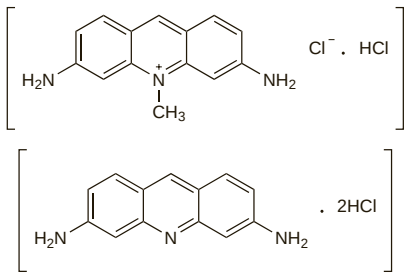
Acriflavinium Chloride *(rINN)*

Acriflavine; Acriflavine Hydrochloride; Acriflavinii Chloridum; Acriflavinii Dichloridum; Acriflavinium, Chlorure d'; Akriflaviniumchlorid; Cloruro de acriflavinio. A mixture of 3,6-diamino-10-methylacridinium chloride hydrochloride and 3,6-diaminoacridine dihydrochloride.

Акрифлавиния Хлорид

CAS — 8063-24-9; 65589-70-0.
ATC — R02AA13.
ATC Vet — QG01AC90; QR02AA13.



NOTE. The nomenclature is confusing. Acriflavinium Chloride is *rINN* but also the *BP* name for Acriflavinium Monochloride (see below).

Acriflavinium Monochloride

Acriflavinii monochloridum; Acriflavinio, monocloruro de; Acriflavinium, monochlorure d'; Akriflavinio monochloridas; Akriflaviniummonoklorid; Akriflaviniummonokloridi; Euflaviini; Euflavin; Euflavine; Euflavinum; Neutral Acriflavine; Neutroflavin. A mixture of 3,6-diamino-10-methylacridinium chloride and 3,6-diaminoacridine monohydrochloride. The latter is usually present to the extent of between 30 and 40%.

CAS — 68518-47-8.
ATC — D08AA03.
ATC Vet — QD08AA03.

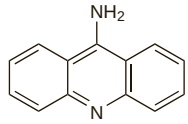
NOTE. The nomenclature is confusing. Although the *BP* name was Acriflavinium Chloride this is also *rINN* for a related compound (see above).

Aminoacridine Hydrochloride *(BANM, rINNM)*

Aminacrine Hydrochloride *(USAN)*; Aminoacridine, Chlorhydrate d'; Aminoacridini Hydrochloridum; Hidrocloruro de aminoacridina; NSC-7571. 9-Aminoacridine hydrochloride monohydrate.

Аминоакридина Гидрохлорид

$C_{13}H_{10}N_2,HCl,H_2O$ = 248.7.
CAS — 90-45-9 (aminoacridine); 134-50-9 (anhydrous aminoacridine hydrochloride).
ATC — D08AA02.
ATC Vet — QD08AA02.



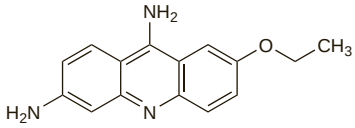
(aminoacridine)

Ethacridine Lactate *(BANM, rINNM)*

Acrinol; Aethacridinium Lacticum; Etakridiinilaktaatti; Etakridinlaktat; Etakridin-laktát; Etakridino laktatas; Etakrydyny mleczan; Éthacridine, lactate d'; Ethacridini lactas; Ethakridin-laktát; Lactato de etacridina; Lactoacridine. 6,9-Diamino-2-ethoxyacridine lactate.

Этакридина Лактат

$C_{15}H_{15}N_3O,C_3H_6O_3$ = 343.4.
CAS — 442-16-0 (ethacridine); 1837-57-6 (ethacridine lactate); 6402-23-9 (ethacridine lactate monohydrate).
ATC — B05CA08; D08AA01.
ATC Vet — QB05CA08; QD08AA01.



(ethacridine)

Pharmacopoeias. *Chin.*, *Eur.* (see p.vii), and *Jpn* describe the monohydrate.

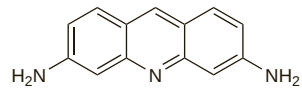
Ph. Eur. 6.2 (Ethacridine Lactate Monohydrate). A yellow crystalline powder. Sparingly soluble in water; very slightly soluble in alcohol; practically insoluble in dichloromethane. A 2% solution in water has a pH of 5.5 to 7.0. Protect from light.

Proflavine Hemisulfate

Proflavine Hemisulphate *(pINNM)*; Hemisulfato de proflavina; Neutral Proflavine Sulphate; Proflavine, Hémisulfate de; Proflavini Hemisulfas. 3,6-Diaminoacridine sulphate dihydrate.

Профлавина Гемисульфат

$(C_{13}H_{11}N_3)_2,H_2SO_4,2H_2O$ = 552.6.
CAS — 92-62-6 (proflavine).



(proflavine)

Profile

The acridine derivatives are slow-acting antiseptics. They are bacteriostatic against many Gram-positive bacteria but less effective against Gram-negative bacteria. They are ineffective against spores. Their activity is increased in alkaline solutions and is not reduced by tissue fluids.

The acridine derivatives have been used for the treatment of infected wounds or burns and for skin disinfection, although they have been largely superseded by other antiseptics or suitable antibacterials. Prolonged treatment may delay healing. They have also been used for the local treatment of ear, oropharyngeal, and genito-urinary infections.

Aminoacridine is reported to be non-staining and is used as the hydrochloride as eye drops in the treatment and prophylaxis of superficial eye infections.

Ethacridine lactate is included in some preparations for the treatment of diarrhoea. It has also been given by extra-amniotic injection for the termination of pregnancy (p.2004) but other methods are usually preferred.

Other acridine derivatives covered elsewhere in *Martindale* include mepacrine (p.836), which is used in the treatment of giardiasis, and pyronaridine (p.612), which is used to treat malaria. Amsacrine (p.681) is a 9-anilinoacridine drug that is used in the treatment of adult leukaemias. Other acridine derivatives are also under investigation as anticancer drugs because of the ability of the acridine chromophore to intercalate DNA and inhibit topoisomerase enzymes.

Hypersensitivity to acridine derivatives has been reported.

◊ References.

1. Wainwright M. Acridine—a neglected antibacterial chromophore. *J Antimicrob Chemother.* 2001; **47:** 1–13.
2. Denny WA. Acridine derivatives as chemotherapeutic agents. *Curr Med Chem* 2002; **9:** 1655–65.

Preparations

BPC 1973: Proflavine Cream.

Proprietary Preparations (details are given in Part 3)
Austral.: Aminopt; ***Ger.:*** Metifex; Neochinosol; Rivanol; Uroseptol†; ***India:*** Emcredil; Vecredil; ***Pol.:*** Rivanol; Rivanolum; Rivel; Rywanol; ***Turk.:*** Rivanol.

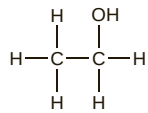
Multi-ingredient: ***Arg.:*** Carnot Topico; Nene Dent; Otocuril; ***Austral.:*** Medijel; ***Austria:*** Dermowund; ***Braz.:*** Acridin; Cystex; Senol†; ***Chile:*** Molca; ***Cz.:*** Tannacomp†; ***Fr.:*** Chromargon; Pyorex; ***Ger.:*** Anaesthesin-Rivanol; Nordapanin N†; Otolitan N mit Rivanol†; Tannacomp; ***Hong Kong:*** Burn Cream†; Medijel; ***Hung.:*** Glycosept; ***India:*** Anaebell†; Emscab; ***Israel:*** Medijel; ***Malaysia:*** Burnol Plus; Medijel; ***NZ:*** Medijel; ***Pol.:*** Septalan; ***S.Afr.:*** Achromide; Daromide; Vagarsol; ***Singapore:*** Burnol Plus; Medijel; ***Spain:*** Antigrietun; Hepro; ***Switz.:*** Euproctol N; Flavangin†; Haemocortin; Haemolan; Tyrothricin; ***Thai.:*** Burnol Plus; Flavinol; ***UK:*** Iglu; Medijel; ***USA:*** Alasulf; Deltavac; DIT1-2.

Alcohol ⊗

Aethanolum; Alcool; Alkol; Etanol; Etanol (96%); Etanol bezwodny; Etanoli; Etanolis; Éthanol; Ethanol; Ethanolum; Ethyl Alcohol.

Алкоголь; Этанол

C_2H_5OH = 46.07.
CAS — 64-17-5.
ATC — D08AX08; V03AB16; V03AZ01.
ATC Vet — QD08AX08; QV03AB16; QV03AZ01.



NOTE. The following terms have been used as 'street names' (see p.vi) or slang names for various forms of alcohol:

Booze; Drinks; Grog; Juice; Jungle juice; Liq; Liquor; Lunch head; Moonshine; Piss; Sauce; Schwillins.

Pharmacopoeias. Various strengths are included in *Br.*, *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, *US*, and *Viet.* Also in *USNF.*

In *Martindale* the term alcohol is used for alcohol 95 or 96% v/v.

Ph. Eur. 6.2 (Ethanol, Anhydrous; Ethanolum Anhydricum; Ethanol BP 2008). It contains not less than 99.5% v/v or 99.2% w/w of C_2H_5OH at 20°. A colourless, clear, volatile, flammable, hygroscopic liquid; it burns with a blue, smokeless flame. B.p. about 78°. Miscible with water and with dichloromethane. Protect from light.

The BP 2008 gives Absolute Alcohol and Dehydrated Alcohol as approved synonyms.

Ph. Eur. 6.2 (Ethanol (96 per cent)). It contains not less than 95.1% v/v or 92.6% w/w and not more than 96.9% v/v or 95.2% w/w of C_2H_5OH at 20°, and water. A colourless, clear, volatile, flammable, hygroscopic liquid; it burns with a blue, smokeless flame. B.p. about 78°. Miscible with water and with dichloromethane. Protect from light.

The BP 2008 gives Alcohol (96 per cent) as an approved synonym.

BP 2008 (Dilute Ethanols). The monograph describes several dilute alcohols containing between 20 and 90% v/v of C_2H_5OH, and one of these, ethanol (90%), is also known as rectified spirit.

USP 31 (Alcohol). It contains not less than 92.3% w/w or 94.9% w/v and not more than 93.8% w/w or 96.0% w/v of C_2H_5OH at 15.56°. A clear, colourless, mobile, volatile liquid with a characteristic odour and burning taste; it is flammable. B.p. about 78°. Miscible with water and with almost all other organic solvents. Store in airtight containers. Protect from light.

USP 31 (Dehydrated Alcohol). It contains not less than 99.5% v/v or 99.2% w/w of C_2H_5OH (sp. gr. not more than 0.7962 at 15.56°). Store in airtight containers. Protect from light.

USNF 26 (Diluted Alcohol). It contains 48.4 to 49.5% v/v or 41 to 42% w/w of C_2H_5OH. Store away from fire in airtight containers.

Alcoholic strength. This is expressed as a percentage by volume of alcohol. It was previously often expressed in terms of *proof spirit*. Proof spirit contained about 57.1% v/v or 49.2% w/w of C_2H_5OH, and was defined as 'that which at the temperature of 51°F weighs exactly twelve-thirteenths of an equal measure of distilled water'. Spirit of such a strength that 100 volumes contained as much ethyl alcohol as 160 volumes of proof spirit was described as '60 OP' (over proof). Spirit of which 100 volumes contained as much alcohol as 40 volumes of proof spirit was described as '60 UP' (under proof).

An alternative method of indicating spirit strength was used on the labels of alcoholic beverages in the UK when the strength was given as a number of degrees, proof spirit being taken as 100°. In the USA alcoholic strength is expressed in degrees, the value of which is equal to twice the percentage by volume. Thus 70° proof (old UK system) is equivalent to 40% v/v, and therefore to 80° proof (USA system).

Adverse Effects

Adverse effects of alcohol arise chiefly from the intake of alcoholic beverages. The concentration of alcohol in the blood producing a state of intoxication varies between individuals.

- Low concentrations (up to 180 mg per 100 mL) of alcohol may result in impaired vision, reaction time, and coordination and emotional lability.
- At low to moderate concentrations (180 to 350 mg per 100 mL), alcohol acts as an apparent stimulant; depression of cortical function causes loss of judgement, slurred speech, diplopia, blurred vision, ataxia, lack of coordination, blackouts, sweating, tachycardia, nausea, vomiting, and incontinence. Alcohol inhibits the release of antidiuretic hormone resulting in enhanced diuresis. Acidosis (especially in children), hypoglycaemia, and hypokalaemia may occur.
- High concentrations (350 to 450 mg per 100 mL) of alcohol result in cold clammy skin, hypothermia, hypotension, stupor, coma, dilated pupils, and depressed or absent tendon reflexes. Severe hypoglycaemia, convulsions, respiratory depression, and metabolic acidosis may occur. Cardiac arrhythmias such as atrial fibrillation and AV block have been recorded.

The median lethal blood-alcohol concentration is generally estimated to be about 400 to 500 mg per 100 mL. Death may occur at lower blood-alcohol concentrations due to inhalation of vomit during unconsciousness.

Chronic excessive consumption of alcohol may cause damage to many organs, particularly the brain and the

liver. Possible direct toxic effects of alcohol on the brain, as well as thiamine deficiency, may lead to Wernicke-Korsakoff syndrome. Fat deposits may occur in the liver and there may be a reduction in various blood-cell counts. Nutritional diseases may occur due to inadequate diet. High alcohol consumption has been associated with pancreatitis, and an increased risk of cardiovascular disease, although some consider that moderate consumption might have a protective effect against ischaemic heart disease.

Alcohol consumption has also been associated with an increased risk of some types of cancer.

The term '**alcoholism**' may be used to denote dependence on alcohol, which is of the barbiturate-alcohol type (see Amobarbital, p.962) and usually involves tolerance to other sedatives and anaesthetics. After prolonged periods of excessive alcohol consumption, a drop in blood-alcohol concentration may precipitate a withdrawal syndrome characterised by tremor, agitation, feelings of dread, nausea, vomiting, and sweating; hallucinations, seizures, and delirium tremens may also develop.

A **fetal alcohol syndrome** has been identified in some infants born to some alcoholic mothers; such infants have a distinctive set of facial anomalies, growth retardation, and significant learning and/or behavioural problems. There have been some reports of the syndrome and other adverse effects on the fetus being associated with moderate alcohol intake in pregnancy. It is therefore generally suggested that alcohol is avoided, or at least intake limited, during pregnancy (see Pregnancy, below).

Frequent application of alcohol to the skin produces irritation and dry skin.

Effects on the skin. A 70% solution of alcohol, containing povidone-iodine, caused partial thickness chemical burns beneath tourniquets in 3 young children.[1] Other adverse effects on the skin reported with the topical application of alcohols have included necrosis after skin cleansing of preterm neonates with methylated spirits[2,3] and haemorrhagic skin necrosis due to the alcohol content of chlorhexidine in spirit used as a disinfectant in umbilical artery catheterisation in preterm infants.[4]

See also Children, under Adverse Effects of Isopropyl Alcohol, p.1651.

1. Dickinson JC, Bailey BN. Chemical burns beneath tourniquets. *BMJ* 1988; **297:** 1513.
2. Harpin V, Rutter N. Percutaneous alcohol absorption and skin necrosis in a preterm infant. *Arch Dis Child* 1982; **57:** 477–9.
3. Murch S, Costelloe K. Hyperosmolality related to propylene glycol in an infant. *BMJ* 1990; **301:** 389.
4. Al-Jawad ST. Percutaneous alcohol absorption and skin necrosis in a preterm infant. *Arch Dis Child* 1983; **58:** 395–6.

Treatment of Adverse Effects

Treatment of acute poisoning with alcohol should include hydration with intravenous fluids, control of nausea and vomiting, and correction of electrolyte imbalances, such as hypomagnesaemia. Protection of the airway is crucial and ventilation may be required in cases of respiratory depression. Glucose is indicated for patients with hypoglycaemia, while thiamine supplementation should be considered for chronic alcoholics. Hypothermia and hypotension should be corrected. Convulsions may be controlled with intravenous benzodiazepines or phenytoin. Haemodialysis is of value in severe alcohol poisoning. Gut decontamination and activated charcoal are unlikely to be of benefit due to the rapid absorption of alcohol through intestinal mucosa. The use of intravenous infusions of fructose to treat severe alcohol poisoning is not recommended.

The management of the alcohol withdrawal syndrome and long-term abstinence following withdrawal are discussed below.

Alcohol withdrawal and abstinence. The alcohol withdrawal syndrome presents in the early stages as a classical hyperadrenergic state with tremor, tachycardia, sweating, and hypertension. Sometimes this is accompanied by mild disorientation, anxiety, impaired concentration, depression, agitation, and gastrointestinal symptoms. Insomnia, nightmares, and transient hallucinations can also be present. The condition may be self-limiting without the need for therapeutic intervention or it may progress to the severe and potentially fatal condition of delirium tremens (DTs), often characterised by delirium, disorientation, and hallucinations. In some cases generalised tonic-clonic seizures occur within 24 hours of alcohol withdrawal and are followed by delirium tremens.

The general management of the alcohol **withdrawal** syndrome and maintenance of abstinence have been the subject of many reviews and discussions.[1-15] In most cases symptoms do not require treatment and disappear within a few days, but more severe cases may require managed withdrawal from alcohol to avoid complications.

Benzodiazepines are usually the drugs of first choice because of their sedative, anxiolytic and anticonvulsant properties. If given promptly, benzodiazepines can prevent progression to seizures and delirium tremens. Longer-acting drugs such as chlordiazepoxide or diazepam may be more effective against withdrawal seizures and provide smoother withdrawal, while shorter-acting ones such as lorazepam or oxazepam have a smaller risk of producing oversedation and may be more suitable for use in the elderly and, since they do not rely on hepatic enzymes for their metabolism, for patients with liver disease. Because of the risk of dependence benzodiazepines should only be given in short courses. Some advocate that benzodiazepine dosage should be adjusted according to the severity of symptoms with special care being paid to patients with a history of withdrawal seizures, comorbid conditions, or those using sedative or hypnotic medication. This reduces the amount of drug required and the duration of treatment but entails regular monitoring by trained nursing staff. For mild to moderate symptoms, standard anxiolytic or muscle-relaxing oral doses of benzodiazepines may be sufficient. For severe symptoms, or for the treatment of delirium tremens, higher doses and use of the intravenous route may be required. *Clomethiazole* appears to be an effective alternative to the benzodiazepines (but see under Interactions of Clomethiazole, p.978); although widely used in Europe, it is not available in the USA. Some centres use phenobarbital but *barbiturates* are generally not recommended for the treatment of alcohol withdrawal syndrome.

Antipsychotics are not usually recommended for use in the control of symptoms of alcohol withdrawal since they do not reduce delirium tremens and some may reduce the seizure threshold. However, they might be considered for use as adjuncts in patients requiring treatment of marked agitation or hallucinations.

The generalised tonic-clonic seizures associated with alcohol withdrawal are usually self-limiting and patients who experience only one or two seizures do not usually require any specific treatment beyond continuing therapy with benzodiazepines or clomethiazole. For recurrent seizures or status epilepticus (p.469) a benzodiazepine may be given intravenously. Other types of seizure may be associated with head trauma or pre-existing seizure disorders (p.465) and should be treated accordingly. Other *antiepileptics* such as carbamazepine have been tried in the treatment of alcohol withdrawal seizures and may be of use as adjuncts in controlling other symptoms of alcohol withdrawal syndrome. As benzodiazepines are effective in preventing withdrawal seizures, other prophylactic drugs are not usually indicated.

Beta blockers can reduce symptoms of autonomic overactivity such as tachycardia, hypertension, tremor, and agitation but because they can mask these symptoms of withdrawal and do not prevent the development of more serious complications they should not be used alone. Some beta blockers such as propranolol that penetrate the CNS may produce CNS effects that complicate therapy. The alpha$_2$-adrenoceptor agonist *clonidine* may be of similar benefit as an adjunct.

Other drugs that have been reported to be of benefit in alcohol withdrawal syndrome include nitrous oxide and gamma-hydroxybutyric acid.

It is essential that in all cases of alcohol withdrawal syndrome hypoglycaemia, dehydration, electrolyte disturbances (in particular magnesium), and vitamin deficiencies be corrected. However, hydration should be undertaken with care as alcoholics may be more prone to develop cerebral oedema, the management of which is discussed under Raised Intracranial Pressure on p.1181. It is usually recommended that all patients should be given thiamine because of their increased risk of developing Wernicke-Korsakoff syndrome (p.1977). It should be noted that giving intravenous glucose before thiamine may precipitate Wernicke's encephalopathy in thiamine-deficient patients.

Abstinence. Once the initial acute withdrawal of alcohol is achieved treatment may be required to maintain long-term abstinence. Pharmacotherapy should only be used as an adjunct to psychotherapy and supportive care. Drugs used to modify alcohol seeking behaviour either sensitise the patient to alcohol (aversive drugs) or reduce or alleviate the craving for alcohol. The main ones used for aversive therapy have historically been *disulfiram* and *calcium carbimide*. A patient who ingests alcohol after taking an adequate dose of one of these drugs will experience a severe and unpleasant reaction (see Adverse Effects of Disulfiram, p.2296). However, the deterrent value of aversive drugs, and their potential toxicity, has long been a matter of debate. Such treatment is likely to be of little use unless it is undertaken with the willing cooperation of the patient and is used with psychotherapy, and even then there is no evidence that it has any effect on the long-term course of alcoholism.

Of those drugs that have been reported to reduce alcohol craving *acamprosate* and *naltrexone* have been the most promising as adjuncts for management of alcohol dependence and have been shown to improve abstinence and reduce relapse rates. Whether benefit is maintained long-term after treatment is stopped is unclear. *Other drugs* tried with varying benefit include aripiprazole, tiapride, gamma-hydroxybutyric acid, bromocriptine, nalmefene, and topiramate. Experimental evidence suggests that serotonin plays a role in the impulsivity and craving and is partly responsible for alcohol dependence. However, studies with SSRIs in alcohol dependence have been disappointing and it would appear that the benefit is in treating underlying depression rather than influencing drinking behaviour. Similar results have been noted with other drugs acting at serotonin receptors such as buspirone, ritanserin, and nefazodone. However, studies with ondansetron have shown some efficacy on drinking frequency and intake.

1. Mayo-Smith MF. American Society of Addiction Medicine Working Group on Pharmacological Management of Alcohol Withdrawal. Pharmacological management of alcohol withdrawal: a meta-analysis and evidence-based practice guideline. *JAMA* 1997; **278:** 144–51.
2. O'Connor PG, Schottenfeld RS. Patients with alcohol problems. *N Engl J Med* 1998; **338:** 592–602.
3. Tinsley JA, *et al.* Developments in the treatment of alcoholism. *Mayo Clin Proc* 1998; **73:** 857–63.
4. Schaffer A, Naraiyo CA. Recommended drug treatment strategies for the alcoholic patient. *Drugs* 1998; **56:** 571–85.
5. Naik PC, Brownell LW. Treatment of psychiatric aspects of alcohol misuse. *Hosp Med* 1999; **60:** 173–7.
6. Garbutt JC, *et al.* Pharmacological treatment of alcohol dependence: a review of the evidence. *JAMA* 1999; **281:** 1318–25.
7. Swift RM. Drug therapy for alcohol dependence. *N Engl J Med* 1999; **340:** 1482–90.
8. Kraemer KL, *et al.* Managing alcohol withdrawal in the elderly. *Drugs Aging* 1999; **14:** 409–25.
9. Myrick H, *et al.* New developments in the pharmacotherapy of alcohol dependence. *Am J Addict* 2001; **10** (suppl): 3–15.
10. Kosten TR, O'Connor PG. Management of drug and alcohol withdrawal. *N Engl J Med* 2003; **348:** 1786–95.
11. Mayo-Smith MF, *et al.* Management of alcohol withdrawal delirium: an evidence-based practice guideline. *Arch Intern Med* 2004; **164:** 1405–12.
12. Mann K. Pharmacotherapy of alcohol dependence: a review of the clinical data. *CNS Drugs* 2004; **18:** 485–504.
13. Kenna GA, *et al.* Pharmacotherapy, pharmacogenomics, and the future of alcohol dependence treatment, part 1. *Am J Health-Syst Pharm* 2004; **61:** 2272–9.
14. Kenna GA, *et al.* Pharmacotherapy, pharmacogenomics, and the future of alcohol dependence treatment, part 2. *Am J Health-Syst Pharm* 2004; **61:** 2380–8.
15. Srisurapanont M, Jarusuraisin N. Opioid antagonists for alcohol dependence. Available in The Cochrane Database of Systemic Reviews; Issue 1. Chichester: John Wiley; 2005 (accessed 15/03/06).

Precautions

Excessive alcohol intake should be avoided. In the UK, the Department of Health advises that men should not drink more than 3 to 4 units of alcohol per day, and women not more than 2 to 3 units of alcohol per day, regardless of whether one drinks every day, once or twice a week, or occasionally. A unit of alcohol is defined as 10 mL of pure alcohol. A normal measure of spirits in a public house contains about 1 unit of alcohol. A pint of ordinary strength lager or cider, a pint of bitter, or 175 mL glass of wine contain about 2 units of alcohol, while a pint of strong lager contains about 3 units of alcohol. Women and the elderly may be more susceptible to the adverse effects of alcohol ingestion.

Alcohol may aggravate peptic ulcer disease or hepatic impairment and impair control of diabetes mellitus or epilepsy. Ingestion of alcohol during pregnancy or breast feeding is not advisable. In chronic alcoholics there may be tolerance to the effects of other CNS depressants including general anaesthetics.

All processes requiring judgement and coordination are affected by alcohol and these include the driving of any form of transport and the operating of machinery. It is an offence in many countries for motorists to drive when the blood-alcohol concentration is above a stated value while in some countries any detectable concentration is an offence. The alcohol concentration in urine and expired air can be used to estimate the blood-alcohol concentration.

It should be remembered that alcohol may be present in a number of pharmaceutical preparations such as elixirs and mouthwashes, and that children may be particularly susceptible to its hypoglycaemic effects.

Breast feeding. The American Academy of Pediatrics[1] states that, although usually compatible with breast feeding, ingestion of large amounts of alcohol by a breast-feeding mother may cause drowsiness, diaphoresis, deep sleep, weakness, decrease in

linear growth, and abnormal weight gain in the infant; maternal ingestion of 1 g/kg or more daily decreases the milk ejection reflex.

1. 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 15/03/06)

Driving. In addition to the legal maximum blood-alcohol concentration permitted for motorists, in the UK there are restrictions on holding a driving licence for those who persistently misuse alcohol, have alcohol dependency, have had an alcohol-related seizure, or have an alcohol-related disorder.[1]

1. Driver and Vehicle Licensing Agency. For medical practitioners: at a glance guide to the current medical standards of fitness to drive (issued February 2008). Available at: http://www.dvla.gov.uk/media/pdf/medical/aagv1.pdf (accessed 14/08/08)

Porphyria. Alcohol has been associated with acute attacks of porphyria and is considered unsafe in porphyric patients.

Pregnancy. Alcohol crosses the placenta and is both teratogenic and fetotoxic in humans.[1,2] Binge drinking or excessive alcohol intake is associated with low birth-weight, behavioural and intellectual difficulties later in life, and fetal alcohol syndrome (see Adverse Effects, above). It is therefore generally agreed that pregnant women should avoid or limit their intake of alcohol although guidance from professional bodies is slightly inconsistent. In the UK, the Royal College of Obstetricians and Gynaecologists[2] states that while the safest approach may be to avoid any alcohol intake during pregnancy, there is no evidence of harm from infrequent or low levels of alcohol intake (no more than one or two units once or twice a week) particularly after the first trimester. NICE[1] suggests limiting alcohol intake to no more than one unit per day. However, in the USA, the Surgeon General's Office[3] and the American Academy of Pediatrics[4] advise women who are pregnant or women who are planning a pregnancy to avoid alcohol use.

1. National Collaborating Centre for Women's and Children's Health/National Institute for Clinical Excellence. Antenatal care: routine care for the healthy pregnant woman (issued October 2003). Available at: http://www.rcog.org.uk/resources/Public/pdf/Antenatal_Care.pdf (accessed 19/09/06)
2. Royal College of Obstetricians and Gynaecologists. RCOG Statement no. 5: alcohol consumption and the outcomes of pregnancy (issued March 2006). Available at: http://www.rcog.org.uk/resources/Public/pdf/alcohol_pregnancy_rcog_statement5a.pdf (accessed 19/09/06)
3. United States Department of Health and Human Services. News release: U.S. Surgeon General releases advisory on alcohol use in pregnancy (issued 21st February 2005). Available at: http://www.hhs.gov/surgeongeneral/pressreleases/sg02222005.html (accessed 19/09/06)
4. American Academy of Pediatrics: Committee on Substance Abuse and Committee on Children With Disabilities. Fetal alcohol syndrome and alcohol-related neurodevelopmental disorders. *Pediatrics* 2000; **106:** 358–61. Also available at: http://www.pediatrics.org/cgi/content/full/106/2/358 (accessed 19/09/06)

Interactions

Reports of interactions between alcohol and other drugs are not consistent, possibly because acute alcohol intake may inhibit drug metabolism while chronic alcohol intake can enhance the induction of drug-metabolising enzymes in the liver.

Alcohol can enhance the acute effects of CNS depressants, such as hypnotics, antihistamines, opioid analgesics, antiepileptics, antidepressants, antipsychotics, and sedatives. In addition 'dose dumping', rapid and potentially fatal release of high doses from modified-release formulations, has occurred when some opioid preparations were taken with alcohol.

Unpleasant reactions, similar to those occurring with disulfiram (p.2296), may occur when alcohol is taken with chlorpropamide, griseofulvin, mepacrine, metronidazole and other nitroimidazoles, the nitrofuran derivatives furazolidone and nifuratel, procarbazine, or some cephalosporins. Alcoholic beverages containing tyramine may cause reactions when taken by patients receiving MAOIs.

Alcohol can cause hypoglycaemic reactions in patients receiving sulfonylurea antidiabetics or insulin, and orthostatic hypotension in patients taking drugs with a vasodilator action. It may enhance the hypotensive effects of antihypertensives and has also increased the sedative effect of indoramin. Alcohol may increase gastric bleeding caused by analgesics and can have a variable effect on oral anticoagulants. It may decrease the antidiuretic effect of vasopressin.

◊ Reviews.

1. McInnes GT. Interactions that matter: alcohol. *Prescribers' J* 1985; **25:** 87–90.
2. Lieber CS. Interaction of alcohol with other drugs and nutrients: implications for the therapy of alcoholic liver disease. *Drugs* 1990; **40** (suppl 3): 23–44.
3. Fraser AG. Pharmacokinetic interactions between alcohol and other drugs. *Clin Pharmacokinet* 1997; **33:** 79–90.
4. Weathermon R, Crabb DW. Alcohol and medication interactions. *Alcohol Res Health* 1999; **23:** 40–54.

Cycloserine. Increased blood-alcohol concentrations have been reported in patients receiving cycloserine.[1]

1. Glass F, *et al.* Beobachtungen und untersuchungen über die gemeinsame wirkung von alkohol und D-cycloserin. *Arzneimittelforschung* 1965; **15:** 684–8.

H_2-antagonists. The existence of an interaction between H_2-antagonists and alcohol is controversial and has not been established. While some studies suggest that *cimetidine*[1-3] and *nizatidine*[3] can increase peak blood-alcohol concentrations the effects of *ranitidine*[2,4] have been variable; *famotidine* appears to have no significant effect.[2] Later studies report that any interaction between H_2-antagonists and alcohol is minor and unlikely to be of clinical importance.[5-8]

1. Caballeria J, *et al.* Effects of cimetidine on gastric alcohol dehydrogenase activity and blood ethanol levels. *Gastroenterology* 1989; **96:** 388–92.
2. DiPadova C, *et al.* Effects of ranitidine on blood alcohol levels after ethanol ingestion: comparison with other H -receptor antagonists. *JAMA* 1992; **267:** 83–6.
3. Holt S, *et al.* Evidence for an interaction between alcohol and certain H receptor antagonists. *Gut* 1991; **32:** A1220.
4. Toon S, *et al.* Lack of effect of high dose ranitidine on the postprandial pharmacokinetics of alcohol. *Gut* 1992; **33** (suppl): S10.
5. Raufman J-P, *et al.* Histamine-2 receptor antagonists do not alter serum ethanol levels in fed, nonalcoholic men. *Ann Intern Med* 1993; **118:** 488–94.
6. Levitt MD. Do histamine-2 receptor antagonists influence the metabolism of ethanol? *Ann Intern Med* 1993; **118:** 564–5.
7. Kleine M-W, Ertl D. Comparative trial in volunteers to investigate possible ethanol-ranitidine interaction. *Ann Pharmacother* 1993; **27:** 841–5.
8. Gugler R. H -antagonists and alcohol: do they interact? *Drug Safety* 1994; **10:** 271–80.

Paracetamol. The effects of paracetamol poisoning may be exacerbated by chronic alcohol consumption (see p.108).

Verapamil. When verapamil has been taken with alcohol there has been a reported increase in peak blood-alcohol concentrations of about 17%.[1] Such an interaction may extend the toxic effects of alcohol and raise its blood concentration above the legal limit for driving.[2]

1. Schumock G, *et al.* Verapamil inhibits ethanol elimination. *Pharmacotherapy* 1989; **9:** 184–5.
2. Anonymous. Does verapamil increase the effects of alcohol? *Pharm J* 1990; **244:** 14.

Pharmacokinetics

Alcohol is rapidly absorbed from the gastrointestinal tract and is distributed throughout the body fluids. It readily crosses the placenta. Alcohol vapour can be absorbed through the lungs. Absorption through intact skin is said to be negligible.

The rate of absorption of alcohol from the gastrointestinal tract may be modified by such factors as the presence of food, the concentration of alcohol, carbonation of the alcoholic beverage, and the period of time during which it is ingested.

Alcohol is mainly metabolised in the liver; it is converted by alcohol dehydrogenase to acetaldehyde and is then further oxidised to acetate. A hepatic microsomal oxidising system is also involved. About 90 to 98% of alcohol is oxidised and the remainder is excreted unchanged by the kidneys and the lungs. It also appears in breast milk, sweat, and other secretions.

The rate of metabolism may be accelerated after repeated excessive intake and by certain substances including insulin.

◊ Reviews.

1. Holford NHG. Clinical pharmacokinetics of ethanol. *Clin Pharmacokinet* 1987; **13:** 273–92.
2. Lotsof J. A revised pharmacokinetic model for alcohol. *Clin Pharmacokinet* 2003; **42:** 585–7.
3. Paton A. Alcohol in the body. *BMJ* 2005; **330:** 85–7.

Uses and Administration

Alcohol has been used and abused for many thousands of years, in the form of alcoholic beverages, for its effects on the CNS. However, it also has pharmaceutical applications.

Alcohol is bacteriostatic at low concentrations but has bactericidal activity at higher concentrations; it does not, however, destroy bacterial spores. The mechanism of action appears to be denaturation of proteins. In the total absence of water, proteins are not denatured as rapidly as when water is present. Its bactericidal activity drops sharply when diluted below a 50% concentration and the optimal bactericidal concentration is 60 to 90% by volume. Alcohol also exhibits some fungicidal and virucidal activity. It is used to disinfect skin before injection, venepuncture, or surgical procedures. It is also used to disinfect hands and clean surfaces. A concentration of 70%, often as methylated spirits (p.1652), is commonly used for disinfection. Alcohol should not be used for disinfection of surgical or dental instruments because of its low efficacy against bacterial spores and inability to penetrate protein-rich materials.

Alcohol also has anhidrotic, rubefacient, and astringent and haemostatic properties. It is sometimes used for its skin-cooling properties and to harden the skin. It is an ingredient of several topical preparations used for skin disorders.

Alcohol is widely used as a solvent and preservative in pharmaceutical preparations.

Alcohol may be used as a neurolytic in the management of severe and chronic pain.

Alcohol is given intravenously in the treatment of acute poisoning from ethylene glycol (p.2300) and methyl alcohol (p.2024).

Alcohol is also used in sclerotherapy.

Pain. The use of alcohol as a neurolytic to produce destructive nerve block (see under Pain, p.1852) has produced variable results, and some consider the risk of complications outweighs the benefits. However, alcohol has been injected into the pituitary gland for relief of severe pain of the head and neck;[1,2] doses of 1 mL of absolute alcohol have been used.[1] It may be useful in coeliac plexus block, and has been injected into the muscle sheath to relieve painful muscle spasms in patients with multiple sclerosis.[1] Alcohol 50 to 100% may be used for peripheral or central nerve block in terminally ill patients with pain that does not respond to drug therapy;[3,4] the block produced by alcohol may occasionally last up to 2 years, even longer than that produced by phenol. However, larger volumes of alcohol than phenol are required, which means that blockade may be less precise due to leakage to proximal sites;[4] in addition, alcohol may exacerbate local pain on injection, because of its irritant effect on the tissues, and injection of a local anaesthetic beforehand, or giving the alcohol combined with a local anaesthetic, may be necessary.[4,5]

Intrathecal injection of alcohol has also been used for the intractable pain of spasticity (p.1887); early use, as soon as spasticity becomes painful and disabling, has been advocated.[6]

1. Lloyd JW. Use of anaesthesia: the anaesthetist and the pain clinic. *BMJ* 1980; **281:** 432–4.
2. Lipton S. Pain relief in active patients with cancer: the early use of nerve blocks improves the quality of life. *BMJ* 1989; **298:** 37–8.
3. Hardy, PAJ. The role of the pain clinic in the management of the terminally ill. *Br J Hosp Med* 1990; **43:** 142–6.
4. Gordin V, *et al.* Acute and chronic pain management in palliative care. *Best Pract Res Clin Obstet Gynaecol* 2001; **15:** 203–34.
5. Kongsgaard UE, *et al.* Nevrolytisk blokade hos kreftpasienter–fortsatt en nyttig behandling. *Tidsskr Nor Laegeforen* 2004; **124:** 481–3.
6. Viel E, *et al.* Spasticité: intérêt du testing par anesthésie locorégionale et blocs thérapeutiques. *Ann Fr Anesth Reanim* 2005; **24:** 667–72.

Sclerotherapy. Alcohol has been used successfully as a sclerosant in a variety of conditions including aldosterone-producing adenoma,[1] parathyroid adenomas,[2] thyroid nodules,[3,4] advanced rectal cancer,[5] hepatocellular carcinoma,[6,7] dysphagia associated with oesophagastric cancer,[8,9] hepatic[10] or renal[11] cysts, and gallbladder obstruction.[12] It has also been used in the sclerotherapy of oesophageal varices,[13,14] although the safety of this procedure has been questioned after a report of complications developing in 13 of 17 patients, 2 of whom died.[15] Other conditions in which alcohol has been used as a sclerosant include bleeding from ruptured hepatomas[16] and in peptic ulcer disease,[17] vascular malformations,[18] and obstructive cardiomyopathies[19] resistant to usual treatment.

Other sclerosants used in oesophageal varices are discussed on p.2346.

1. Hokotate H, *et al.* Aldosteronomas: experience with superselective adrenal arterial embolization in 33 cases. *Radiology* 2003; **227:** 401–6.
2. Vergès B, *et al.* Traitement des adénomes parathyroïdiens par alcoolisation sous contrôle échographique. *Ann Chir* 2000; **125:** 457–60.
3. Monzani F, *et al.* Autonomous thyroid nodule and percutaneous ethanol injection. *Lancet* 1991; **337:** 743.
4. Bennedbaek FN, Hegedüs L. Alcohol sclerotherapy for benign solitary solid cold thyroid nodules. *Lancet* 1995; **346:** 1227.
5. Payne-James J, *et al.* Advanced rectal cancer. *BMJ* 1990; **300:** 746.
6. Lencioni R, *et al.* Alcoolizzazione percutanea dell'epatocarcinoma: risultati a lungo termine. *Radiol Med (Torino)* 1997; **94:** 8–13.

7. Ebara M, *et al*. Percutaneous ethanol injection for small hepatocellular carcinoma: therapeutic efficacy based on 20-year observation. *J Hepatol* 2005; **43:** 458–64.
8. Payne-James JJ, *et al.* Use of ethanol-induced tumor necrosis to palliate dysphagia in patients with esophagogastric cancer. *Gastrointest Endosc* 1990; **36:** 43–6.
9. Stanners AJ, *et al.* Alcohol injection for palliation of malignant oesophageal disease. *Lancet* 1993; **341:** 767.
10. Larsen TB, *et al*. Single-session alcohol sclerotherapy in symptomatic benign hepatic cysts: long-term results. *Acta Radiol* 1999; **40:** 636–8.
11. Mohsen T, Gomha MA. Treatment of symptomatic simple renal cysts by percutaneous aspiration and ethanol sclerotherapy. *BJU Int* 2005; **96:** 1369–72.
12. Asfar S, *et al*. Percutaneous sclerosis of gallbladder. *Lancet* 1989; **ii:** 387.
13. Meirelles-Santos JO, *et al.* Absolute ethanol and 5% ethanolamine oleate are comparable for sclerotherapy of esophageal varices. *Gastrointest Endosc* 2000; **51:** 573 6.
14. Ferrari AP, *et al*. Efficacy of absolute alcohol injection compared with band ligation in the eradication of esophageal varices. *Arq Gastroenterol* 2005; **42:** 72–6.
15. Bhargava DK, *et al.* Endoscopic sclerotherapy using absolute alcohol. *Gut* 1986; **27:** 1518.
16. Chung SCS, *et al*. Injection of alcohol to control bleeding from ruptured hepatomas. *BMJ* 1990; **301:** 421.
17. Lin HJ, *et al*. Heat probe thermocoagulation and pure alcohol injection in massive peptic ulcer haemorrhage: a prospective, randomised controlled trial. *Gut* 1990; **31:** 753–7.
18. Deveikis JP. Percutaneous ethanol sclerotherapy for vascular malformations in the head and neck. *Arch Facial Plast Surg* 2005; **7:** 322–5.
19. Sigwart U. Non-surgical myocardial reduction for hypertrophic obstructive cardiomyopathy. *Lancet* 1995; **346:** 211–14.

Preparations

USP 31: Alcohol in Dextrose Injection; Dehydrated Alcohol Injection; Rubbing Alcohol.

Proprietary Preparations (details are given in Part 3)
Austral.: Microshield Antimicrobial Hand Gel; ***Canad.:*** Avagard D; Biobase; Dial†; Duonalc-E Mild; Instant Hand Sanitizer; One Step Hand Sanitizer; President's Choice Hand Sanitizer; Purell; ***Fr.:*** Curethyl; Optrex; Pharmadose alcool; ***Ger.:*** AHD 2000; Amphisept E; Fugaten; Klosterfrau Franzbranntwein Menthol; Manusept HD†; Sterillium Virugard; ***Hung.:*** Saletanol D†; ***Indon.:*** Handy Clean; ***Malaysia:*** QuicKlean; ***Philipp.:*** AHD 2000; ***Switz.:*** Amphisept†; ***USA:*** Alcare; Bodi Line Action; Gel-Stat; Kleen-Handz†.

Multi-ingredient: ***Austral.:*** Dermatech Liquid; Johnsons Clean & Clear Invisible Blemish Treatment†; Johnsons Clean & Clear Oil Controlling Toner; Microshield Handrub; Microshield Tincture; ***Austria:*** Dodesept; Dodesept Gefarbt; Dodesept N; Skinsept; Skinsept mucosa; ***Belg.:*** Sabenyl; Solution Antiseptique Stella†; ***Canad.:*** Avagard CHG; Biobase-G; Chase Kolik Gripe Water; Dilusol AHA†; Dilusol†; Duonalc-E; Franzbranns†; Green Antiseptic Mouthwash & Gargle; Mouthwash Antiseptic & Gargle†; MRX†; Sans-Acne†; ***Chile:*** Abboderm†; Acnoxyl Locion Tonica; Alcolex; Listerine; Listermint Con Fluor; Oralfresh Citrus; Oralfresh Clasico; Oralfresh Menta; ***Cz.:*** Promanum N; Skinsept mucosa†; Softa-Man; ***Fin.:*** Otiborin; Somanol + Ethanol; ***Fr.:*** Alco-Aloe; Aniospray 29; Chlorispray†; Parogencyl gencives fragilisees†; ***Ger.:*** Aerodesin; Autoderm Extra; Bacillol; Bacillol AF; Betaseptic; Desderman N†; Franzbranntwein mit Fichtennadelol†; Freka-Derm; Freka-Nol; Freka-Sept 80; Hospidermin; Hospisept; Incidin; Incidin Spezial; Incidur Spray†; Klosterfrau Franzbranntwein; Klosterfrau Franzbranntwein Latschenkiefer; Mucasept-A; Promanum N; Riwa Franzbranntwein; Skinsept G; Skinsept mucosa; Softa Man; Softasept N; Spitacid; ***Gr.:*** Faragel-Forte; ***Hong Kong:*** Listerine; Listerine Tartar Control; ***Hung.:*** Fructosol E†; ***India:*** Daslin; Dettolin; ***Indon.:*** Allerin; Benadryl CM; Berlifed; Chlorphemin; Coricidin; Dactylen; Domeryl; Eksedryl Expectorant; Inadryl; Inadryl Plus; Koffex; Listerine; Listerine Coolmint; Neo Novapon; Nichodryl; OBH; Paradryl; ***Israel:*** Alcosept; Oxy Clean Medicated; Salisol; Septadine; Spirit Salicyl; V-Tabur; ***Ital.:*** Bemonalcool; Citroclorex; Citromed 80 and 85; Citromed Chirurgico; Citrosil Alcolico Azzuro; Citrosil Alcolico Bruno; Citrosil Alcolico Incolore; Citrosteril Strumenti; Clorexan Ferri; Eso Ferri Alcolico; Esoalcolico Incolore; Esoform Alcolico; Forbrand; Formedico; Incidin Spezial; Incidur Spray; Jodieci; Melsept Spray; Neomedil; Panseptil; Sekumatic; Simpottantacinque; Softa Man; ***Neth.:*** Softa-Man; ***Philipp.:*** BSI Medicated Spray; Dermablend Clarifying; Listerine Coolmint; Listerine Original; Zilactin; Ziladent; ***Port.:*** Promanum; Softasept; ***S.Afr.:*** Clearasil Medicated Facial Cleanser; Dry & Clear Medicated Skin Cleanser; Listerine Antiseptic; Oxipor VHC; Specific Nerve Pain Remedy; ***Singapore:*** Hexodane Handrub; Listerine; Listerine Cool Mint; Listerine Fresh Burst; Listerine Tartar Control; Tri-Cidal†; ***Spain:*** Alcohocel; Alcohol Benzalconio; Alcohol Cetil†; Alcohol Cetilpi Cuve†; Alcohol CL Benz; Alcohol Poten; Alcohol Potenciado; Beta Alcanforado; Beta Romero; Embrocacion Gras; Farmalcohol; Linimento Naion; Menalcol; Mercrotona; ***Switz.:*** Betaseptic; Desitur†; Frekaderm†; Promanum N; Sclerovein; Softasept N; ***Thai.:*** Hand Joy; ***UK:*** Brushtox; Clearasil Pore Cleansing Lotion; Medi-Wipe; Oxy Cleanser; Oxy Duo Pads; Spectrum; ***USA:*** Banadyne-3; Clearasil Double Clear; Clearasil Double Textured Pads; Lipmagik; Maximum Strength Anbesol; Orasol; Stri-Dex Pads; ***Venez.:*** Frixonil.

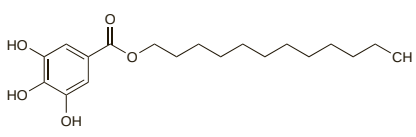
Alkyl Gallates

Galatos de alquilo.

Dodecyl Gallate

Dodecilo galatas; Dodécyle, gallate de; Dodecylgallat; Dodecylgallát; Dodecylis gallas; Dodekyyligallaatti; E312; Galato de dodecilo; Lauryl Gallate; Laurylum Gallicum. Dodecyl 3,4,5-trihydroxybenzoate.

$C_{19}H_{30}O_5$ = 338.4.
CAS — 1166-52-5.

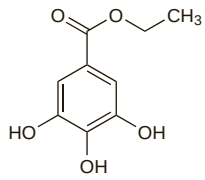


Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Dodecyl Gallate). A white or almost white crystalline powder. M.p. about 96°. Very slightly soluble or practically insoluble in water; freely soluble in alcohol; slightly soluble in dichloromethane. Store in nonmetallic containers. Protect from light.

Ethyl Gallate

Galato de etilo. Ethyl 3,4,5-trihydroxybenzoate.

$C_9H_{10}O_5$ = 198.2.
CAS — 831-61-8.



Pharmacopoeias. In *Br.*
BP 2008 (Ethyl Gallate). A white to creamy-white, odourless or almost odourless, crystalline powder. Slightly soluble in water; freely soluble in alcohol and in ether; practically insoluble in arachis oil. Protect from light. Avoid contact with metals.

Octil Gallate

E311; Galato de octilo; Octyl Gallate; Octyle, gallate d'; Octylis gallas; Oktilo galatas; Oktylgallat; Oktyl-gallát; Oktyyligallaatti. Octyl 3,4,5-trihydroxybenzoate.

$C_{15}H_{22}O_5$ = 282.3.
CAS — 1034-01-1.

Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Octyl Gallate). A white or almost white crystalline powder. Practically insoluble in water and in dichloromethane; freely soluble in alcohol. Store in nonmetallic containers. Protect from light.

Propyl Gallate

E310; Galato de propilo; Propil-gallát; Propilo galatas; Propyle, gallate de; Propylgallat; Propyl-gallát; Propylis gallas; Propylu galusan; Propylum Gallicum; Propyyligallaatti. Propyl 3,4,5-trihydroxybenzoate.

$C_{10}H_{12}O_5$ = 212.2.
CAS — 121-79-9.

Pharmacopoeias. In *Eur.* (see p.vii). Also in *USNF.*
Ph. Eur. 6.2 (Propyl Gallate). A white or almost white, crystalline powder. Very slightly soluble in water; freely soluble in alcohol; dissolves in dilute solutions of alkali hydroxides. Protect from light.
USNF 26 (Propyl Gallate). A white crystalline powder with a slight characteristic odour. Slightly soluble in water; freely soluble in alcohol. Store in airtight containers. Avoid contact with metals. Protect from light.

Adverse Effects and Precautions

The alkyl gallates may cause contact sensitivity and skin reactions.

Effects on the blood. Methaemoglobinaemia associated with the antoxidants (butylated hydroxyanisole, butylated hydroxytoluene, and propyl gallate) used to preserve the oil in a soybean infant feed formula has been reported.[1] Propyl gallate was suspected of being the most likely cause because its chemical structure is similar to pyrogallol (p.1611), a methaemoglobinaemia inducer.

1. Nitzan M, *et al*. Infantile methemoglobinemia caused by food additives. *Clin Toxicol* 1979; **15:** 273–80.

Uses

The alkyl esters of gallic acid (3,4,5-trihydroxybenzoic acid) have antoxidant properties and are used as preservatives in pharmaceuticals and cosmetics. Alkyl gallates are also used as antoxidants in foods and are useful in preventing deterioration and rancidity of fats and oils. They are used in concentrations of 0.001 to 0.1%.

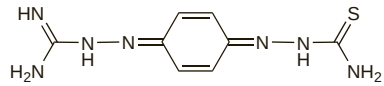
To improve acceptability and efficacy, the alkyl gallates are frequently used with other antoxidants such as butylated hydroxyanisole or butylated hydroxytoluene and with sequestrants and synergists such as citric acid and zinc salts.

The alkyl gallates have also been reported to have limited antibacterial and antifungal activity.

Ambazone *(BAN, rINN)*

Ambatsoni; Ambazon; Ambazona; Ambazonum. 4-Amidinohydrazonocyclohexa-1,4-dien-3-one thiosemicarbazone monohydrate.

Амбазон
$C_8H_{11}N_7S,H_2O$ = 255.3.
CAS — 539-21-9 (anhydrous ambazone); 6011-12-7 (ambazone monohydrate).
ATC — R02AA01.
ATC Vet — QR02AA01.



Profile

Ambazone is an antiseptic that is used in the form of lozenges for minor infections of the mouth and pharynx.

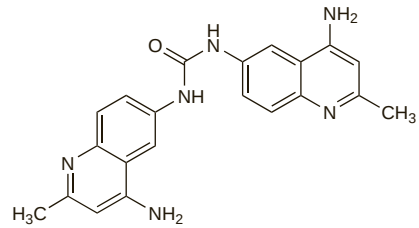
Preparations

Proprietary Preparations (details are given in Part 3)
Cz.: Faringosept†; ***Hung.:*** Faringosept†; ***Pol.:*** Faringosept; ***Rus.:*** Faringosept (Фарингосепт).

Aminoquinuride Hydrochloride *(rINNM)*

Aminoquinuride, Chlorhydrate d'; Aminoquinuridi Hydrochloridum; Hidrocloruro de aminoquinurida. 1,3-Bis(4-amino-2-methyl-6-quinolyl)urea dihydrochloride.

Аминохинурида Гидрохлорид
$C_{21}H_{20}N_6O,2HCl$ = 445.3.
CAS — 3811-56-1 (aminoquinuride); 5424-37-3 (aminoquinuride hydrochloride).



(aminoquinuride)

Profile

Aminoquinuride hydrochloride is an antiseptic that has been used in topical preparations for the treatment of mouth and skin disorders.

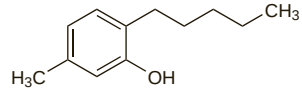
Preparations

Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Austria:*** Herviros; ***Ger.:*** Herviros†.

Amylmetacresol *(BAN, rINN)*

Amilmetacresol; Amilmetakrezol; Amylmétacrésol; Amylmetacresolum; Amylmetakresol; Amyylimetakresoli. 6-Pentyl-*m*-cresol; 5-Methyl-2-pentylphenol.

Амилметакрезол
$C_{12}H_{18}O$ = 178.3.
CAS — 1300-94-3.



Pharmacopoeias. In *Br.*
BP 2008 (Amylmetacresol). A clear or almost clear liquid or a solid crystalline mass with a characteristic odour, colourless or slightly yellow when freshly prepared; it darkens on keeping. F.p. about 22°. Practically insoluble in water; soluble in alcohol, in ether, and in fixed and volatile oils. Protect from light.

Profile

Amylmetacresol is a phenolic antiseptic used chiefly as an ingredient of lozenges in the treatment of minor infections of the mouth and throat.

Preparations

Proprietary Preparations (details are given in Part 3)
UK: Antiseptic Throat Lozenges; Throaties Anti-Bacterial Pastilles.

Multi-ingredient: ***Austral.:*** Sore Throat Chewing Gum†; Strepsils; Strepsils Plus; ***Austria:*** Coldangin; Neo-Angin; ***Belg.:*** Strepsils; Strepsils + Lidocaine; Strepsils Menthol; Strepsils Vit C; ***Canad.:*** Strepsils; Strepsils Cherry†; ***Cz.:*** Neo-Angin; Strepsils; Strepsils Menthol a Eucalyptus; Strepsils Plus; Strepsils Vitamin C; ***Denm.:*** Strepsils; ***Fin.:*** Strepsils; Strepsils Menthol;