **16:** 253–64.
8. Mato JM, *et al.* S-Adenosylmethionine in alcoholic liver cirrhosis: a randomized, placebo-controlled, double-blind, multicenter clinical trial. *J Hepatol* 1999; **30:** 1081–9.
9. Rambaldi A, Gluud C. S-Adenosyl-L-methionine for alcoholic liver diseases. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2006 (accessed 01/04/08).

Osteoarthritis. Ademetionine has been reported to possess therapeutic efficacy in the treatment of osteoarthritis (p.11) and similar conditions, possibly due to an effect on cartilage metabolism and formation of anti-inflammatory mediators within the cell; it may also inhibit leukotrienes but does not appear markedly to interfere with prostaglandin synthesis.

References.

1. Domljan Z, *et al.* A double-blind trial of ademethionine vs naproxen in activated gonarthrosis. *Int J Clin Pharmacol Ther Toxicol* 1989; **27:** 329–33.
2. Bradley JD, *et al.* A randomized, double blind, placebo controlled trial of intravenous loading with S-adenosylmethionine (SAM) followed by oral SAM therapy in patients with knee osteoarthritis. *J Rheumatol* 1994; **21:** 905–11.
3. Soeken KL, *et al.* Safety and efficacy of S-adenosylmethionine (SAMe) for osteoarthritis. *J Fam Pract* 2002; **51:** 425–30.
4. Najm WI, *et al.* S-Adenosyl methionine (SAMe) versus celecoxib for the treatment of osteoarthritis symptoms: a double-blind cross-over trial. *BMC Musculoskelet Disord* 2004; **5:** 6.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Transmetil†; Tunik; ***Austral.:*** MoodLift†; ***Cz.:*** Transmetil; ***Ger.:*** Gumbaral; ***Ital.:*** Donamet; Isimet†; Samyr; Transmetil; ***Mex.:*** Samyr; ***Rus.:*** Heptor (Гептор); Heptral (Гептрал); ***Spain:*** S Amet†.

Multi-ingredient: ***Arg.:*** Tunik B12.

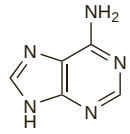
Adenine

Adeniini; Adenin; Adenina; Adeninas; Adénine; Adeninum; Vitamin B_4; Vitamina B_4. 6-Aminopurine; 1,6-Dihydro-6-iminopurine.

Аденин

$C_5H_5N_5$ = 135.1.

CAS — 73-24-5.



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

Ph. Eur. 6.2 (Adenine). A white or almost white powder. Very slightly soluble in water and in alcohol; dissolves in dilute mineral acids and in dilute solutions of alkali hydroxides.

USP 31 (Adenine). Odourless white crystals or crystalline powder. Very slightly soluble in water; sparingly soluble in boiling water; slightly soluble in alcohol; practically insoluble in chloroform and in ether.

Profile

Adenine is a purine base and one of the components of adenosine nucleotides that form nucleic acids (p.2355). It is also a constituent of many coenzymes. It has been used to extend the storage life of whole blood (p.1056) and has also been given for the management of white blood cell disorders and alcoholism. Adenine hydrochloride has been used similarly.

Preparations

USP 31: Anticoagulant Citrate Phosphate Dextrose Adenine Solution.

Proprietary Preparations (details are given in Part 3)
Fr.: Leuco-4.

Multi-ingredient: ***Fr.:*** TTD-B -B ; ***Philipp.:*** Godex; ***Rus.:*** Lidevine (Лидевин); ***Spain:*** Hepadif.

Adenosine Phosphate *(BAN, USAN, rINN)*

Adenosine Monophosphate; Adenosine 5′-Monophosphate; Adénosine, Phosphate d'; Adenosine-5′-(dihydrogen phosphate); Adenosine-5′-phosphoric Acid; Adenosini Phosphas; 5′-Adenylic Acid; AMP; A-5MP; Fosfato de adenosina; Monophosadénine; Muscle Adenylic Acid; NSC-20264. 6-Amino-9-β-D-ribofuranosylpurine 5′-(dihydrogen phosphate).

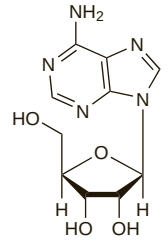
Аденозина Фосфат

$C_{10}H_{14}N_5O_7P$ = 347.2.

CAS — 61-19-8.

ATC — C01EB10.

ATC Vet — QC01EB10.



(adenosine)

Pharmacopoeias. *Ger.* includes the disodium salt ($C_{10}H_{12}N_5Na_2O_7P,xH_2O$).

Profile

Adenosine phosphate is an endogenous adenine nucleotide involved in many biological processes. Adenosine monophosphate (AMP) is a vasodilator and has been included in preparations for venous insufficiency, haemorrhoids, and varicose veins. It has also been used in pain and inflammation. Adenosine diphosphate and its disodium salt have also been used. AMP is also used in bronchial challenge tests to assess airway hyper-responsiveness in asthma and other respiratory disorders.

Unlike adenosine (p.1202) or adenosine triphosphate (below), adenosine phosphate is not used in supraventricular tachycardias.

Preparations

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

Multi-ingredient: ***Cz.:*** Laevadosin†; ***S.Afr.:*** Lipostabil†; ***Spain:*** Artri; Taurobetina†.

Adenosine Triphosphate

Adenosina, trifosfato de; Adenosine 5′-Triphosphate; 5′-Adenyldiphosphoric Acid; Adenylpyrophosphoric Acid; ATP; Trifosadenina; Triphosadénine. Adenosine 5′-(tetrahydrogen triphosphate).

Аденозинтрифосфат

$C_{10}H_{16}N_5O_{13}P_3$ = 507.2.

CAS — 56-65-5.

ATC — C01EB10.

ATC Vet — QC01EB10.

Pharmacopoeias. *Ger.* includes the disodium salt ($C_{10}H_{14}N_5Na_2O_{13}P_3$ = 551.1).

Profile

Adenosine triphosphate (ATP) is an endogenous adenine nucleotide with a fundamental role in cellular energy transformation; ATP is hydrolysed to adenosine diphosphate (ADP) releasing energy stored in phosphate bonds. In addition, extracellular ATP influences many biological processes.

ATP is a vasodilator that has been used in varied disorders. The sodium and disodium salts have been used in cerebral and peripheral vascular disorders and also for the treatment of supraventricular tachycardias, although adenosine (p.1202) is the form generally used as an antiarrhythmic. ATP has also been investigated for use in cachexia in patients with cancer.

◊ Reviews.

1. Agteresch HJ, *et al.* Adenosine triphosphate: established and potential clinical applications. *Drugs* 1999; **58:** 211–32.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Atepadene†; ***Fr.:*** Atepadene; Striadyne; ***Hong Kong:*** ATP-Daiichi; ***Jpn:*** Adetphos; ***Philipp.:*** Nutaphake; ***Rus.:*** Fosfobion (Фосфобион)†; ***Spain:*** Atepodin.

Multi-ingredient: ***Cz.:*** Laevadosin†; ***Indon.:*** Enerplus; Myoviton; Vitap; ***Spain:*** Refulgin.

Adiphenine *(rINN)*

Adifenina; Adiphénine; Adipheninum. 2-Diethylaminoethyl diphenylacetate.

Адифенин

$C_{20}H_{25}NO_2$ = 311.4.

CAS — 64-95-9.