cyanides, lithium, malathion, clofenotane, and some organic solvents such as methyl alcohol or ethylene glycol. Adsorption characteristics can be influenced by the charcoal's particle size, thus different responses may be obtained with different preparations.

Activated charcoal is given by mouth usually as a slurry in water. A usual adult dose for reduction of absorption is 50 g, but higher doses have been used. Children 1 to 12 years old may be given 25 to 50 g and infants under 1 year 1 g/kg. For maximum efficacy, activated charcoal should be given as soon as possible (within 1 hour) after ingestion of the toxic compound. However, it may be effective several hours after poisoning with certain drugs that slow gastric emptying. In the case of drugs that undergo enterohepatic or enteroenteric recycling (e.g. phenobarbital and theophylline) *repeated doses* of activated charcoal are of value in enhancing faecal elimination. Adult doses for repeated administration in active elimination have varied but typically 50 g may be given every 4 hours or 25 g every 2 hours. Doses in children and infants are similar to those used above for reduction of absorption and may be given every 4 to 6 hours. Administration may also be via a nasogastric tube.

Mixtures such as 'universal antidote' that contained activated charcoal, magnesium oxide, and tannic acid should not be used; activated charcoal alone is more effective and tannic acid may cause hepatotoxicity.

In treatment of poisoning using charcoal haemoperfusion, activated charcoal is used to remove drugs from the bloodstream. Where available, it may be of value in acute severe poisoning by drugs such as the barbiturates, glutethimide, or theophylline when other intensive measures fail to improve the condition of the patient.

Activated charcoal is used in dressings for ulcers and suppurating wounds (p.1585) to reduce malodour and may improve the rate of healing.

Activated charcoal has been used as a marker of intestinal transit and has also been tried in the treatment of flatulence. Both activated charcoal and vegetable charcoal (wood charcoal; carbo ligni) are included in preparations for various gastrointestinal disorders.

Technical grades of activated charcoal have been used as purifying and decolorising agents, for the removal of residual gases in low-pressure apparatus, and in respirators as a protection against toxic gases.

Administration. Activated charcoal is most commonly given as a slurry in water but this is often unpalatable because of the colour, gritty taste, lack of flavour, and difficulty in swallowing.[1] Flavourings and other excipients are often added in an attempt to improve palatability, although the effect of any additives on the adsorptive capacity of charcoal needs to be considered. Studies *in vitro* or in healthy subjects indicated that some foods such as ice cream, milk, and cocoa might inhibit the adsorptive capacity of activated charcoal, whereas starches and jams appeared to have no effect.[2,3] Carmellose has improved palatability although it might also reduce adsorptive capacity.[4-6] Saccharin sodium, sucrose, or sorbitol may be suitable additives,[7] although there may be problems associated with sorbitol-containing products (see under Poisoning, below). Chocolate syrup has also been used but the sweetness and flavour may disappear after a few minutes of contact with the activated charcoal.[1] A more recent study[8] of charcoal use in children with suspected poisoning found no evidence that use of flavourings improved the success of administration.

1. Scholtz EC, *et al.* Evaluation of five activated charcoal formulations for inhibition of aspirin absorption and palatability in man. *Am J Hosp Pharm* 1978; **35:** 1355–9.
2. Levy G, *et al.* Inhibition by ice cream of the antidotal efficacy of activated charcoal. *Am J Hosp Pharm* 1975; **32:** 289–91.
3. De Neve R. Antidotal efficacy of activated charcoal in presence of jam, starch and milk. *Am J Hosp Pharm* 1976; **33:** 965–6.
4. Mathur LK, *et al.* Activated charcoal–carboxymethylcellulose gel formulation as an antidotal agent for orally ingested aspirin. *Am J Hosp Pharm* 1976; **33:** 717–19.
5. Manes M. Effect of carboxymethylcellulose on the adsorptive capacity of charcoal. *Am J Hosp Pharm* 1976; **33:** 1120, 1122.
6. Mathur LK, *et al.* Effect of carboxymethylcellulose on the adsorptive capacity of charcoal. *Am J Hosp Pharm* 1976; **33:** 1122.
7. Cooney DO. Palatability of sucrose-, sorbitol-, and saccharin-sweetened activated charcoal formulations. *Am J Hosp Pharm* 1980; **37:** 237–9.
8. Osterhoudt KC, *et al.* Activated charcoal administration in a pediatric emergency department. *Pediatr Emerg Care* 2004; **20:** 493–8.

Poisoning. The management of acute poisoning is discussed on p.1435. The use of a *single oral dose* of activated charcoal has become a widespread method of preventing the absorption of ingested compounds and may be superior to gastric emptying. The American Academy of Clinical Toxicology (AACT) and the European Association of Poisons Centres and Clinical Toxicologists (EAPCCT) consider[1] that activated charcoal may be used if a patient presents within 1 hour of ingesting a potentially toxic amount of a poison known to be adsorbed by charcoal. There are insufficient data to support general use beyond 1 hour after ingestion.[1-3] In addition, *multiple oral doses* of activated charcoal have been found to enhance the elimination of some drugs and toxic substances even after systemic absorption. Mechanisms by which activated charcoal may increase drug elimination from the body include interruption of the enterohepatic circulation of drugs excreted into the bile, reduction of the reabsorption of drugs which diffuse or are actively secreted into the intestines, and increased elimination of the drug via the gastrointestinal tract when given with a laxative to decrease gastrointestinal transit time, although the practice of using charcoal with a laxative has been questioned.[4-6] Repeated oral doses of activated charcoal may therefore be considered for compounds that undergo enterohepatic or enteroenteric circulation, have a small volume of distribution, are not extensively bound to plasma proteins, and have a low endogenous clearance. Following a review of the literature[6] the AACT and EAPCCT recommended that multiple doses of charcoal should be considered only if a patient has ingested a life-threatening amount of carbamazepine, dapsone, phenobarbital, quinine, or theophylline. Anecdotal reports and studies in acutely poisoned patients indicate that a technique of giving multiple doses of charcoal may offer an alternative to charcoal haemoperfusion or haemodialysis. However, while activated charcoal is generally well tolerated, major complications do occasionally occur, including pulmonary aspiration and bowel obstruction.[7] Also, use of multiple doses of charcoal preparations containing sorbitol or sodium bicarbonate can result in increased vomiting[8] or in electrolyte disturbances.[4,9,10]

1. American Academy of Clinical Toxicology; European Association of Poisons Centres and Clinical Toxicologists. Position paper: single-dose activated charcoal. *J Toxicol Clin Toxicol* 2005; **43:** 61–87. Also available at: http://www.clintox.org/Pos_Statements/SingleDoseActivatedCharcoal.pdf (accessed 27/09/05)
2. Green R, *et al.* How long after drug ingestion is activated charcoal still effective? *J Toxicol Clin Toxicol* 2001; **39:** 601–5.
3. Cooper GM, *et al.* A randomized clinical trial of activated charcoal for the routine management of oral drug overdose. *QJM* 2005; **98:** 655–60.
4. Neuvonen PJ, Olkkola KT. Oral activated charcoal in the treatment of intoxications: role of single and repeated doses. *Med Toxicol* 1988; **3:** 33–58.
5. Neuvonen PJ, Olkkola KT. Effect of purgatives on antidotal efficacy of oral activated charcoal. *Hum Toxicol* 1986; **5:** 255–63.
6. American Academy of Clinical Toxicology; European Association of Poisons Centres and Clinical Toxicologists. Position statement and practice guidelines on the use of multi-dose activated charcoal in the treatment of acute poisoning. *J Toxicol Clin Toxicol* 1999; **37:** 731–51. Also available at: http://www.clintox.org/Pos_Statements/MultipleDoseActivatedCharcoal.pdf (accessed 27/09/05)
7. Palatnick W, Tenenbein M. Activated charcoal in the treatment of drug overdose: an update. *Drug Safety* 1992; **7:** 3–7.
8. McFarland AK, Chyka PA. Selection of activated charcoal products for the treatment of poisonings. *Ann Pharmacother* 1993; **27:** 358–61.
9. McLuckie A, *et al.* Role of repeated doses of oral activated charcoal in the treatment of acute intoxications. *Anaesth Intensive Care* 1990; **18:** 375–84.
10. Tenenbein M. Multiple doses of activated charcoal: time for reappraisal? *Ann Emerg Med* 1991; **20:** 529–31.

HAEMOPERFUSION. Haemoperfusion involves the passage of blood through an adsorbent material such as activated charcoal or synthetic hydrophobic polystyrene resins that can retain certain drugs and toxic agents. Early problems with charcoal haemoperfusion such as charcoal embolism, marked thrombocytopenia, fibrinogen loss, and pyrogen reactions have been largely overcome by purification procedures and by coating the carbon with biocompatible polymers. However, transient falls in platelet count, leucocyte count, and circulatory concentrations of clotting factors, calcium, glucose, urea, creatinine, and urate have been reported during haemoperfusion. While there is no substitute for supportive measures, haemoperfusion can significantly reduce the body burden of certain compounds with a low volume of distribution within 4 to 6 hours in some severely poisoned patients; haemoperfusion is not effective for drugs or poisons with very large volumes of distribution.

References.

1. Winchester JF. Dialysis and hemoperfusion in poisoning. *Adv Ren Replace Ther* 2002; **9:** 26–30.

Porphyria. Activated charcoal may be used as part of the management of erythropoietic protoporphyria, one of the non-acute porphyrias (p.1448). It acts as a sorbent in the gut lumen, interrupting the enterohepatic recycling of protoporphyrin. It may also have a role in congenital erythropoietic porphyria, a very rare porphyria. In a patient[1] with photomutilation due to this condition, activated charcoal 30 g given orally every 3 hours for 36 hours reduced the plasma-porphyrin concentration to normal values by 20 hours and was more effective than colestyramine or red cell transfusion. After discontinuation of activated charcoal, plasma-porphyrin concentrations rose rapidly to near pretreatment levels within 10 days. Long-term treatment with oral charcoal over a 9-month period produced a clinical remission with low concentrations of plasma and skin porphyrin and an absence of photocutaneous activity. The optimal dose was determined to be 60 g three times daily. However, exacerbation after an initial period of remission has been reported in another patient[2] and total lack of efficacy in a third.[3]

Activated charcoal has also been tried in variegate porphyria, but a study[4] in 8 patients found that oral charcoal led to clinical and biochemical deterioration with an increase in skin lesions and in urinary and plasma porphyrins.

1. Pimstone NR, *et al.* Therapeutic efficacy of oral charcoal in congenital erythropoietic porphyria. *N Engl J Med* 1987; **316:** 390–3.
2. Hift RJ, *et al.* The effect of oral activated charcoal on the course of congenital erythropoietic porphyria. *Br J Dermatol* 1993; **129:** 14–17.
3. Minder EI, *et al.* Lack of effect of oral charcoal in congenital erythropoietic porphyria. *N Engl J Med* 1994; **330:** 1092–4.
4. Hift RJ, *et al.* Administration of oral activated charcoal in variegate porphyria results in a paradoxical clinical and biochemical deterioration. *Br J Dermatol* 2003; **149:** 1266–9.

Pruritus. Activated charcoal has been tried in pruritus (p.1582) associated with renal failure. In a double-blind crossover study,[1] activated charcoal 6 g daily by mouth for 8 weeks was more effective than placebo in relieving generalised pruritus in 11 patients undergoing maintenance haemodialysis. Another study[2] found that activated charcoal completely relieved pruritus in 10 of 23 haemodialysis patients, with a partial response in a further 10; treatment was generally well tolerated.

1. Pederson JA, *et al.* Relief of idiopathic generalized pruritus in dialysis patients treated with activated oral charcoal. *Ann Intern Med* 1980; **93:** 446–8.
2. Giovannetti S, *et al.* Oral activated charcoal in patients with uremic pruritus. *Nephron* 1995; **70:** 193–6.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Mamograf; Minicam Carb; ***Austral.:*** Ad-Sorb; Carbosorb; Charcocaps; Karbons†; ***Austria:*** Norit; Norit-Carbomix; ***Belg.:*** Norit; Norit-Carbomix; ***Braz.:*** Neocarbon†; ***Canad.:*** Charac; Charcodote Aqueous; ***Cz.:*** Carbosorb; Norit; ***Fin.:*** Carbomix; ***Fr.:*** Alione Charbon; Carbactive; Carbomix; Carbonet; Charbon de Belloc; Colocarb; Formocarbine; Splenocarbine; Toxicarb; ***Ger.:*** Kohle-Compretten; Kohle-Hevert; Kohle-Pulvis; Kohle-Tabletten; Ultracarbon; ***Gr.:*** Carbomix†; Norit; Toxicarb; ***Hong Kong:*** Charcodote; ***Indon.:*** Bekarbon; ***Irl.:*** Carbomix; Carbonet; ***Israel:*** Norit; ***Ital.:*** Carbomix; ***Mex.:*** Carbotural; ***Neth.:*** Norit; ***Norw.:*** Kohle-Compretten; ***NZ:*** Carbosorb X; ***Port.:*** Askina Carbsorb†; Norit; ***Singapore:*** Aqueous Charcodote; Ultracarbon; ***Spain:*** Arkocapsulas Carbon Vegetal; Ultra Adsorb; ***Swed.:*** Carbomix; Kolsuspension; Medikol; ***Thai.:*** Ca-R-Bon; Ultracarbon; ***Turk.:*** Charflo Aqua; ***UK:*** Actidose-Aqua; Bragg's Medicinal Charcoal; Carbomix; Carbonet; Charcodote; Clinisorb; Legius; Lyofoam C; Modern Herbals Trapped Wind & Indigestion; Norit; ***USA:*** Actidose-Aqua; Charcoaid; Charcoal Plus; Charcocaps; Liqui-Char.

Multi-ingredient: ***Arg.:*** Carbogasol; Carbon Tabs; Diarrocalmol; Estreptocarbocaftiazol; Karbonetas; Lefa Enteril†; Opocarbon; ***Austral.:*** Carboflex†; Carbosorb S; No Gas†; ***Austria:*** Eucarbon; Eucarbon Herbal; Intestinol; Sabatif; ***Belg.:*** Carbobel; Carbolactanose; ***Canad.:*** Carboflex†; Charac Tol; Charcodote; ***Chile:*** Carbon Sulfaguanidina; ***Cz.:*** Carbocit; Carbotox; ***Fr.:*** Acticarbine; Actisorb Ag ; Carboflex; Carbolevure; Carbophos; Carbosylane; Carbosymag; Notgaz; ***Ger.:*** Actisorb Silver†; ***Gr.:*** Carbosylane; ***India:*** Distenil; Molzyme†; Nutrozyme; Papytazyme; Unienzyme; ***Irl.:*** Actisorb Silver; ***Israel:*** Carbosylane; Charcodote; Eucarbon; Kaltocarb; Novicarbon; ***Ital.:*** Actisorb Plus; Carbone Composto; Carbonesia; Carboyoghurt; Eucarbon; No-Gas; ***Malaysia:*** Eucarbon†; ***Mex.:*** Acilin; Dipecfur; ***NZ:*** Carbosorb S†; Carbosorb XS; ***Pol.:*** Rapacholin AC; Rapacholin C; ***Port.:*** Carboflex†; ***S.Afr.:*** Rubilax†; ***Switz.:*** Carbolevure; Carboticon; Carvon†; ***Thai.:*** Belacid; Bicobon†; Biodan†; Carbonpectate; Delta Charcoal; Papytazyme†; Pepsitase; Polyenzyme-I; ***Turk.:*** Charflo Sorbitol; Eucarbon; Intestinol; Karboseptin; ***UK:*** Acidosis; Actisorb Silver; Carbellon; ***USA:*** Actidose with Sorbitol; Flatulex; Poison Antidote Kit; ***Venez.:*** Carbargal; Carbargal con Atropina; Guanicar.

Amifostine *(BAN, USAN, rINN)*

Amifostiini; Amifostin; Amifostina; Amifostinum; Ethiofos; Gammaphos; NSC-296961; WR-2721. *S*-[2-(3-Aminopropylamino)ethyl] dihydrogen phosphorothioate.

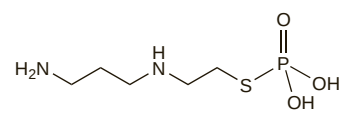
Амифостин

$C_5H_{15}N_2O_3PS$ = 214.2.

CAS — 20537-88-6 (amifostine); 63717-27-1 (amifostine monohydrate).

ATC — V03AF05.

ATC Vet — QV03AF05.



Pharmacopoeias. *US* includes the trihydrate.

USP 31 (Amifostine). The trihydrate is a white crystalline powder. Freely soluble in water. pH of a 5% solution in water is between 6.5 and 7.5. Store in airtight containers at a temperature of 2° to 8°. Protect from light.

Incompatibility. Amifostine has been reported[1] to be physically incompatible with aciclovir sodium, amphotericin B, cefoperazone sodium, chlorpromazine hydrochloride, cisplatin, ganciclovir sodium, hydroxyzine hydrochloride, miconazole,

minocycline hydrochloride, and prochlorperazine edisilate during simulated Y-site administration.

1. Trissel LA, Martinez JF. Compatibility of amifostine with selected drugs during simulated Y-site administration. *Am J Health-Syst Pharm* 1995; **52:** 2208–12.

Adverse Effects, Treatment, and Precautions

Amifostine may cause a transient reduction, usually in systolic, or, less frequently, in diastolic blood pressure. However, more pronounced reductions in blood pressure may occur and transient loss of consciousness has been reported very rarely. To minimise hypotension, patients should be adequately hydrated before treatment begins and should be in a supine position. Amifostine is contra-indicated in patients who are hypotensive or dehydrated. Patients taking antihypertensive drugs should discontinue treatment 24 hours before starting amifostine. Arterial blood pressure must be monitored during the amifostine infusion and if systolic blood pressure decreases significantly, the infusion must stop. It may be continued if blood pressure returns to normal within 5 minutes.

Nausea and vomiting are frequently reported and concurrent antiemetic therapy is recommended.

Amifostine reduces serum-calcium concentrations, although clinical hypocalcaemia has occurred only very rarely in patients who received multiple doses of amifostine within 24 hours. Serum-calcium concentrations should be monitored in patients at risk of hypocalcaemia.

Other adverse effects include flushing, chills, somnolence, hiccups, and sneezing. Hypersensitivity reactions and anaphylactoid reactions have been reported. Skin rashes may occur and there have been reports of more severe skin reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis, in some cases resulting in fatality.

Administration of amifostine over a longer period than the recommended 15 minutes is associated with a higher incidence of adverse effects.

Effects on the skin. Amifostine has been associated with severe skin reactions, including Stevens-Johnson syndrome[1,2] and toxic epidermal necrolysis,[1,2] and fatalities have occurred.[2] The reactions appear to be more common in patients receiving radiotherapy.[2]

1. Lale Atahan I, *et al*. Two cases of Stevens-Johnson syndrome: toxic epidermal necrolysis possibly induced by amifostine during radiotherapy. *Br J Dermatol* 2000; **143:** 1072–3.
2. Boccia R, *et al*. Assessment and management of cutaneous reactions with amifostine administration: findings of the ethyol (amifostine) cutaneous treatment advisory panel (ECTAP). *Int J Radiat Oncol Biol Phys* 2004; **60:** 302–9.

Pharmacokinetics

Amifostine is rapidly cleared from the plasma after intravenous administration and is dephosphorylated by alkaline phosphatase to the active metabolite WR-1065, a free thiol compound. The elimination half-life of amifostine after a 15-minute infusion is less than 10 minutes. About 6% or less of a dose is excreted in the urine.

Uses and Administration

Amifostine, an aminothiol compound, is a cytoprotective agent. It is converted in the body to its active metabolite WR-1065, which protects noncancerous cells against the toxic effects of antineoplastics and ionising radiation. It is used in patients with advanced ovarian cancer to reduce neutropenia-related infection associated with cyclophosphamide and cisplatin therapy and, in patients with advanced solid tumours of non-germ cell origin, to reduce the cumulative renal toxicity associated with repeated cisplatin use. It is also used to reduce the incidence of xerostomia (dry mouth) in patients undergoing radiation therapy for head and neck cancer. Amifostine is under investigation in ameliorating the adverse effects of other antineoplastics and in the treatment of myelodysplasia.

In chemotherapy, amifostine is given by intravenous infusion over 15 minutes starting no more than 30 minutes before the antineoplastic therapy. The dose in adults is 910 mg/m^2 once daily. Subsequent doses should be reduced to 740 mg/m^2 in patients unable to tolerate the full dose. A dose of 740 mg/m^2 is also recommended for the reduction of renal toxicity of cisplatin if doses of cisplatin of less than 100 mg/m^2 are used.

In the prevention of xerostomia, amifostine is given in a dose of 200 mg/m^2 daily as a 3-minute intravenous infusion started 15 to 30 minutes before radiotherapy.

Cytoprotection. WR-1065, the active metabolite of amifostine, readily enters non-malignant cells where it deactivates cytotoxics such as alkylating and platinum-containing antineoplastics and protects against the effects of ionising radiation.[1-3] The cytoprotective effects of amifostine are reported to be selective for normal cells and not to interfere with the cytotoxic effects of antineoplastics and radiation on malignant cells. Several factors contribute to this selectivity, including the lower alkaline phosphatase content of malignant cells compared with normal cells, and the lower pH of malignant tissues, both of which decrease the formation and uptake of WR-1065 by malignant cells.[2,3]

Benefit has been reported with amifostine in various malignancies and the American Society of Clinical Oncology currently recommends[4] that its use may be considered in patients receiving cisplatin- or alkylating agent-based chemotherapy, and in patients receiving radiation therapy in the head and neck region. Although it is usually given intravenously, there is some evidence[5,6] that the subcutaneous route may be effective and may be associated with fewer adverse effects.

1. Foster-Nora JA, Siden R. Amifostine for protection from antineoplastic drug toxicity. *Am J Health-Syst Pharm* 1997; **54:** 787–800.
2. Mabro M, *et al*. A risk-benefit assessment of amifostine in cytoprotection. *Drug Safety* 1999; **21:** 367–87.
3. Culy CR, Spencer CM. Amifostine: an update on its clinical status as a cytoprotectant in patients with cancer receiving chemotherapy or radiotherapy and its potential therapeutic application in myelodysplastic syndrome. *Drugs* 2001; **61:** 641–84.
4. Schuchter LM, *et al*. 2002 update of recommendations for the use of chemotherapy and radiotherapy protectants: clinical practice guidelines of the American Society of Clinical Oncology. *J Clin Oncol* 2002; **20:** 2895–903. Also available at: http://www.jco.org/cgi/reprint/20/12/2895.pdf (accessed 4/10/05)
5. Koukourakis MI, *et al*. Subcutaneous administration of amifostine during fractionated radiotherapy: a randomized phase II study. *J Clin Oncol* 2000; **18:** 2226–33.
6. Bonner HS, Shaw LM. New dosing regimens for amifostine: a pilot study to compare the relative bioavailability of oral and subcutaneous administration with intravenous infusion. *J Clin Pharmacol* 2002; **42:** 166–74.

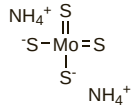
Preparations

USP 31: Amifostine for Injection.

Proprietary Preparations (details are given in Part 3)
Arg.: Erifostine; Ethyol†; ***Austral.:*** Ethyol; ***Belg.:*** Ethyol; ***Braz.:*** Ethyol; ***Chile:*** Ethyol; ***Cz.:*** Ethyol; ***Denm.:*** Ethyol; ***Fin.:*** Ethyol; ***Fr.:*** Ethyol; ***Ger.:*** Ethyol; ***Gr.:*** Ethyol; ***Hong Kong:*** Ethyol†; ***Hung.:*** Ethyol†; ***India:*** Amiphos; ***Israel:*** Ethyol; ***Ital.:*** Ethyol; ***Malaysia:*** Ethyol†; ***Mex.:*** Ethyol; ***Neth.:*** Ethyol; ***NZ:*** Ethyol; ***Philipp.:*** Ethyol; ***Pol.:*** Ethyol; ***Port.:*** Ethyol; ***S.Afr.:*** Ethyol; ***Singapore:*** Ethyol†; ***Spain:*** Ethyol; ***Swed.:*** Ethyol; ***Switz.:*** Ethyol; ***Thai.:*** Cytofos; Ethyol; ***Turk.:*** Ethyol; ***UK:*** Ethyol†; ***USA:*** Ethyol; ***Venez.:*** Ethyol.

Ammonium Tetrathiomolybdate

Tetratiomolibdato de amonio.
$(NH_4)_2MoS_4$ = 260.3.
CAS — 15060-55-6.



Profile

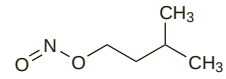
Ammonium tetrathiomolybdate is a chelator that aids the elimination of copper from the body. It is under investigation in the treatment of Wilson's disease.

Wilson's disease. Ammonium tetrathiomolybdate forms a complex with protein and copper. When it is taken with food it blocks the intestinal absorption of copper, and when given between meals it combines with albumin- and caeruloplasmin-bound copper. Ammonium tetrathiomolybdate is under investigation for the initial reduction of copper levels in patients with Wilson's disease (p.1459); it may be particularly suitable for patients with neurological symptoms.[1] Bone marrow depression[1,2] and raised liver enzymes[1] have been reported; both have responded to temporary withdrawal or dose reduction.

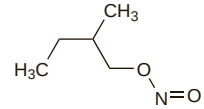
1. Brewer GJ, *et al*. Treatment of Wilson disease with ammonium tetrathiomolybdate III: initial therapy in a total of 55 neurologically affected patients and follow-up with zinc therapy. *Arch Neurol* 2003; **60:** 379–85.
2. Harper PL, Walshe JM. Reversible pancytopenia secondary to treatment with tetrathiomolybdate. *Br J Haematol* 1986; **64:** 851–3.

Amyl Nitrite

Amyli Nitris; Amylis Nitris; Amylium Nitrosum; Amylnitrit; Amyylinitriitti; Azotito de Amilo; Isoamyl Nitrite; Isopentyl Nitrite; Nitrito de amilo; Pentanolis Nitris.
$C_5H_{11}NO_2$ = 117.1.
ATC — V03AB22.
ATC Vet — QV03AB22.



and



NOTE. The following terms have been used as 'street names' (see p.vi) or slang names for various forms of amyl nitrite:
60 second trip; Aimes; Aimies; Ames; Amys; Boppers; Hard on; Pearls; Poppers; Sixty second trip; Snappers; Whiffenpoppers.

Pharmacopoeias. In *Jpn* and *US*.
USP 31 (Amyl Nitrite). A mixture of the nitrite esters of 3-methyl-1-butanol and 2-methyl-1-butanol. A clear, yellowish liquid having a peculiar, ethereal, fruity odour. It is very flammable. It is volatile even at low temperatures. B.p. about 96°. Practically insoluble in water; miscible with alcohol and with ether. Store in a cool place in airtight containers. Protect from light.

Stability. Amyl nitrite is liable to decompose with evolution of nitrogen, particularly if it has become acid in reaction.

Adverse Effects, Treatment, and Precautions

Amyl nitrite inhalation commonly causes flushing, headache, and dizziness; nausea and vomiting, hypotension, restlessness, and tachycardia may also occur. Overdosage may result in cyanosis, syncope, dyspnoea, and muscular weakness, due to vasodilatation and methaemoglobinaemia. Methylthioninium chloride may be required for severe methaemoglobinaemia but should not be used if cyanide poisoning is suspected since cyanide may be displaced.

Amyl nitrite may increase intra-ocular and intracranial pressure and should be used with caution in patients with glaucoma, recent head trauma, or cerebral haemorrhage.

Abuse. Volatile nitrites (commonly known as 'poppers'), including amyl, butyl, or isobutyl nitrite, have been abused in the belief that they expand creativity, stimulate music appreciation, promote a sense of abandon in dancing, and intensify sexual experience.[1,2]

Inhalation causes headache, tachycardia, syncope, acute psychosis, increased intra-ocular pressure, transient hemiparesis, methaemoglobinaemia, coma, and, rarely, sudden death. Haemolytic anaemia has also been reported;[3-5] in some subjects, Heinz body formation has been detected.[3] Methaemoglobinaemia may be severe,[6] and has also been reported after ingestion of volatile nitrites.[7-10] Symptoms are similar to those of hypoxia[9] and may be reversed by methylthioninium chloride.[6-10]

Amyl nitrite inhalation has led to severe and extensive contact dermatitis around the face with secondary spread elsewhere on the body.[11]

1. Sigell LT, *et al*. Popping and snorting volatile nitrites: a current fad for getting high. *Am J Psychiatry* 1978; **135:** 1216–18.
2. Lockwood B. Poppers: volatile nitrite inhalants. *Pharm J* 1996; **257:** 154–5.
3. Romeril KR, Concannon AJ. Heinz body haemolytic anaemia after sniffing volatile nitrites. *Med J Aust* 1981; **1:** 302–3.
4. Brandes JC, *et al*. Amyl nitrite-induced hemolytic anemia. *Am J Med* 1989; **86:** 252–4.
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Handling and storage. Amyl nitrite is very flammable and must not be used where it may be ignited.

Uses and Administration

Amyl nitrite is rapidly absorbed on inhalation and has been used in the immediate treatment of patients with definite cyanide poisoning (p.2045) to induce the formation of methaemoglobin, which combines with the cyanide to form non-toxic cyanmethaemoglobin. The value of such treatment has been questioned since only low levels of methaemoglobin are formed, but other mechanisms may also be important. A suggested procedure has