Adverse effects from ingestion of ephedrine-containing OTC preparations, including herbal products (usually in high doses and/or long term) have included coronary artery thrombosis,[10] myocardial infarction, seizures,[11] psychotic reactions,[12] nephrolithiasis,[13-15] and myocarditis;[16] a number of fatalities have been reported. Frank dependence has been reported in female weightlifters following long-term use of high doses.[17]

For a report of urinary calculi developing in a patient who had ingested a preparation containing guaifenesin and ephedrine, see Abuse, under Guaifenesin, p.1561.

1. WHO. Recommendations from the Expert Committee on Drug Dependence. *WHO Drug Inf* 1998; **12:** 227–9.
2. Cockings JGL, Brown MA. Ephedrine abuse causing acute myocardial infarction. *Med J Aust* 1997; **167:** 199–200.
3. Zahn KA, *et al.* Cardiovascular toxicity after ingestion of "herbal ecstacy" [sic]. *J Emerg Med* 1999; **17:** 289–91.
4. James LP, *et al.* Sympathomimetic drug use in adolescents presenting to a pediatric emergency department with chest pain. *J Toxicol Clin Toxicol* 1998; **36:** 321–8.
5. Tinsley JA, Watkins DD. Over-the-counter stimulants: abuse and addiction. *Mayo Clin Proc* 1998; **73:** 977–82.
6. Haller CA, Benowitz NL. Adverse cardiovascular and central nervous system events associated with dietary supplements containing ephedra alkaloids. *N Engl J Med* 2000; **343:** 1833–8.
7. Dennehy CE, *et al.* Dietary supplement-related adverse events reported to the California Poison Control System. *Am J Health-Syst Pharm* 2005; **62:** 1476–82.
8. Samenuk D, *et al.* Adverse cardiovascular events temporally associated with ma huang, an herbal source of ephedrine. *Mayo Clin Proc* 2002; **77:** 12–16.
9. Haller CA, *et al.* Short-term metabolic and hemodynamic effects of ephedra and guarana combinations. *Clin Pharmacol Ther* 2005; **77:** 560–71.
10. Sola S, *et al.* Coronary dissection and thrombosis after ingestion of ephedra. *Am J Med* 2004; **116:** 645–6.
11. Anonymous. Adverse events associated with ephedrine-containing products—Texas, December 1993-September 1995. *JAMA* 1996; **276:** 1711–12.
12. Doyle H, Kargin M. Herbal stimulant containing ephedrine has also caused psychosis. *BMJ* 1996; **313:** 756.
13. Powell T, *et al.* Ma-huang strikes again: ephedrine nephrolithiasis. *Am J Kidney Dis* 1998; **32:** 153–9.
14. Blau JJ. Ephedrine nephrolithiasis associated with chronic ephedrine abuse. *J Urol (Baltimore)* 1998; **160:** 825.
15. Hoffman N, *et al.* Resolution of ephedrine stones with dissolution therapy. *Urology* 2003; **61:** 1035.
16. Zaacks SM, *et al.* Hypersensitivity myocarditis associated with ephedra use. *J Toxicol Clin Toxicol* 1999; **37:** 485–9.
17. Gruber AJ, Pope HG. Ephedrine abuse among 36 female weightlifters. *Am J Addict* 1998; **7:** 256–61.

Interactions

As for Sympathomimetics, p.1407. Ephedrine has direct and indirect actions and may cause a hypertensive crisis in patients receiving an MAOI (including a RIMA); the possibility of such an interaction after intranasal use of ephedrine should also be borne in mind. See also under Phenelzine (p.418) and Moclobemide (p.411). Since ephedrine has both alpha- and beta-agonist properties it should be avoided or used with care in patients undergoing anaesthesia with cyclopropane, halothane, or other volatile anaesthetics. An increased risk of arrhythmias may occur if given to patients receiving cardiac glycosides, quinidine, or tricyclic antidepressants, and there is an increased risk of vasoconstrictor or pressor effects in patients receiving ergot alkaloids or oxytocin. The rate of metabolism of some other drugs is increased by ephedrine. For mention of the potential additive stimulant effects seen with caffeine and ephedrine, see Sympathomimetics, under Caffeine, p.1118.

Pharmacokinetics

Ephedrine is readily and completely absorbed from the gastrointestinal tract. It is excreted largely unchanged in the urine, with small amounts of metabolites produced by hepatic metabolism. Ephedrine has been variously reported to have a plasma half-life ranging from 3 to 6 hours depending on urinary pH; elimination is enhanced and half-life accordingly shorter in acid urine.

◊ References.

1. Welling PG, *et al.* Urinary excretion of ephedrine in man without pH control following oral administration of three commercial ephedrine sulfate preparations. *J Pharm Sci* 1971; **60:** 1629–34.
2. Sever PS, *et al.* The metabolism of (−)-ephedrine in man. *Eur J Clin Pharmacol* 1975; **9:** 193–8.
3. Pickup ME, *et al.* The pharmacokinetics of ephedrine after oral dosage in asthmatics receiving acute and chronic treatment. *Br J Clin Pharmacol* 1976; **3:** 123–34.

Uses and Administration

Ephedrine is a sympathomimetic (p.1408) with direct and indirect effects on adrenergic receptors. It has alpha- and beta-adrenergic activity and has pronounced stimulating effects on the CNS. It has a more prolonged though less potent action than adrenaline. In therapeutic doses it raises the blood pressure by increasing cardiac output and also by inducing peripheral vasoconstriction. Tachycardia may occur but is less frequent than with adrenaline. Ephedrine also causes bronchodilatation, reduces intestinal tone and motility, relaxes the bladder wall while contracting the sphincter muscle but relaxes the detrusor muscle of the bladder and usually reduces the activity of the uterus. It has a stimulant action on the respiratory centre. It dilates the pupil but does not affect the light reflexes. After ephedrine has been used for a short while, tachyphylaxis may develop.

Ephedrine salts are used, either alone or in combination preparations, in the symptomatic relief of nasal congestion (p.1548). They may be given orally, or topically as nasal drops or sprays. Ephedrine salts have sometimes been used in motion sickness in combination preparations with hyoscine or an antihistamine and have been tried for postoperative nausea and vomiting (p.1700).

Ephedrine salts have been given parenterally to combat a fall in blood pressure during spinal or epidural anaesthesia. Ephedrine is of little value in hypotensive crises due to shock, circulatory collapse, or haemorrhage. It is no longer generally advocated for orthostatic hypotension.

Ephedrine salts have been used as bronchodilators, but the more $beta_2$-selective sympathomimetics, such as salbutamol, are now preferred.

Other uses of ephedrine salts include diabetic neuropathic oedema, in which they may provide marked relief. They have also been used in micturition disorders.

Nasal drops or sprays usually containing ephedrine 0.5 or 1% are used in the treatment of **nasal congestion**. Ephedrine salts have also been given by oral inhalation.

To reverse **hypotension** induced by spinal or epidural anaesthesia, a solution containing ephedrine hydrochloride 3 mg/mL is given by slow intravenous injection in doses of 3 to 6 mg (or at most 9 mg) repeated every 3 to 4 minutes as required; the maximum total dose is 30 mg. Ephedrine salts have also been given by intramuscular or subcutaneous injection.

The *BNF* suggests an oral dose of 30 to 60 mg of ephedrine hydrochloride three times daily in the treatment of **diabetic neuropathic oedema**.

Several other salts of ephedrine have been given including the camsilate, the levulinate, and the tannate. Racephedrine hydrochloride has also been used.

For children's doses, see Administration in Children, below.

Administration in children. Over-the-counter cough and cold preparations containing sympathomimetic decongestants (including ephedrine) should be used with caution in children and generally avoided in those under 2 years of age (see p.1547). However, the *BNFC* suggests that, in certain circumstances, specialists may prescribe ephedrine nasal drops for children under 2 years in the short-term treatment of severe **nasal congestion** that has not responded to sodium chloride nasal drops or inhalation of warm moist air. Nasal drops or sprays containing ephedrine hydrochloride 0.5% are licensed to treat nasal congestion in young children over 3 months of age. Although not licensed for such use, the *BNFC* recommends a strength of 0.25% for use in children aged 1 to 3 months.

Ephedrine is rarely needed in children for reversal of **hypotension** induced by spinal or epidural anaesthesia, but if it is used the *BNFC* suggests the following doses of a solution containing ephedrine hydrochloride 3 mg/mL, given by slow intravenous injection via a central line:

- 1 to 12 years: 500 to 750 micrograms/kg or 17 to 25 mg/m^2 every 3 to 4 minutes according to response up to a maximum total dose of 30 mg
- 12 to 18 years: 3 to 7.5 mg (maximum 9 mg) repeated every 3 to 4 minutes according to response up to a maximum total dose of 30 mg

Micturition disorders. Ephedrine salts have been used in nocturnal enuresis, although other treatments are usually preferred, and have been tried in patients with stress incontinence but the value of such treatment is not clear.

Spinal anaesthesia. Parenteral sympathomimetics such as ephedrine and phenylephrine have been advocated for the correction of hypotension associated with local anaesthesia. The risk of hypotension with spinal or epidural block is greater than many other forms of nerve block (see Adverse Effects of Central Block, p.1850). Ephedrine has been used[1,2] although not always successfully[3] for the correction of such hypotension. It has also been used prophylactically,[4,5] although prophylactic use during labour has been associated with fetal tachycardia,[5] and adequate hydration of the patient beforehand is more important in minimising hypotension.

1. Hall PA, *et al.* Spinal anaesthesia for Caesarean section: comparison of infusions of phenylephrine and ephedrine. *Br J Anaesth* 1994; **73:** 471–4.
2. Thomas DG, *et al.* Randomized trial of bolus phenylephrine or ephedrine for maintenance of arterial pressure during spinal anaesthesia for Caesarean section. *Br J Anaesth* 1996; **76:** 61–5.
3. Critchley LAH, *et al.* Hypotension during subarachnoid anaesthesia: haemodynamic effects of ephedrine. *Br J Anaesth* 1995; **74:** 373–8.
4. Sternlo J-E, *et al.* Prophylactic im ephedrine in bupivacaine spinal anaesthesia. *Br J Anaesth* 1995; **74:** 517–20.
5. Cleary-Goldman J, *et al.* Prophylactic ephedrine and combined spinal epidural: maternal blood pressure and fetal heart rate patterns. *Obstet Gynecol* 2005; **106:** 466–72.

Preparations

BP 2008: Ephedrine Elixir; Ephedrine Hydrochloride Tablets; Ephedrine Nasal Drops;
USP 31: Ephedrine Sulfate Capsules; Ephedrine Sulfate Injection; Ephedrine Sulfate Nasal Solution; Ephedrine Sulfate Syrup; Theophylline, Ephedrine Hydrochloride, and Phenobarbital Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Muchan; ***Belg.:*** Ephedronguent; ***Braz.:*** Unifedrine; ***Chile:*** Efedrosan; ***Gr.:*** Neo Rhinovit; Rhinolex; ***Hung.:*** Epherit; ***Mex.:*** Tendrin; ***Pol.:*** Efrinol; ***Port.:*** Spinefe; ***Turk.:*** Rinitalmit; ***UK:*** CAM; ***USA:*** Kondon's Nasal; ***Venez.:*** Boref†; Colirio Iris.

Multi-ingredient: Numerous preparations are listed in Part 3.

Eprazinone Hydrochloride *(rINNM)*

CE-746; Éprazinone, Chlorhydrate d'; Eprazinoni Hydrochloridum; Hidrocloruro de eprazinona. 3-[4-(β-Ethoxyphenethyl)piperazin-1-yl]-2-methylpropiophenone dihydrochloride.

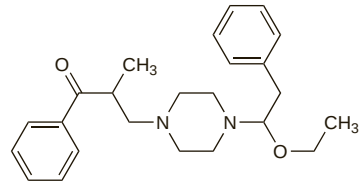
Эпразинона Гидрохлорид

$C_{24}H_{32}N_2O_2.2HCl$ = 453.4.

CAS — 10402-90-1 (eprazinone); 10402-53-6 (eprazinone hydrochloride).

ATC — R05CB04.

ATC Vet — QR05CB04.



(eprazinone)

Profile

Eprazinone hydrochloride has been variously described as having mucolytic or expectorant properties (p.1547) as well as a direct relaxant action on bronchial smooth muscle. It is given in oral doses of 50 to 100 mg three times daily. It has also been given rectally.

Effects on the skin. Skin eruptions have been associated with the oral use of eprazinone.[1,2]

1. Faber M, *et al.* Eprazinonexanthem mit subkornealer Pustelbildung. *Hautarzt* 1984; **35:** 200–3.
2. Tanabe K, *et al.* Non-pigmented fixed drug eruption induced by eprazinone hydrochloride. *Dermatol Online J* 2005; **11:** 25.

Overdosage. Symptoms in two 22-month-old children who received an overdose of 800 mg of eprazinone included somnolence, ataxia, and seizures.[1]

1. Merigot P, *et al.* Les convulsions avec trois antitussifs dérivés substitués de la pipérazine: (zipéprol, éprazinone, éprozinol). *Ann Pediatr (Paris)* 1985; **32:** 504–11.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Eftapan; ***Belg.:*** Isilung; ***Ger.:*** Eftapan.

Multi-ingredient: ***Austria:*** Eftapan Tetra.

Eprozinol Hydrochloride *(rINNM)*

Éprozinol, Chlorhydrate d'; Eprozinoli Hydrochloridum; Hidrocloruro de eprozinol. 3-[4-(β-Methoxyphenethyl)piperazin-1-yl]-1-phenylpropan-1-ol dihydrochloride.

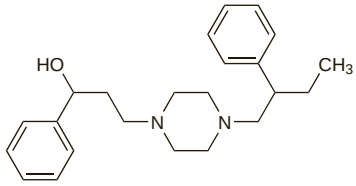
Эпрозинола Гидрохлорид

$C_{22}H_{30}N_2O_2,2HCl$ = 427.4.

CAS — 32665-36-4 (eprozinol).

ATC — R03DX02.

ATC Vet — QR03DX02.



(eprozinol)

Profile

Eprozinol hydrochloride has been given orally for its mucolytic or expectorant properties.

Adverse effects. Convulsions and coma were reported in a 19-year-old patient after taking eprozinol.[1]

1. Merigot P, *et al.* Les convulsions avec trois antitussifs dérivés substitués de la pipérazine: (zipéprol, éprazinone, éprozinol). *Ann Pediatr (Paris)* 1985; **32:** 504–11.

Preparations

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

Erdosteine *(rINN)*

Erdosteiini; Erdostein; Erdosteína; Erdostéine; Erdosteinum. (±)-({[(Tetrahydro-2-oxo-3-thienyl)carbamoyl]methyl}thio)acetic acid.

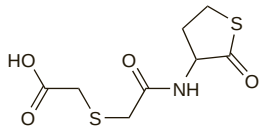
Эрдостеин

$C_8H_{11}NO_4S_2$ = 249.3.

CAS — 84611-23-4.

ATC — R05CB15.

ATC Vet — QR05CB15.



Adverse Effects and Precautions

Gastrointestinal disturbances may occur with erdosteine. Headache, dyspnoea, taste alterations, urticaria, erythema, and dermatitis have been reported rarely. Licensed product information for erdosteine suggests that it should not be used in patients with active peptic ulcer disease.

Pharmacokinetics

Erdosteine is rapidly absorbed after oral use; absorption is unaffected by food. Peak plasma concentrations are reached after about an hour. Erdosteine undergoes first-pass metabolism to an active metabolite, *N*-thiodiglycolyl-homocysteine. Plasma protein binding is about 64.5%. The elimination half-life is about 1.46 hours for erdosteine, and about 1.62 hours for the metabolite. Excretion is mainly via the urine, as metabolites; faecal elimination is negligible.

Uses and Administration

Erdosteine is a mucolytic that is used in the treatment of disorders of the respiratory tract characterised by productive cough (p.1547). It is given in usual oral doses of 300 mg twice daily for a maximum of 10 days.

Administration in hepatic and renal impairment. Exposure to erdosteine is increased in patients with hepatic impairment. UK licensed product information states that no increase in adverse effects has been observed in patients with mild liver failure, but restricts the dose in these patients to a maximum of 300 mg daily by mouth. Erdosteine is contra-indicated in severe hepatic impairment.

Although no difference in absorption or elimination has been seen in patients with moderate renal impairment, the risk of accumulation of metabolites cannot be excluded. For this reason, use of erdosteine is contra-indicated in patients with a creatinine clearance of less than 25 mL/minute.

Chronic obstructive pulmonary disease. Erdosteine has been used[1-3] in the management of chronic obstructive pulmonary disease (p.1112) but the value of mucolytics in this disorder is controversial.

1. Dechant KL, Noble S. Erdosteine. *Drugs* 1996; **52:** 875–81.
2. Marchioni CF, *et al.* Evaluation of efficacy and safety of erdosteine in patients affected by chronic bronchitis during an infective exacerbation phase and receiving amoxycillin as basic treatment (ECOBES, European Chronic Obstructive Bronchitis Erdosteine Study). *Int J Clin Pharmacol Ther* 1995; **33:** 612–18.
3. Moretti M, *et al.* The effect of long-term treatment with erdosteine on chronic obstructive pulmonary disease: the EQUAL-IFE Study. *Drugs Exp Clin Res* 2004; **30:** 143–52.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Amuctol†; Fluidasa; ***Austria:*** Erdomed; ***Belg.:*** Mucothera†; ***Braz.:*** Erdotin†; Flusten; ***Chile:*** Biopulmin; ***Cz.:*** Erdomed; ***Denm.:*** Erdotin; ***Fin.:*** Erdopect; ***Fr.:*** Edirel†; Vectrine; ***Gr.:*** Theovix; Tusselin; ***Hung.:*** Erdomed; ***Indon.:*** Vectrine; ***Ital.:*** Erdotin; ***Mex.:*** Dostein; Esteclin; ***Philipp.:*** Ectrin; ***Port.:*** Erdotin; ***Switz.:*** Mucofor; ***Turk.:*** Erdostin; ***UK:*** Erdotin.

Multi-ingredient: ***Mex.:*** Esteclin Bac.

Eriodictyon

Hierba santa; Mountain Balm; Yerba Santa.

Эриодиктион калифорнийский

CAS — 8013-08-9.

Profile

Eriodictyon consists of the dried leaves of *Eriodictyon californicum* (Hydrophyllaceae). It has been used as an expectorant. It has also been used in the treatment of dry mouth and to mask the taste of bitter drugs.

Preparations

Proprietary Preparations (details are given in Part 3)
Canad.: Mouth Kote; ***Hong Kong:*** Pretz†.

Multi-ingredient: ***Ital.:*** Broncosedina; ***UK:*** Saliva Natura; ***USA:*** Feminease; ***Venez.:*** Yerba Santa.

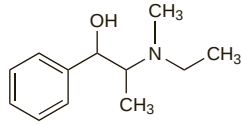
Etafedrine Hydrochloride *(BANM, USAN, rINNM)* ⊗

Étafédrine, Chlorhydrate d'; Etafedrini Hydrochloridum; Ethylephedrine Hydrochloride; Hidrocloruro de etafedrina. (–)-2-(Ethylmethylamino)-1-phenylpropan-1-ol hydrochloride.

Этафедрина Гидрохлорид

$C_{12}H_{19}NO,HCl$ = 229.7.

CAS — 7681-79-0 (etafedrine); 48141-64-6 ((–)-etafedrine); 5591-29-7 (etafedrine hydrochloride).



(etafedrine)

Profile

Etafedrine hydrochloride is a sympathomimetic related to ephedrine (p.1558). It is used for its bronchodilator effects in combination preparations for the relief of cough and associated respiratory-tract disorders.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Braz.:*** Broncolex†; EMS Expectorante; Revenil; Revenil Dospan; Revenil Expectorante; ***Canad.:*** Dalmacol; ratio-Calmydone; ***Indon.:*** Decolsin; ***S.Afr.:*** Nethaprin Dospan; Nethaprin Expectorant; ***Thai.:*** Brondil.

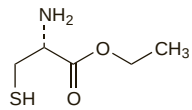
Ethyl Cysteine Hydrochloride

Etilcisteína, hidrocloruro de. Ethyl L-2-amino-3-mercaptopropionate hydrochloride.

Этиловый Эфир Цистеина Гидрохлорида

$C_5H_{11}NO_2S,HCl$ = 185.7.

CAS — 3411-58-3 (ethyl cysteine); 868-59-7 (ethyl cysteine hydrochloride).



(ethyl cysteine)

Pharmacopoeias. In *Jpn*.

Profile

Ethyl cysteine hydrochloride is a mucolytic that has been used in the treatment of disorders of the respiratory tract associated with productive cough.

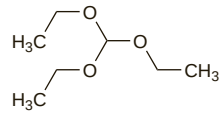
Ethyl Orthoformate

Ether de Kay; Triethoxymethane; Trietoximetano. Triethyl orthoformate.

Этиловый Эфир Ортомуравьиной Кислоты

$C_7H_{16}O_3$ = 148.2.

CAS — 122-51-0.



Pharmacopoeias. In *Fr.*

Profile

Ethyl orthoformate is a cough suppressant (see p.1547). It is reported to be a respiratory antispasmodic and has been given by mouth or rectally.

Fedrilate *(rINN)*

Fédrilate; Fedrilato; Fedrilatum; UCB-3928. 1-Methyl-3-morpholinopropyl perhydro-4-phenylpyran-4-carboxylate.

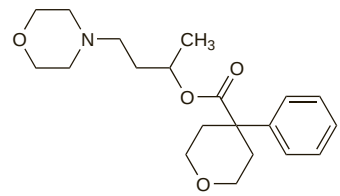
Федрилат

$C_{20}H_{29}NO_4$ = 347.4.

CAS — 23271-74-1.

ATC — R05DB14.

ATC Vet — QR05DB14.



Profile

Fedrilate is a cough suppressant used orally for non-productive cough.

Preparations

Proprietary Preparations (details are given in Part 3)
Braz.: Gotas Binelli.

Fenoxazoline Hydrochloride *(rINNM)* ⊗

Fénoxazoline, Chlorhydrate de; Fenoxazolini Hydrochloridum; Hidrocloruro de fenoxazolina. 2-(2-Isopropylphenoxymethyl)-2-imidazoline hydrochloride.

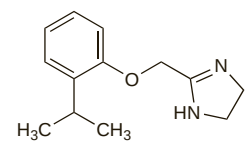
Феноксазолина Гидрохлорид

$C_{13}H_{18}N_2O,HCl$ = 254.8.

CAS — 4846-91-7 (fenoxazoline); 21370-21-8 (fenoxazoline hydrochloride).

ATC — R01AA12.

ATC Vet — QR01AA12.



(fenoxazoline)

Profile

Fenoxazoline hydrochloride is a sympathomimetic with effects similar to those of naphazoline (p.1565) that has been used topically for its vasoconstrictor properties in the symptomatic treatment of nasal congestion.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Nebulicina; ***Braz.:*** Aturgyl†; Nasofelin.
