Cocaine *(BAN)* ⊗

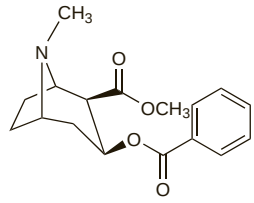
Cocaína; Cocainum; Kokaiini; Kokain; Methyl Benzoylecgonine. (1*R*,2*R*,3*S*,5*S*)-2-(Methoxycarbonyl)tropan-3-yl benzoate.

$C_{17}H_{21}NO_4$ = 303.4.

CAS — 50-36-2.

ATC — N01BC01; R02AD03; S01HA01; S02DA02.

ATC Vet — QN01BC01; QR02AD03; QS01HA01; QS02DA02.



NOTE. The following terms have been used as 'street names' (see p.vi) or slang names for various forms of cocaine:
24-7; 151; 256; A1-Yola; All-American drug; Angie; Apple jacks; Aspirin; Aunt; Aunt Nora; Baby T; Bad; Badrock; Bahsay; Baise; Ball; Balls Mahoney; Bane; Barbs; Basa; Base; Baseball; Basing; Basuco; Batman; Bazooka; Bazulco; Beak; Beam; Beamers; Beans; Beat; Beautiful boulders; Bebe; Beemers; Berni; Bernice; Bernie; Bernie's flakes; Bernie's gold dust; Big bloke; Big C; Big flake; Big rush; Bill blass; Billie hoke; Bing; Bing Crosby; Bings; Birdie powder; Biscuits; Bjs; BJ's; B.J.'s; Black rock; Blanca; Blanco; Blast; Blizzard; Blotter; Blow; Blowcaine; Blowout; Blue; Bobo; Bogota Bullion; Bolivian; Bolivian marching powder; Bollo; Bolo; Bomb; Bonecrusher; Bones; Booger; Booger Sugar; Boost; Booth; Bopper; Botray; Boubou; Boulder; Boulya; Bouncing powder; Boutros; Boy; Branco; Breakfast of champions; Brick; Brooke Shields; Bubble gum; Bugar sugar; Buger sugar; Bullia capital; Bullion; Bump; Bumper; Bunk; Burese; Burnese; Bush; Butler; Butter; Butter Sandwich; Butter Sandwiches; Butu; C; Cabello; Cadillac; Caine; Cakes; California cornflakes; Came; Candy; Candy C; Candy cane; Candy sugar; Candycaine; Cane; Cap; Caps; Capsula; Carnie; Carrie; Carrie Nation; Casper; Casper the ghost; Cat's pee; Caviar; CDs; C-dust; Cecil; C-game; Cha; Chabbie; Chach; Chalk; Champagne; Champagne of drugs; Chan; Chandi; Chang; Charlie; Charlie girl; Chaz; Cheap basing; Cheddar; Cheese; Chemical; Chewies; Chez; Chinese Sky Candy; Ching; Chippy; Choe; Cholly; Climax; Cloud; Cloud nine; Coc; Co-caee-na; Coca; Coca-Cola; Coco; Coconut; Cokane; Coke; Cola; Colombian Dancing Dust; Colombian Foot Soldiers; Colombian Marching Powder; Colombo; Colorado; Combol; Cookie; Cookies; Coover; Coovers; Corine; Cornbread; Corrine; Corrinne; Crack; Crackers; Crank; Crib; Crill; Cristaux; Crow; Crumbs; Crunch & Munch; Crusty treats; Crystal; Cubes; Cuch; Dama blanca; Demo; Demolish; Devil drug; Devil's dandruff; Devilsmoke; Dice; Dime; Dime special; Dip; Dirty basing; Divits; DOA; Double bubble; Double yoke; Dream; Duct; Dust; Dutch Bliss; Eastside player; Egg; Eggs; El Perico; Electric koolaid; Esnortiar; Eve; Everclear; Eye opener; Eye openers; Famous dimes; Farlopa; Fast white lady; Fat bags; Fifty-one; Fish scales; Flake; Flave; Florida snow; Foo Foo; Foo foo stuff; Foo-foo dust; Foolish powder; Freebase; Freeze; French fries; Fries; Friskie powder; Fry; Gak; Garbage rock; Gas; Gear; Geek; Get your own; Gift-of-the-sun; Gift-of-the-sun-god; Gin; Girl; Girlfriend; Glad stuff; Glo; Gold; Gold dust; Gold star; Golf ball; Golf balls; Gooka; Gravel; Green gold; Grit; Grits; Groceries; Gulosa; Gutter glitter; Hail; Half track; Hamburger; Hamburger helper; Hamburgers; Handball; Happy dust; Happy powder; Happy trails; Hard; Hard ball; Hard line; Hard rock; Hardball; Have a dust; Haven dust; Heaven; Heaven dust; Heavy stuff; Hell; Henry VIII; Her; Hit; Hocus-Pocus; Hollywood; Homer; Hooter; Hoove; Hotcakes; How do you like me now?; Hubba; Hubba, I am back; Hubbas; Hunter; I am back; Ice; Ice cube; Icing; Inca message; Incentive; Issues; Ivory flakes; Jam; Jejo; Jelly; Jelly beans; Jessica Simpson; "Jiffy"; Johnny; Johnson; Joy powder; Junk; Kangaroo; Kangoroo; Kate; Kibbles & Bits; King; King's habit; Kitty; Kokomo; Kryptonite; Kubba; Kubs; Kuff; Lady; Lady C; Lady caine; Lady snow; Late night; Leaf; Lido; Line; Lines; Liquid lady; Llello; Love; Love affair; Lucifer Left-Nostril; Ma'a; Mama coca; Marching dust; Marching powder; Mayo; Merca; Merck; Merk; Mighty white; Mix; Mixed jive; Mobbeles; Mojo; Monster; Mosquitos; Movie star drug; Mr. B.; Mujer; Munch; Neige; Neve; New addition; Nieve; Nighttrain; Nose; Nose candy; Nose powder; Nose stuff; Nuggets; Number 3; One-fifty-one; One-to-one; Oyster stew; Pala; Paradise; Paradise white; Pariba; Parlay; Partying; Pasta; Paste; Patico; Pearl; Pebbles; Pee Wee; Pepsi; Percia; Percio; Perico; Peruvian; Peruvian flake; Peruvian lady; Peruvian Marching Powder; P.F.; Picnic in Stevenage; Piece; Piedra; Piedras; Pile; Piles; Pimp; Polvo blanco; Pony; Pop; Powder; Powder diamonds; Press; Prime time; Primo; Product; Purple caps; Purple haze; Quick; Quik; Quill; Race horse Charlie; Racehorse Charlie; Railers; Rane; Raw; Ready rock; Real tops; Red caps; Regular "P"; Rest in peace; Ringer; Ringers; Roca; Rock; Rock attack; Rocks; Rocks of hell; Rocky III; Rooster; Rox; Roxanne; Royalty; Roz; Rush; Schmeck; Schoolboy; Schoolcraft; Scorpion; Scottie; Scotty; Scrabble; Scramble; Scruples; Serpico 21; Seven-Up; Sevenup; Shabu; Shake; She; Sherms; Shit; Shnazzle; Shneg; Shootin' Caine; Showbiz Sherbert; Shrile; Sightball; Skeeter; Skeezell; Slab; Sleet; Sleigh ride; Smack; Smoke; Snai; Sniff; Snort; Snow; Snow bird; Snow coke; Snow cone; Snow soke; Snow toke; Snow Train; Snow white; Snowcones; Soap; Society high; Soda; Soft; Soup; Space; Space dust; Speed; Speed boat; Square time Bob; Squares; Squib; Squirrel; Star; Star dust; Star-spangled powder; Stardust; Stone; Stones; Strawberry; Street Caviar; Studio fuel; Suga buga; Sugar; Sugar block; Sugar boogers; Super cloud; Sutta; Sweet stuff; Swell up; T; Talco; Tardust; Teenager; Teeth; Tension; The champagne of stimulants; The devil; The great white hope; Thing; Tissue; Tony; Toot; Tootie; Top gun; Topo; Tornado; Toss up; Toss-ups; Trails; Trey; Troop; Turkey; Turtle stuff; Tutti-frutti; Tweaks; Twenty rock; Twinkie; Ultimate; Uptown; Uzi; Wacky dust; Wash; Washed rock; Wave; Weasel dust; Whack; White; White ball; White boy; White cloud; White Devil; White dragon; White dust; White ghost; White girl; White horse; White lade; White lady; White Lion; White mosquito; White Pony; White powder; White stuff; White sugar; White tornado; Whites; Whiz bang; Window pane; Wings; Witch; Woolies; Wrecking crew; Yada; Yadidi; Yahoo; Yak; Yale; Yam; Yams; Ya Yo; Yao; Yay; Yayo; Yayoo; Yay-yo; Yeah-O; Yeaho; Yee Yoo; Yeo; Yeyo; Yimyom; Yiz; Yola; Zing; Zip; Zulu.

Pharmacopoeias. In *Br.* and *US.*

BP 2008 (Cocaine). It may be obtained from the leaves of *Erythroxylum coca* and other spp. of *Erythroxylum*, or by synthesis. Colourless crystals or a white, crystalline powder. It is slightly volatile. M.p. 96° to 98°. Practically insoluble in water; freely soluble in alcohol and in ether; very soluble in chloroform; soluble in arachis oil; slightly soluble in liquid paraffin.

USP 31 (Cocaine). Colourless to white crystals or white, crystalline powder. M.p. 96° to 98°. Soluble 1 in 600 of water, 1 in 7 of alcohol, 1 in 1 of chloroform, 1 in 3.5 of ether, 1 in 12 of olive oil, and 1 in 80 to 100 of liquid paraffin. A saturated solution in water is alkaline to litmus. Protect from light.

Cocaine Hydrochloride *(BANM)* ⊗

Chloridrato de Cocaína; Cocaína, hidrocloruro de; Cocaïne, chlorhydrate de; Cocaine Hydrochlor.; Cocaini hydrochloridum; Cocainium Chloratum; Kokaiinihydrokloridi; Kokain-hidroklorid; Kokain-hydrochlorid; Kokainhydroklorid; Kokaino hidrochloridas; Kokainy chlorowodorek.

$C_{17}H_{21}NO_4$,HCl = 339.8.

CAS — 53-21-4.

ATC — N01BC01; R02AD03; S01HA01; S02DA02.

ATC Vet — QN01BC01; QR02AD03; QS01HA01; QS02DA02.

NOTE. CCN is a code approved by the BP 2008 for use on single unit doses of eye drops containing cocaine hydrochloride where the individual containers may be too small to bear all the appropriate labelling information.

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

Ph. Eur. 6.2 (Cocaine Hydrochloride). Colourless crystals or a white or almost white crystalline powder. M.p. about 197° with decomposition. Very soluble in water; freely soluble in alcohol. Protect from moisture and light.

USP 31 (Cocaine Hydrochloride). Colourless crystals or white, crystalline powder. Soluble 1 in 0.5 of water, 1 in 3.5 of alcohol, and 1 in 15 of chloroform; soluble in glycerol; insoluble in ether. Protect from light.

Stability in solutions. ***ALKALIS***. Solutions of cocaine hydrochloride are adversely affected by alkalis.

PHENOL. A stability study[1] was conducted in response to queries over conflicting data on the incompatibility of cocaine hydrochloride solutions and phenol. Some pharmacists had reported that cocaine hydrochloride eye drops preserved with phenol had shown no sign of physical incompatibility. The BPC 1973 states that cocaine hydrochloride is incompatible with phenol but suggests that cocaine hydrochloride solutions may be preserved with chlorocresol. The study found that there was no sign of physical incompatibility in aqueous solutions containing cocaine hydrochloride 5% and phenol 0.5% stored for a year at temperatures of 0° to 37° but there was a fall in pH, greatest at the higher temperatures, which was suggestive of chemical change. It was recommended that such solutions should be stored in a cool place.

1. *PSGB Lab Report P/75/14* 1975.

Adverse Effects

Because the therapeutic use of cocaine is now very restricted many reports of adverse effects occur in the context of abuse. However, both systemic and local effects have followed its use as a surface anaesthetic. Although some effects are similar to those of other local anaesthetics (p.1850), cocaine differs in that it acts as a potent indirect-acting sympathomimetic. It stimulates the CNS causing agitation, dilated pupils, tachycardia, hypertension, hallucinations, hypertonia, and hyperreflexia. Convulsions, coma, and metabolic acidosis may develop. Symptoms of CNS stimulation and sympathetic overactivity are very marked in overdosage with cocaine. A single oral dose of 1 g may be fatal, but some persons have a cocaine idiosyncrasy and severe toxicity may occur after doses of only 10 mg intravenously. Systemic absorption of small doses may slow the heart, but with increasing doses tachycardia, hypertension, and ventricular fibrillation occur.

High concentrations of cocaine should not be used topically as, in addition to risks of systemic toxicity after absorption, lasting local damage may occur.

Topical application of cocaine to the cornea can cause corneal damage with clouding, pitting, sloughing, and occasionally ulceration. Topical application to the nose or mouth has been reported to cause loss of smell and taste respectively.

Prolonged use of cocaine by nasal inhalation may cause mucosal damage or perforation of the nasal septum.

Abuse. Cocaine abuse and its effects have been discussed in a number of reviews.[1-6]

Cocaine abuse was once only in the form of chewing of coca leaves containing small amounts of cocaine, but processing of the leaves has led to abuse with a variety of more dangerous preparations containing higher concentrations of cocaine.[7] Coca paste, produced by maceration of the leaves with petrol and sulfuric acid, contains about 40 to 90% of cocaine sulfate and is smoked with tobacco or cannabis. Treatment of coca paste with hydrochloric acid produces cocaine hydrochloride, which is abused by intravenous injection, either alone or with diamorphine, or by sniffing to achieve nasal absorption. Alkaloidal cocaine (cocaine base; 'freebase'), which is abused by smoking, is produced by treating cocaine hydrochloride with alkali, followed either by heating (to form 'crack' cocaine) or by extracting the base from ether or another organic solvent. The route by which cocaine is taken determines the rate and extent of its absorption, and hence the abuse potential, although once absorbed, the pharmacokinetics are independent of route. Intravenous cocaine hydrochloride and smoked cocaine base have a greater potential for abuse than intranasal cocaine hydrochloride because of their greater rapidity and intensity of effects.

The psychological effects of cocaine abuse may be described by a cycle of initial euphoria followed by dysphoria and finally schizophreniform psychosis.[7,8] Euphoria may be accompanied by other symptoms of stimulation such as sexual arousal, anorexia, insomnia, hyperexcitability, loquacity, and grandiosity, and users may appear manic. After a short time these feelings are replaced by symptoms of dysphoria including considerable anxiety, fear, depression, apathy, irritability, and suspiciousness. Dysphoria may be ameliorated by repeated use, so the user develops the need to take the drug continuously to feel relatively well, but repeated use appears to diminish the intensity of the effects.[7] During euphoria and dysphoria users may experience a wide range of physical symptoms including palpitations, headache, dizziness, gastrointestinal effects, hyperhidrosis, tremors, tachycardia, hypertension, fever, and myoclonic jerks. Seizures can also occur after repeated use. In chronic abusers psychological deterioration may eventually occur, resulting in loss of mental function, compulsive disorders, suicidal ideation, psychopathic disorders, and ultimately a psychosis resembling acute paranoid schizophrenia similar to that seen with amfetamines.[7,8] Symptoms may include paranoia, stereotyped behaviour, delusions, loss of impulse control, violence, and visual, olfactory, auditory, gustatory, and tactile hallucinations. Overdosage can result in death due to status epilepticus, hyperthermia, ventricular tachycardia, and cardiac or respiratory arrest.[7]

For further details of the adverse effects of cocaine abuse, including effects due to use during pregnancy, see below.

1. Johanson C-E, Fischman MW. The pharmacology of cocaine related to its abuse. *Pharmacol Rev* 1989; **41:** 3–52.
2. Warner EA. Cocaine abuse. *Ann Intern Med* 1993: **119:** 226–35.
3. Strang J, *et al.* Cocaine in the UK—1991. *Br J Psychiatry* 1993; **162:** 1–13.
4. Das G. Cocaine abuse in North America: a milestone in history. *J Clin Pharmacol* 1993; **33:** 296–310.
5. Hatsukami DK, Fischman MW. Crack cocaine and cocaine hydrochloride: are the differences myth or reality? *JAMA* 1996; **276:** 1580–8.
6. Brownlow HA, Pappachan J. Pathophysiology of cocaine abuse. *Eur J Anaesthesiol* 2002; **19:** 395–414.
7. Arif A, ed. *Adverse health consequences of cocaine abuse.* Geneva: WHO, 1987.
8. Leikin JB, *et al.* Clinical features and management of intoxication due to hallucinogenic drugs. *Med Toxicol Adverse Drug Exp* 1989; **4:** 324–50.

ADULTERATION. For a report of methaemoglobinaemia as a result of the ingestion of cocaine adulterated with benzocaine, see Abuse under Adverse Effects of Benzocaine, p.1854.

BREAST FEEDING. The American Academy of Pediatrics[1] has stated that, when used as a drug of abuse by breast-feeding mothers, cocaine has caused signs of intoxication in the infant, notably diarrhoea, vomiting, irritability, seizures, and tremulousness.

Acute intoxication has been reported in a breast-fed child whose mother was using cocaine intranasally.[2]

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 02/06/04)
2. Chasnoff IJ, *et al.* Cocaine intoxication in a breast-fed infant. *Pediatrics* 1987; **80:** 836–8.

EFFECTS ON THE BLOOD. References.

1. Leissinger CA. Severe thrombocytopenia associated with cocaine use. *Ann Intern Med* 1990; **112:** 708–10.

EFFECTS ON THE CARDIOVASCULAR SYSTEM. There appears to be no relationship between underlying heart disease and the risk of cocaine-induced cardiac effects and cardiac events can occur regardless of the route of abuse.[1] Cardiovascular toxicity due to cocaine may be related to individual sensitivity and therefore may not be predictable or dose dependent.[2] Patients with plasma cholinesterase deficiency are particularly at risk for sudden death.[3] Other risk factors for cardiovascular disease, such as cigarette smoking or pre-existing atherosclerosis, may exacerbate the cardiac toxicity of cocaine.[4-6] Cocaine blocks reuptake of catecholamines at adrenergic nerve endings and thus produces sympathetic stimulation of the cardiovascular system. Accumulation of catecholamines predisposes the myocardium to arrhythmias,[7] and sinus tachycardia, supraventricular or ventricular tachyarrhythmias, myocarditis, and sudden arrhythmic death may occur.[7-9] Severe hypertension can lead to cerebrovascular accidents and stroke has occurred even in young adults without other predisposing conditions.[10,11] However, the exact mechanism of cocaine-induced stroke remains unclear and other implicated effects include vasospasm, cerebral vasculitis, enhanced platelet aggregation, and cardioembolism.[12] Aortic dissection and rupture of the aorta have also occurred.[6] Up to 25% of emergency admissions to US urban hospitals with nontraumatic chest pain have detectable amounts of cocaine or its metabolites in their urine, but only a minority of these have myocardial infarction,[6] as chest pain without signs of myocardial infarction also commonly occurs.[8] Asymptomatic myocardial ischaemia manifesting as episodes of ST segment elevation has also been reported during withdrawal of cocaine.[13] The mechanism for these changes is probably multifactional, including increased myocardial oxygen demand, coronary vasoconstriction, and enhanced platelet aggregation and thrombus formation.[6,14] The immediate vasoconstrictor effect of cocaine may be followed by delayed or recurrent vasoconstriction due to its active metabolites, benzoylecgonine and ethyl methyl ecgonine.[6]

Vasoconstriction may also produce ischaemia in the fingers, toes, spinal cord,[8] spleen,[15] and intestines.[16] Renal ischaemia and infarction may also occur.[17,18] Other reported cardiovascular effects include dilated cardiomyopathy and premature atherosclerosis.[6]

1. VanDette JM, Cornish LA. Medical complications of illicit cocaine use. *Clin Pharm* 1989; **8:** 401–11.
2. Thadani PV. Cardiovascular toxicity of cocaine: underlying mechanisms. *J Appl Cardiol* 1990; **5:** 317–20.
3. Cregler LL, Mark H. Medical complications of cocaine abuse. *N Engl J Med* 1986; **315:** 1495–1500.
4. Moliterno DJ, *et al.* Coronary-artery vasoconstriction induced by cocaine, cigarette smoking, or both. *N Engl J Med* 1994; **330:** 454–9.
5. Higgins ST, *et al.* Influence of cocaine use on cigarette smoking. *JAMA* 1994; **272:** 1724.
6. Lange RA, Hillis LD. Cardiovascular complications of cocaine use. *N Engl J Med* 2001; **345:** 351–8. Correction. *ibid.*; 1432.
7. Loper KA. Clinical toxicology of cocaine. *Med Toxicol Adverse Drug Exp* 1989; **4:** 174–85.
8. Anonymous. Acute reactions to drugs of abuse. *Med Lett Drugs Ther* 1990; **32:** 92–4.
9. Bauman JL, *et al.* Cocaine-related sudden cardiac death: a hypothesis correlating basic science and clinical observations. *J Clin Pharmacol* 1994; **34:** 902–11.
10. Kaku DA, Lowenstein DH. Emergence of recreational drug abuse as a major risk factor for stroke in young adults. *Ann Intern Med* 1990; **113:** 821–7.
11. Levine SR, *et al.* Cerebrovascular complications of the use of the "crack" form of alkaloidal cocaine. *N Engl J Med* 1990; **323:** 699–704.
12. Treadwell SD, Robinson TG. Cocaine use and stroke. *Postgrad Med J* 2007; **83:** 389–94.
13. Nademanee K, *et al.* Myocardial ischemia during cocaine withdrawal. *Ann Intern Med* 1989; **111:** 876–80.
14. Rezkalla SH, Kloner RA. Cocaine-induced acute myocardial infarction. *Clin Med Res* 2007; **5:** 172–6.
15. Novielli KD, Chambers CV. Splenic infarction after cocaine use. *Ann Intern Med* 1991; **114:** 251–2.
16. Freudenberger RS, *et al.* Intestinal infarction after intravenous cocaine administration. *Ann Intern Med* 1990; **113:** 715–16.
17. Sharff JA. Renal infarction associated with intravenous cocaine use. *Ann Emerg Med* 1984; **13:** 1145–7.
18. Bemanian S, *et al.* Cocaine-induced renal infarction: report of a case and review of the literature. *BMC Nephrol* 2005; **6:** 10. Available at: http://www.biomedcentral.com/1471-2369/6/10 (accessed 22/06/06)

EFFECTS ON THE CNS. Severe CNS depression with deep coma has been seen in a few cocaine abusers after prolonged binges.[1]

1. Roberts JR, Greenberg MI. Cocaine washout syndrome. *Ann Intern Med* 2000; **132:** 679–80.

EFFECTS ON THE KIDNEYS. For reference to renal failure following rhabdomyolysis associated with cocaine abuse, see under Effects on the Muscles, below. There has been a report[1] of acute renal failure occurring in a 16-year-old girl secondary to cocaine abuse but without evidence of rhabdomyolysis.

For reference to renal ischaemia and infarction due to cocaine abuse, see under Effects on the Cardiovascular System, above.

1. Leblanc M, *et al.* Cocaine-induced acute renal failure without rhabdomyolysis. *Ann Intern Med* 1994; **121:** 721–2.

EFFECTS ON THE LUNGS. Smoking the free base has resulted in pulmonary complications not encountered with other methods of abuse for cocaine. Associated adverse effects have included pulmonary oedema, hypersensitivity pneumonitis, pulmonary haemorrhage, obliterative bronchiolitis, abnormalities of pulmonary function, pneumomediastinum, and pneumothorax.[1] Severe or life-threatening exacerbations of asthma have also been reported.[2]

1. Ettinger NA, *et al.* A review of the respiratory effects of smoking cocaine. *Am J Med* 1989; **87:** 664–8.
2. Rubin RB, Neugarten J. Cocaine-associated asthma. *Am J Med* 1990; **88:** 438–9.

EFFECTS ON THE MOUTH. Abuse of cocaine can produce several adverse effects in the oral cavity including perforation of the palate (usually after perforation of the nasal septum), gingival lesions, and erosions of the teeth.[1]

1. Brand HS, *et al.* Cocaine and oral health. *Br Dent J* 2008; **204:** 365–9.

EFFECTS ON THE MUSCLES. Rhabdomyolysis, sometimes progressing to renal failure, has been associated with free-base smoking or injection of cocaine hydrochloride.[1-3]

1. Roth D, *et al.* Acute rhabdomyolysis associated with cocaine intoxication. *N Engl J Med* 1988; **319:** 673–7.
2. Herzlich BC, *et al.* Rhabdomyolysis related to cocaine abuse. *Ann Intern Med* 1988; **109:** 335–6.
3. Pogue VA, Nurse HM. Cocaine-associated acute myoglobinuric renal failure. *Am J Med* 1989; **86:** 183–6.

EFFECTS ON SEXUAL FUNCTION. While the initial euphoria of cocaine abuse may be accompanied by sexual arousal, sexual dysfunction can occur[1] and male infertility has been reported.[2] Priapism associated with cocaine abuse has also occurred.[3]

1. Cregler LL, Mark H. Medical complications of cocaine abuse. *N Engl J Med* 1986; **315:** 1495–1500.
2. Bracken MB, *et al.* Association of cocaine use with sperm concentration, motility, and morphology. *Fertil Steril* 1990; **53:** 315–22.
3. Altman AL, *et al.* Cocaine associated priapism. *J Urol* 1999; **161:** 1817–18.

EFFECTS ON THE SKIN. Urticarial vasculitis occurred in a young man after intranasal abuse of cocaine.[1]

1. Hofbauer GFL, *et al.* Uritcarial vasculitis following cocaine use. *Br J Dermatol* 1999; **141:** 600–601.

OVERDOSAGE. References to fatal overdosage from cocaine abuse.

1. Greenland VC, *et al.* Vaginally administered cocaine overdose in a pregnant woman. *Obstet Gynecol* 1989; **74:** 476–7.
2. Peretti FJ, *et al.* Cocaine fatality: an unexplained blood concentration in a fatal overdose. *Forensic Sci Int* 1990; **48:** 135–8.
3. Karch SB, *et al.* Relating cocaine blood concentrations to toxicity–an autopsy study of 99 cases. *J Forensic Sci* 1998; **43:** 41–5.

PREGNANCY. The effects of cocaine abuse during pregnancy have been reviewed.[1-4] Women who abuse cocaine during pregnancy appear to have an increased risk of spontaneous abortion,[5] abruptio placentae[6,7] and associated still-births,[8] premature labour,[9-11] and other birth complications.[9-11] These effects may be due to vasoconstriction by cocaine increasing maternal blood pressure and reducing placental blood flow.[12] Uterine rupture[13] during pregnancy and rupture of ectopic pregnancies[14] have also been associated with cocaine. Neonates born to mothers abusing cocaine have an increased risk of intra-uterine growth retardation and may have lower birthweight, smaller head size, and shorter length.[6,8-10,15-17] Cocaine is possibly teratogenic and congenital abnormalities associated with abuse include cardiovascular abnormalities,[9,18,19] limb reduction defects,[20] intestinal atresia or infarction,[20] skull defects,[8] and genito-urinary tract anomalies.[21] Neurobehavioural impairment[22] and signs of transient CNS irritability[23] may also occur. Some workers[24,25] have found effects on cognition and motor delays while others have found effects on arousal and attention regulation rather than cognitive processes.[26] Cocaine can increase neonatal cerebral blood flow[27] and cerebral infarction and associated seizures have occurred in neonates whose mothers took cocaine near to the onset of labour.[28] Evidence on the risk of intraventricular haemorrhage is conflicting.[7,24]

1. Slutsker L. Risks associated with cocaine use during pregnancy. *Obstet Gynecol* 1992; **79:** 778–89.
2. Volpe JJ. Effects of cocaine use on the fetus. *N Engl J Med* 1992; **327:** 399–407. Correction. *ibid.*; 1039.
3. Wiggins RC. Pharmacokinetics of cocaine in pregnancy and effects on fetal maturation. *Clin Pharmacokinet* 1992; **22:** 85–93.
4. Fajemirokun-Odudeyi O, Lindow SW. Obstetric implications of cocaine use in pregnancy: a literature review. *Eur J Obstet Gynecol Reprod Biol* 2004; **112:** 2–8.
5. Chasnoff IJ, *et al.* Cocaine use in pregnancy. *N Engl J Med* 1985; **313:** 666–9.
6. Dombrowski MP, *et al.* Cocaine abuse is associated with abruptio placentae and decreased birth weight, but not shorter labor. *Obstet Gynecol* 1991; **77:** 139–41.
7. Dusick AM, *et al.* Risk of intracranial hemorrhage and other adverse outcomes after cocaine exposure in a cohort of 323 very low birth weight infants. *J Pediatr* 1993; **122:** 438–45.
8. Bingol N, *et al.* Teratogenicity of cocaine in humans. *J Pediatr* 1987; **110:** 93–6.
9. Little BB, *et al.* Cocaine abuse during pregnancy: maternal and fetal implications. *Obstet Gynecol* 1989; **73:** 157–60.
10. Mastrogiannis DS, *et al.* Perinatal outcome after recent cocaine usage. *Obstet Gynecol* 1990; **76:** 8–11.
11. Spence MR, *et al.* The relationship between recent cocaine use and pregnancy outcome. *Obstet Gynecol* 1991; **78:** 326–9.
12. Farrar HC, Kearns GL. Cocaine: clinical pharmacology and toxicology. *J Pediatr* 1989; **115:** 665–75.
13. Gonsoulin W, *et al.* Rupture of unscarred uterus in primigravid woman in association with cocaine abuse. *Am J Obstet Gynecol* 1990; **163:** 526–7.
14. Thatcher SS, *et al.* Cocaine use and acute rupture of ectopic pregnancies. *Obstet Gynecol* 1989; **74:** 478–9.
15. Zuckerman B, *et al.* Effects of maternal marijuana and cocaine use on fetal growth. *N Engl J Med* 1989; **320:** 762–8.
16. Chasnoff IJ, *et al.* Temporal patterns of cocaine use in pregnancy: perinatal outcome. *JAMA* 1989; **261:** 1741–4.
17. Little BB, Snell LM. Brain growth among fetuses exposed to cocaine in utero: asymmetrical growth retardation. *Obstet Gynecol* 1991; **77:** 361–4.
18. Lipshultz SE, *et al.* Cardiovascular abnormalities in infants prenatally exposed to cocaine. *J Pediatr* 1991; **118:** 44–51.
19. Shaw GM, *et al.* Maternal use of cocaine during pregnancy and congenital cardiac anomalies. *J Pediatr* 1991; **118:** 167–8.
20. Hoyme HE, *et al.* Prenatal cocaine exposure and fetal vascular disruption. *Pediatrics* 1990; **85:** 743–7.
21. Chávez GF, *et al.* Maternal cocaine use during early pregnancy as a risk factor for congenital urogenital anomalies. *JAMA* 1989; **262:** 795–8.
22. Singer LT, *et al.* Neurobehavioural sequelae of fetal cocaine exposure. *J Pediatr* 1991; **119:** 667–72.
23. Doberczak TM, *et al.* Neonatal neurologic and electroencephalographic effects of intrauterine cocaine exposure. *J Pediatr* 1988; **113:** 354–8.
24. Singer LT, *et al.* Increased incidence of intraventricular hemorrhage and developmental delay in cocaine-exposed, very low birth weight infants. *J Pediatr* 1994; **124:** 765–71.
25. Azuma SD, Chasnoff IJ. Outcome of children prenatally exposed to cocaine and other drugs: a path analysis of three-year data. *Pediatrics* 1993; **92:** 396–402.
26. Mayes LC, *et al.* Information processing and developmental assessments in 3-month-old infants exposed prenatally to cocaine. *Pediatrics* 1995; **95:** 539–45.
27. van der Bor M, *et al.* Increased cerebral blood flow velocity in infants of mothers who abuse cocaine. *Pediatrics* 1990; **85:** 733–6.
28. Chasnoff IJ, *et al.* Perinatal cerebral infarction and maternal cocaine use. *J Pediatr* 1986; **108:** 456–9.

Treatment of Adverse Effects

As for Local Anaesthetics in general, p.1851.

Cocaine overdosage. In the emergency management of overdosage with cocaine the general aims are to establish adequate ventilation and support the circulation. If oral ingestion of a large amount is suspected the stomach should be emptied and activated charcoal given.[1] A tourniquet may be applied to limit absorption if the drug was injected. Patients who have swallowed packages containing cocaine for the purpose of smuggling, may be given laxatives but surgical intervention may be required if signs of toxicity appear.[2]

Sedation with intravenous diazepam may be sufficient to manage the symptoms of cocaine overdose. Sedation with benzodiazepines may also be appropriate initial therapy for hypertension or tachyarrhythmias since the excessive sympathetic tone is largely centrally mediated.[3] Severe life-threatening arrhythmias may require treatment with intravenous propranolol although, following a report of paradoxical hypertension presumably due to unopposed α-adrenergic stimulation, a beta blocker with both α- and β-adrenergic effects such as labetalol is preferred by some if hypertension is also present;[2,4] sodium nitroprusside[3,4] or phentolamine[3,5] may also be used. Although labetalol can reduce the hypertension it does not alleviate cocaine-induced coronary vasoconstriction;[6] it has therefore been suggested that glyceryl trinitrate would be preferable for patients with cocaine-induced chest pain.[5,6] Chest pain may also be treated with aspirin. Calcium-channel blockers such as verapamil may also be of use as an antagonist for coronary artery vasoconstriction induced by cocaine.[5] There is concern about the use of lidocaine for the treatment of cocaine-induced arrhythmias as lidocaine may enhance toxicity.[5] Diazepam should be used to manage seizures[1,4] but if they cannot be controlled phenytoin can be used as an adjunct.[1] Hyperthermia should be treated with physical cooling but the use of dantrolene may also be necessary.[1] Control of anxiety and agitation with benzodiazepines when combined with rapid cooling may also have the effect of decreasing heat production in hyperthermic patients.[3] Metabolic acidosis should be monitored and treated where necessary.[1,4] Short-acting barbiturates or benzodiazepines may be used for dysphoric agitation but drugs that lower the seizure threshold or aggravate hyperthermia such as phenothiazines or haloperidol should be avoided.[1]

1. Loper KA. Clinical toxicology of cocaine. *Med Toxicol Adverse Drug Exp* 1989; **4:** 174–85.
2. Ramrakha P, Barton I. Drug smuggler's delirium. *BMJ* 1993; **306:** 470–1.
3. Anonymous. Acute reactions to drugs of abuse. *Med Lett Drugs Ther* 1996; **38:** 43–6.
4. Farrar HC, Kearns GL. Cocaine: clinical pharmacology and toxicology. *J Pediatr* 1989; **115:** 665–75.
5. Hollander JE. The management of cocaine-associated myocardial ischemia. *N Engl J Med* 1995; **333:** 1267–72.
6. Boehrer JD, *et al.* Influence of labetalol on cocaine-induced coronary vasoconstriction in humans. *Am J Med* 1993; **94:** 608–10.

Cocaine withdrawal syndrome. Cocaine can produce psychological dependence but does not produce a major physical withdrawal syndrome. The management of cocaine abuse and dependence has been reviewed.[1-3] There is no advantage to gradual withdrawal and it is best for the patient to stop the drug abruptly.[1,4] The three major psychiatric complications associated with cocaine withdrawal are dysphoric agitation, severe depression, and psychotic symptoms.[1] Such complications are initially managed with psychosocial treatments. However patients with more severe dependence or those who fail to respond to psychosocial treatments should be considered for drug therapies. Dysphoric agitation is best treated with diazepam; propranolol may also be used in more persistent cases. Depressive symptoms during the acute post-cocaine phase are usually transient and require no treatment other than close observation. Desipramine has been used with equivocal results; it appears to be of most benefit in patients who have antecedent or consequent symptoms of severe depression.[3] Trazodone and imipramine have also been tried but had more adverse effects than desipramine.[3] Furthermore, a systematic review has concluded that there was no evidence to support the use of antidepressants[5] in the treatment of cocaine dependence. Antipsychotics such as chlorpromazine, haloperidol, and promazine have been used to manage patients with psychotic symptoms associated with cocaine dependence.[1]

Several drugs have been tried in the maintenance of abstinence from cocaine.[1] Lithium may be useful in patients with bipolar disorder or cyclothymic personality. Methylphenidate may be helpful in patients with attention deficit disorders but has potential for abuse itself. Phenothiazine derivatives have been tried in the control of impulsive behaviour and to decrease cocaine craving, although adverse effects may limit their acceptability. Carbamazepine has been reported to suppress the craving for cocaine although this has not been supported by subsequent studies.[3] Buprenorphine has been investigated to suppress cocaine and opioid use in patients dependent on both drugs.[3] Anxiolytics or antidepressants are considered unlikely to be of benefit in maintaining abstinence.[3] MAOIs such as phenelzine have been used in a manner analogous to the use of disulfiram in alcohol abuse to provoke unpleasant reactions if patients relapse.[6] Disulfiram itself has also been tried with some success (see below).

There is evidence to suggest that cocaine use affects the dopaminergic modulation of CNS function, and several drugs that interact with the dopamine system have been tried in the treatment of cocaine abuse and dependence.[3,7] For most drugs the results have been disappointing or equivocal although disulfiram and selegiline may warrant further investigation.[7]

1. Arif A, ed. *Adverse health consequences of cocaine abuse*. Geneva: WHO, 1987.
2. Kleber HD. Pharmacotherapy, current and potential, for the treatment of cocaine dependence. *Clin Neuropharmacol* 1995; **18** (suppl 1): S96–S109.
3. Mendelson JH, Mello NK. Management of cocaine abuse and dependence. *N Engl J Med* 1996; **334:** 965–72.
4. DoH. *Drug misuse and dependence: guidelines on clinical management*. London: HMSO, 1999. Also available at: http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/04.00dh/04.00en/documents/digitalasset/dh_4078198.pdf (accessed 11/08/08)
5. Lima MS, *et al.* Antidepressants for cocaine dependence. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2003 (accessed 21/04/08).
6. Brewer C. Cocaine and crack. *BMJ* 1989; **299:** 792.
7. Gorelick DA, *et al.* Agents in development for the management of cocaine abuse. *Drugs* 2004; **64:** 1547–73.

Precautions

As for Local Anaesthetics in general, p.1851.

Since some patients have a marked sensitivity to cocaine, giving a test dose before use on mucous membranes has been suggested. Cocaine should not be applied to damaged mucosa because of the risk of systemic toxicity from enhanced absorption. Ophthalmic preparations of cocaine should not be applied to the eyes for prolonged periods as damage to the cornea may occur not only from the local action of cocaine, but also from loss of the protective eyelid reflexes. As with other mydriatics, there is also a risk of cocaine precipitating angle-closure glaucoma in patients predisposed to the condition. Patients receiving cocaine for surface anaesthesia should be monitored for possible cardiovascular effects. Cocaine should be used with great caution in patients with hypertension, cardiovascular disease, or thyrotoxicosis. It is not recommended for use during pregnancy or breast feeding.

Abuse. Cocaine is subject to abuse. See under Adverse Effects, above.

Gilles de la Tourette's syndrome. Gilles de la Tourette's syndrome, which had been well controlled for 10 years by haloperidol, was precipitated in a 27-year-old man after intranasal use of cocaine on one occasion.[1]

1. Mesulam M-M. Cocaine and Tourette's syndrome. *N Engl J Med* 1986; **315:** 398.

Myasthenia gravis. Report of a patient in whom cocaine abuse first unmasked and then exacerbated myasthenia gravis.[1]

1. Berciano J, *et al.* Myasthenia gravis unmasked by cocaine abuse. *N Engl J Med* 1991; **325:** 892.

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

Interactions

For interactions associated with local anaesthetics, see p.1851.

Cocaine and adrenaline enhance each other's sympathomimetic effects and should preferably not be used together. Caution is needed if cocaine is used with other drugs that may also potentiate the action of catecholamines such as guanethidine or MAOIs.

Adrenaline. In a report[1] of 3 cases of arrhythmias associated with the use of a paste containing cocaine 25% and adrenaline 0.18% for local anaesthesia of the nasal mucosa, the amount of cocaine applied to the nasal mucosa ranged from about 2.5 to 4.5 mg/kg. The maximum recommended dose of cocaine alone in healthy adults is 1.5 mg/kg.

1. Nicholson KEA, Rogers JEG. Cocaine and adrenaline paste: a fatal combination? *BMJ* 1995; **311:** 250–1.

Alcohol. In the presence of alcohol, cocaine is metabolised to its ethyl homologue cocaethylene.[1] Cocaethylene appears to have the same stimulant effects as cocaine but it has a longer half-life and *animal* studies suggest that it is more toxic than the parent drug. However, a review of the literature concluded that the use of cocaine with alcohol did not cause more cardiovascular problems than expected from the additive effects of each drug.[2]

1. Randall T. Cocaine, alcohol mix in body to form even longer lasting, more lethal drug. *JAMA* 1992; **267:** 1043–4.
2. Pennings EJM, *et al.* Effects of concurrent use of alcohol and cocaine. *Addiction* 2002; **97:** 773–83.

Beta blockers. *Propranolol* potentiated cocaine-induced coronary vasoconstriction after intranasal dosage of cocaine in a placebo-controlled study.[1] Because of a possible risk of paradoxical hypertension associated with the use of propranolol to manage arrhythmias associated with cocaine overdosage some prefer the use of labetalol for this indication (see under Treatment of Adverse Effects, above).

1. Lange RA, *et al.* Potentiation of cocaine-induced coronary vasoconstriction by beta-adrenergic blockade. *Ann Intern Med* 1990; **112:** 897–903.

Haloperidol. For the effect of haloperidol in cocaine abusers, see under Chlorpromazine, p.974.

Pharmacokinetics

Cocaine may be slowly absorbed from some sites because of the vasoconstriction it produces, but absorption occurs from all sites of application, including mucous membranes and the gastrointestinal tract, and may be enhanced when there is inflammation. Cocaine is rapidly absorbed when smoked.

Cocaine is rapidly metabolised by plasma esterases and hepatic esterases to ecgonine methyl ester. Benzoylecgonine, another major metabolite of cocaine, may be produced by spontaneous hydrolysis. Cocaine is also demethylated to the active metabolite norcocaine which is not excreted but undergoes further metabolism. There is considerable interindividual variation in the plasma half-life of cocaine possibly due to differences in esterase activity.

Cocaine and its metabolites are excreted in the urine, about 10% appearing as unchanged drug; they may be detectable in urine for several days or even weeks after use. Cocaine crosses the blood-brain barrier and accumulates within the CNS. It does not appear to undergo rapid metabolism within the brain and concentrations in the CNS after acute intoxication may greatly exceed those in plasma.

Cocaine crosses the placenta and the presence of its metabolites in neonatal hair has been used to indicate intra-uterine exposure. Cocaine is distributed into breast milk.

See also under Local Anaesthetics, p.1852.

◊ References.

1. Busto U, *et al.* Clinical pharmacokinetics of non-opiate abused drugs. *Clin Pharmacokinet* 1989; **16:** 1–26.
2. Graham K, *et al.* Determination of gestational cocaine exposure by hair analysis. *JAMA* 1989; **262:** 3328–30.
3. Burke WM, Ravi NV. Urinary excretion of cocaine. *Ann Intern Med* 1990; **112:** 548–9.
4. Ravi NV, Burke WM. Cocaine and traffic accident fatalities in New York City. *JAMA* 1990; **263:** 2887.
5. Schenker S, *et al.* The transfer of cocaine and its metabolites across the term human placenta. *Clin Pharmacol Ther* 1993; **53:** 329–39.

Absorption. Cocaine is rapidly absorbed from the pulmonary vasculature when smoked and the speed of onset of its effects is similar to that obtained after intravenous injection.[1] Absorption from mucous membranes is delayed by vasoconstriction and peak plasma concentrations of up to 474 nanograms/mL have been obtained 15 to 120 minutes after application of doses of 1.5 to 2 mg/kg to the nasal mucosa as a 10% cocaine hydrochloride solution;[2,3] cocaine may still be detectable in the nose several hours later and this may result in prolonged systemic absorption.[2] In a study it was estimated that only 5% of the total dose of cocaine hydrochloride used prior to nasal surgery was absorbed from the nasal mucosa following application of 500 mg of cocaine hydrochloride as a 25% paste with adrenaline or 200 mg as a 10% solution with adrenaline (Moffett's solution) and blood concentrations were well below those associated with toxicity[4] (but see also Adrenaline, under Interactions, above). Peak serum concentrations of cocaine have been obtained after 50 to 90 minutes after oral use and are similar to those obtained after nasal application.[3]

1. Farrar HC, Kearns GL. Cocaine: clinical pharmacology and toxicology. *J Pediatr* 1989; **115:** 665–75.
2. Van Dyke C, *et al.* Cocaine: plasma concentrations after intranasal application in man. *Science* 1976; **191:** 859–61.
3. Van Dyke C, *et al.* Oral cocaine: plasma concentrations and central effects. *Science* 1978; **200:** 211–13.
4. Quiney RE. Intranasal topical cocaine: Moffett's method or topical cocaine paste? *J Laryngol Otol* 1986; **100:** 279–83.

Uses and Administration

Cocaine, a benzoic acid ester, is a local anaesthetic with actions and uses similar to those described on p.1852. It is used as a surface anaesthetic but, because of systemic adverse effects and its abuse potential, its use is now almost entirely restricted to surgery of the ear, nose, and throat. It has been largely replaced by other drugs in ophthalmology because of its corneal toxicity, although it may still be useful in removal or debridement of the corneal epithelium. Cocaine also blocks the uptake of catecholamines at adrenergic nerve endings and potentiates the action of catecholamines. Its sympathomimetic actions cause tachycardia, peripheral vasoconstriction, a rise in blood pressure, and mydriasis. The use of cocaine with sympathomimetics such as adrenaline increases the risk of cardiac arrhythmias. Despite this hazard some use this combination in otolaryngology to improve the operative field and reduce absorption.

When applied to mucous membranes, surface anaesthesia develops rapidly and persists for 30 minutes or longer depending on the concentration of cocaine used, the dose, and on the vascularity of the tissue.

Cocaine hydrochloride is used in aqueous solutions; cocaine hydrochloride 1.12 g is equivalent to about 1 g of cocaine. Solutions containing up to 4% have been used in ophthalmology (but precautions for ophthalmic use should be considered, see above).

Solutions containing up to 10% of cocaine are applied to the nasal mucosa in otolaryngological procedures. Pastes containing up to 25% of cocaine have also been applied.

In order to avoid systemic effects, the usual maximum total dose recommended for application to the nasal mucosa in healthy adults is 1.5 mg/kg. It should be used only by those skilled in the precautions needed to minimise absorption and the consequent risk of arrhythmias.

Cocaine was used with diamorphine or morphine for the relief of severe pain, especially in terminal illness, but this use is now obsolete.

Cocaine solutions should *never* be given by injection; other local anaesthetics are equally effective and much safer.

◊ References.

1. Middleton RM, Kirkpatrick MB. Clinical use of cocaine: a review of the risks and benefits. *Drug Safety* 1993; **9:** 212–17.
2. Latorre F, Klimek L. Does cocaine still have a role in nasal surgery? *Drug Safety* 1999; **20:** 9–13.

Preparations

BP 2008: Cocaine Eye Drops;
USP 31: Cocaine and Tetracaine Hydrochlorides and Epinephrine Topical Solution; Cocaine Hydrochloride Tablets for Topical Solution.

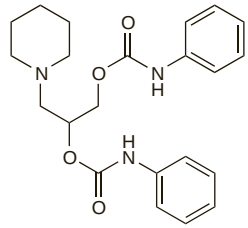
Diperodon Hydrochloride *(BANM, rINNM)*

Diperocaine Hydrochloride; Dipérodon, Chlorhydrate de; Diperodoni Hydrochloridum; Hidrocloruro de diperodón. 3-Piperidinopropylene bis(phenylcarbamate) hydrochloride.

Диперодона Гидрохлорид

$C_{22}H_{27}N_3O_4$,HCl = 433.9.

CAS — 101-08-6 (anhydrous diperodon); 51552-99-9 (diperodon monohydrate); 537-12-2 (diperodon hydrochloride).



(diperodon)

Profile

Diperodon is a local anaesthetic (p.1850) that has been used as the base or the hydrochloride for surface anaesthesia.

Dyclonine Hydrochloride *(BANM, rINNM)*

Dyclocaine Hydrochloride; Dyclocaini Chloridum; Dyclonine, Chlorhydrate de; Dyclonini Hydrochloridum; Hidrocloruro de diclonina. 4′-Butoxy-3-piperidinopropiophenone hydrochloride.

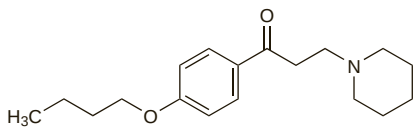
Диклонина Гидрохлорид

$C_{18}H_{27}NO_2$,HCl = 325.9.

CAS — 586-60-7 (dyclonine); 536-43-6 (dyclonine hydrochloride).

ATC — N01BX02; R02AD04.

ATC Vet — QN01BX02; QR02AD04.



(dyclonine)

Pharmacopoeias. In *US*.
USP 31 (Dyclonine Hydrochloride). White crystals or white crystalline powder, with a slight odour. Soluble 1 in 60 of water, 1 in 24 of alcohol, and 1 in 2.3 of chloroform; soluble in acetone; practically insoluble in ether and in hexane. A 1% solution in water has a pH of 4.0 to 7.0. Store in airtight containers. Protect from light.

Profile

Dyclonine hydrochloride is a local anaesthetic (p.1850) used topically for surface anaesthesia of the skin and mucous membranes. Lozenges containing up to 3 mg and throat sprays containing 0.1% of dyclonine hydrochloride have been used for the temporary relief of pain associated with sore throats or mouth irritation; a 1% gel has also been used. A concentration of 0.75% has been used on the skin. It may cause irritation at the site of application.

Preparations

USP 31: Dyclonine Hydrochloride Gel; Dyclonine Hydrochloride Topical Solution.

Proprietary Preparations (details are given in Part 3)

Canad.: Cepacol Spray; Sucrets; Sucrets for Kids; ***Israel:*** Childrens Cherry Sucrets†; Sucrets Children's Formula†; Sucrets Maximum Strength†; ***USA:*** Dyclone†; Sucrets Childrens Formula; Sucrets Original Formula Sore Throat Wild Cherry; Sucrets Throat Spray.

Multi-ingredient: ***Canad.:*** Tanac†; ***USA:*** Cepacol Maximum Strength Sore Throat; Skin Shield; Sucrets Complete; Sucrets Maximum Strength Sore Throat; Tanac.

Ethyl Chloride

Aethylium Chloratum; Chlorethyl; Cloruro de etilo; Ethyli Chloridum; Ethylis Chloridum; Etylklorid; Etylu chlorek; Etyylikloridi; Hydrochloric Ether; Monochlorethane. Chloroethane.

C_2H_5Cl = 64.51.

CAS — 75-00-3.

ATC — N01BX01.

ATC Vet — QN01BX01.

Pharmacopoeias. In *Pol.* and *US*.
USP 31 (Ethyl Chloride). A colourless, mobile, very volatile liquid at low temperatures or under pressure, with a characteristic ethereal odour. B.p. 12° to 13°. Slightly soluble in water; freely soluble in alcohol and in ether. Store in airtight containers, preferably hermetically sealed.

Stability. Ethyl chloride is highly flammable and mixtures of the gas with 5 to 15% of air are explosive.

Adverse Effects and Precautions

As for Chloroform, p.1781.

Cutaneous sensitisation can occur rarely. Thawing of frozen tissue following surgery may be painful and prolonged spraying onto the skin can cause chemical frostbite. Freezing may also distort the histological structure of biopsy specimens. Ethyl chloride should not be applied to broken skin or mucous membranes.

Uses and Administration

Owing to its low boiling-point and the intense cold produced by evaporation, ethyl chloride has been used as a local anaesthetic in minor surgery but such use is not generally recommended. It has also been used topically for the relief of pain and to test the effectiveness of regional anaesthesia. Ethyl chloride was formerly used as an inhalational anaesthetic but has no place in modern anaesthetic practice.

Preparations

Proprietary Preparations (details are given in Part 3)
Ger.: Chloraethyl Dr Henning; WariActiv; ***Hong Kong:*** WariActiv; ***Hung.:*** Chloraethyl†; ***Israel:*** Chloraethyl Dr Henning; ***Mex.:*** Traumazol; ***Spain:*** Cloretilo Chemirosa; ***Switz.:*** Chlorethyl; ***UK:*** Cryogesic.

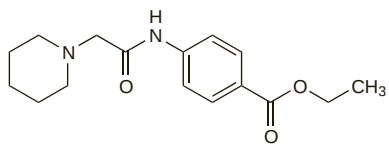
Multi-ingredient: ***USA:*** Fluro-Ethyl.

Ethyl *p*-Piperidinoacetylaminobenzoate

EPAB; *p*-Piperidinoacetilaminobenzoato de etilo; SA-7. 4-[(1-Piperidinylacetyl)amino]benzoic acid ethyl ester.

$C_{16}H_{22}N_2O_3$ = 290.4.

CAS — 41653-21-8.



Profile

Ethyl *p*-piperidinoacetylaminobenzoate is an amide local anaesthetic (p.1850) that has been given orally for the symptomatic relief of gastritis.

Preparations

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

Multi-ingredient: ***Hong Kong:*** Sulcain†; ***Singapore:*** Sulcain†; ***Thai.:*** Sulcain†.

Etidocaine *(BAN, USAN, rINN)*

Etidocaína; Étidocaïne; Etidocainum; Etidokaiini; Etidokain. (±)-2-(*N*-Ethylpropylamino)-butyro-2′,6′-xylidide.

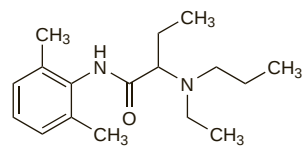
Этидокаин

$C_{17}H_{28}N_2O$ = 276.4.

CAS — 36637-18-0.

ATC — N01BB07.

ATC Vet — QN01BB07.



Etidocaine Hydrochloride *(BANM, rINNM)*

Étidocaïne, Chlorhydrate d'; Etidocaini Hydrochloridum; Hidrocloruro de etidocaína; W-19053.

Этидокаина Гидрохлорид

$C_{17}H_{28}N_2O$,HCl = 312.9.

CAS — 36637-19-1.

ATC — N01BB07.

ATC Vet — QN01BB07.

Adverse Effects, Treatment, and Precautions

As for Local Anaesthetics in general, p.1850.

Effects on the cardiovascular system. For a discussion of the cardiotoxicity of etidocaine, see under the Adverse Effects of Bupivacaine Hydrochloride, p.1855.

Porphyria. Etidocaine is considered to be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in *animals*.

Interactions

For interactions associated with local anaesthetics, see p.1851.

Pharmacokinetics

Etidocaine is rapidly absorbed into the circulation after parenteral injection and is about 95% bound to plasma proteins. It crosses the placenta but the ratio of fetal to maternal concentrations is relatively low. It also diffuses across the blood-brain barrier. Etidocaine is metabolised in the liver and its numerous metabolites are excreted in the urine; less than 10% of the drug is excreted unchanged. The plasma elimination half-life of etidocaine is 2 to 3 hours in adults.

See also under Local Anaesthetics, p.1852.

Pregnancy. After maternal injection etidocaine rapidly crosses the placenta[1] but the degree of transfer is less than for other local anaesthetics including bupivacaine.[2] The ratio of fetal to maternal concentrations of etidocaine varies but values up to about 0.35 are usual.[1,2] Some metabolites appear to be transferred to a greater degree than the parent compound[1]. Etidocaine is highly protein bound but the fraction of unbound drug in plasma increases in pregnant women during delivery.[1] Protein binding of etidocaine is also reduced in fetal plasma.[3] Although neonates are able to metabolise etidocaine it appears that they are less able to do so than adults; a mean elimination half-life of 6.42 hours has been reported in neonates.[3]

1. Morgan DJ, *et al*. Disposition and placental transfer of etidocaine in pregnancy. *Eur J Clin Pharmacol* 1977; **12:** 359–65.
2. Poppers PJ. Evaluation of local anaesthetic agents for regional anaesthesia in obstetrics. *Br J Anaesth* 1975; **47:** 322–7.
3. Morgan D, *et al*. Pharmacokinetics and metabolism of the anilide local anaesthetics in neonates: 11: etidocaine. *Eur J Clin Pharmacol* 1978; **13:** 365–71.

Uses and Administration

Etidocaine hydrochloride is a local anaesthetic of the amide type with actions and uses similar to those described on p.1852. It has a rapid onset and a long duration of action. Etidocaine has been used for infiltration anaesthesia, peripheral nerve block, and epidural block, usually with adrenaline 1 in 200 000. (Local anaesthetic techniques are discussed on p.1853.)

Preparations

Proprietary Preparations (details are given in Part 3)
USA: Duranest†.

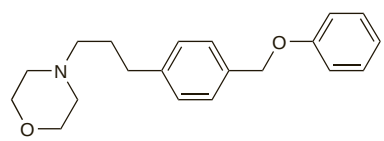
Fomocaine Hydrochloride *(BANM, rINNM)*

Fomocaïne, Chlorhydrate de; Fomocaini Hydrochloridum; Hidrocloruro de fomocaína. 4-[3-(α-Phenoxy-*p*-tolyl)propyl]morpholine hydrochloride.

Фомокаина Гидрохлорид

$C_{20}H_{25}NO_2$,HCl = 347.9.

CAS — 17692-39-6 (fomocaine); 56583-43-8 (fomocaine hydrochloride).



(fomocaine)

Profile

Fomocaine is a local anaesthetic that has been included, as the hydrochloride, in mixed products intended for use in infected skin conditions.