Precautions

Disulfiram is contra-indicated in the presence of cardiovascular disease or psychosis or severe personality disorders, and should not be given to patients known to be hypersensitive to it or to other thiuram compounds, such as those used in rubber vulcanisation or pesticides. It should be used with caution in the presence of diabetes mellitus, epilepsy, impaired hepatic or renal function, respiratory disorders, cerebral damage, or hypothyroidism. Caution is also advised when giving disulfiram to those who are addicted to other drugs in addition to alcohol. It is probably best avoided in pregnancy.

Disulfiram should not be given until at least 24 hours after the last ingestion of alcohol. Patients beginning therapy should be fully aware of the disulfiram-alcohol reaction and should be warned to avoid alcohol in any form, including alcohol-containing medicines and alcohol-based topical preparations. Reactions to alcohol may occur as long as 2 weeks after the cessation of disulfiram.

The US manufacturers have recommended that regular blood counts and liver function tests should be performed during long-term therapy.

Pregnancy. A report of 2 infants with severe limb-reduction anomalies whose mothers had taken disulfiram during pregnancy.[1] Only 2 similar cases had previously been reported.

1. Nora AH, *et al.* Limb-reduction anomalies in infants born to disulfiram-treated alcoholic mothers. *Lancet* 1977; **ii:** 664.

Interactions

Disulfiram inhibits hepatic enzymes and may interfere with the metabolism of other drugs taken at the same time. It enhances the effects of phenytoin and coumarin anticoagulants and their dosage may need to be reduced. It also inhibits the metabolism and excretion of rifampicin. Toxic reactions have occurred when disulfiram was given with isoniazid or metronidazole. Disulfiram may inhibit the metabolism of paraldehyde leading to an accumulation of acetaldehyde and these drugs should not be used together.

◊ In a study[1] to evaluate the effects of disulfiram on cytochrome P450 isoenzymes, the results suggested that disulfiram-mediated inhibition is mainly selective for CYP2E1 after both acute and chronic dosage.

1. Frye RF, Branch RA. Effect of chronic disulfiram administration on the activities of CYP1A2, CYP2C19, CYP2D6, CYP2E1, and N-acetyltransferase in healthy human subjects. *Br J Clin Pharmacol* 2002; **53:** 155–62.

Analgesics. The potential of disulfiram to impair drug metabolism was shown[1] when it was found to prolong the plasma half-life of *phenazone*, probably by inhibiting the hepatic microsomal mixed function oxidases. It was also suggested[1] that disulfiram alters catecholamine metabolism since urinary excretion of vanilmandelic acid was significantly reduced and that of homovanillic acid was increased.

1. Vesell ES, *et al.* Impairment of drug metabolism by disulfiram in man. *Clin Pharmacol Ther* 1971; **12:** 785–92.

Antidepressants. It has been reported[1] that *amitriptyline* appeared to enhance the disulfiram-alcohol reaction. There is the potential for serious interactions during the disulfiram-alcohol reaction with drugs having CNS actions mediated by noradrenaline or dopamine, such as *tricyclic antidepressants* or those inhibiting the same enzymes as disulfiram, such as *MAOIs*.[2]

1. MacCallum WAG. Drug interactions in alcoholism treatment. *Lancet* 1969; **i:** 313.
2. Sellers EM, *et al.* Drugs to decrease alcohol consumption. *N Engl J Med* 1981; **305:** 1255–62.

Antiprotozoals. For reference to toxicity associated with *metronidazole* given to alcoholic patients who were also receiving disulfiram, see Alcohol, under Interactions of Metronidazole, p.838.

Antipsychotics. It has been suggested[1] that phenothiazine antiemetics such as *chlorpromazine* might increase hypotension because of their α-adrenoceptor blocking activity and should therefore be contra-indicated in patients taking disulfiram. There is the potential for serious interactions during the disulfiram-alcohol reaction with drugs having CNS actions mediated by noradrenaline or dopamine, such as *phenothiazines*.[2]

1. Kwentus J, Major LF. Disulfiram in the treatment of alcoholism: a review. *J Stud Alcohol* 1979; **40:** 428–46.
2. Sellers EM, *et al.* Drugs to decrease alcohol consumption. *N Engl J Med* 1981; **305:** 1255–62.

Benzodiazepines. *Diazepam* was reported[1] to reduce the intensity of the disulfiram-alcohol reaction.

1. MacCallum WAG. Drug interactions in alcoholism treatment. *Lancet* 1969; **i:** 313.

Cannabis. For a suggestion that a combination of disulfiram and *cannabis* may produce a hypomanic state, see p.2275.

Cardiovascular drugs. Clinically serious pharmacodynamic interactions might be anticipated during the disulfiram-alcohol reaction in patients taking other drugs that impair blood pressure regulation, such as *alpha blockers*, *beta blockers*, or *vasodilators*.[1]

1. Sellers EM, *et al.* Drugs to decrease alcohol consumption. *N Engl J Med* 1981; **305:** 1255–62.

Macrolides. Fatal toxic epidermal necrolysis and fulminant hepatitis have been reported[1] after starting *clarithromycin* treatment in a patient who was receiving disulfiram.

1. Masiá M, *et al.* Fulminant hepatitis and fatal toxic epidermal necrolysis (Lyell disease) coincident with clarithromycin administration in an alcoholic patient receiving disulfiram therapy. *Arch Intern Med* 2002; **162:** 474–6.

Pharmacokinetics

Disulfiram is absorbed variably from the gastrointestinal tract and is rapidly reduced to diethyldithiocarbamate (ditiocarb, p.1445), principally by the glutathione reductase system in the erythrocytes; reduction may also occur in the liver. Diethyldithiocarbamate is metabolised in the liver to its glucuronide and methyl ester and to diethylamine, carbon disulfide, and sulfate ions. Metabolites are excreted primarily in the urine; carbon disulfide is exhaled in the breath.

◊ There was marked intersubject variability in plasma concentrations of disulfiram and its metabolites in a study of 15 male alcoholics given single 250-mg doses of disulfiram by mouth and repeated dosing with 250 mg daily for 12 days.[1] Variability might result from the marked lipid solubility of disulfiram, differences in plasma protein binding, or enterohepatic cycling. Average times to reach peak plasma concentrations after single or repeated doses were 8 to 10 hours for disulfiram, diethyldithiocarbamate, diethyldithiocarbamate-methyl ester, and diethylamine, and for carbon disulfide in breath; peak plasma concentrations of carbon disulfide occurred after 5 to 6 hours. Plasma concentrations of disulfiram were negligible within 48 hours of a dose, although concentrations of some metabolites were still raised. In urine, 1.7 and 8.3% of a disulfiram dose was eliminated as diethyldithiocarbamate-glucuronide in the 24 hours after a single and repeated dose respectively, while diethylamine accounted for 1.6 and 5.7%, respectively. In the 24 hours after a single and repeated dose 22.4 and 31.3%, respectively, was eliminated as carbon disulfide in the breath.

1. Faiman MD, *et al.* Elimination kinetics of disulfiram in alcoholics after single and repeated doses. *Clin Pharmacol Ther* 1984; **36:** 520–6.

Uses and Administration

Disulfiram is used as an adjunct in the treatment of chronic alcoholism (see Alcohol Withdrawal and Abstinence, p.1626). Disulfiram is not a cure and the treatment is likely to be of little value unless it is undertaken with the willing cooperation of the patient and is used with supportive psychotherapy.

Disulfiram inhibits aldehyde dehydrogenase, the enzyme responsible for the oxidation of acetaldehyde, a metabolite of alcohol. The resulting accumulation of acetaldehyde in the blood is widely believed to be responsible for many of the unpleasant symptoms of the disulfiram-alcohol reaction which occur when alcohol is taken, even in small quantities, after disulfiram (see Adverse Effects and Treatment, above). Symptoms can arise within 10 minutes of the ingestion of alcohol and last from half an hour in mild cases to several hours in severe cases. It is advisable to carry out the initial treatment in hospital or in a specialised unit where the patient can be kept under close supervision.

Disulfiram is given by mouth. In the UK, the dose is 800 mg, taken as a single dose, on the first day of treatment, reduced by 200 mg daily to a maintenance dose which is usually 100 to 200 mg daily. In the USA, where doses above 500 mg daily are not recommended, an initial dose of 500 mg daily for 1 to 2 weeks is given, followed by a maintenance dose of 250 mg daily or within the range of 125 to 500 mg daily. Treatment should be reviewed after no longer than 6 months. Maintenance therapy with disulfiram may need to be continued for months or years, until the patient is fully recovered socially and a basis for permanent self-control has been established.

A test dose of alcohol has been given under close supervision when the patient is receiving maintenance doses of disulfiram, in order to demonstrate the nature of the disulfiram-alcohol reaction. However, these challenge tests are not routinely recommended, and should not in any case be used in patients over 50 years of age. Many authorities consider that an explicit description of the reaction is sufficient.

Disulfiram implants have been used in an attempt to overcome problems of patient compliance but have been largely abandoned due to lack of clinical efficacy.

Alcoholism. References.

1. Wright C, Moore RD. Disulfiram treatment of alcoholism. *Am J Med* 1990; **88:** 647–55.
2. Hughes JC, Cook CCH. The efficacy of disulfiram: a review of outcome studies. *Addiction* 1997; **92:** 381–95.
3. O'Shea B. Disulfiram revisited. *Hosp Med* 2000; **61:** 849–51.
4. Brewer C, *et al.* Does disulfiram help to prevent relapse in alcohol abuse? *CNS Drugs* 2000; **14:** 329–341.
5. Suh JJ, *et al.* The status of disulfiram: a half of a century later. *J Clin Psychopharmacol* 2006; **26:** 290–302.

Cocaine dependence. Cocaine use may affect the dopaminergic modulation of CNS function; disulfiram is one of several drugs that interact with dopaminergic systems and have been tried in treatment of cocaine abuse and dependence (see Cocaine Withdrawal Syndrome, p.1860).

References.

1. Carroll KM, *et al.* Efficacy of disulfiram and cognitive behavior therapy in cocaine-dependent outpatients: a randomized placebo-controlled trial. *Arch Gen Psychiatry* 2004; **61:** 264–72.

Preparations

BP 2008: Disulfiram Tablets;
USP 31: Disulfiram Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Abstensyl; Vandisul†; ***Austral.:*** Antabuse; ***Austria:*** Antabus; ***Belg.:*** Antabuse; ***Braz.:*** Antietanol; Sarcoton; ***Chile:*** Antabus; Tolerane; ***Cz.:*** Antabus; ***Denm.:*** Antabus; ***Fin.:*** Antabus; ***Fr.:*** Esperal; ***Ger.:*** Antabus; ***Hung.:*** Antaethyl; ***India:*** Esperal; ***Irl.:*** Antabuse; ***Israel:*** Antabuse†; ***Ital.:*** Antabuse; Etiltox; ***Mex.:*** Etabus; ***Neth.:*** Antabus; Refusal; ***Norw.:*** Antabus; ***NZ:*** Antabuse; ***Pol.:*** Anticol; ***Port.:*** Tetradin; ***Rus.:*** Esperal (Эспераль); ***S.Afr.:*** Antabuse; ***Spain:*** Antabus; ***Swed.:*** Antabus; ***Switz.:*** Antabus; ***Thai.:*** Antabuse†; Difiram; ***Turk.:*** Antabus; ***UK:*** Antabuse; ***USA:*** Antabuse.

Multi-ingredient: ***Fr.:*** TTD-B -B ; ***Rus.:*** Lidevine (Лидевин); ***Swed.:*** Tenutex.

Dizocilpine Maleate *(USAN, rINNM)*

Dizocilpine, Maléate de; Dizocilpini Maleas; Maleato de dizocilpina; MK-801. (+)-10,11-Dihydro-5-methyl-5*H*-dibenzo[*a*,*d*]-cyclohepten-5,10-imine maleate.

Дизоцилпина Малеат

$C_{16}H_{15}N,C_4H_4O_4$ = 337.4.

CAS — 77086-21-6 (dizocilpine); 77086-22-7 (dizocilpine maleate).

Profile

Dizocilpine is an antagonist of the excitatory neurotransmitter *N*-methyl-D-aspartate (NMDA). It has been investigated for its antiepileptic properties as well as for a potential role in various other neurological disorders including the prevention of damage due to cerebral ischaemia.

◊ Dizocilpine has good anticonvulsant activity but as it causes alarming psychotropic effects it was abandoned as a possible therapy for epilepsy.[1] Interest in its use as a possible therapy for stroke continued.

1. Richens A. New antiepileptic drugs. *Br J Hosp Med* 1990; **44:** 241.

Dolomite

Profile

Dolomite is a naturally occurring mineral composed of calcium and magnesium carbonate. It has been used as a nutritional supplement but may contain lead and other toxic metals and is not generally recommended.

Preparations

Proprietary Preparations (details are given in Part 3)
Port.: Frutin; ***USA:*** Dolomite.

Multi-ingredient: ***Austral.:*** Prosteo†.

Dong Quai

Angelica Sinensis; Chinese Angelica; Dang Gui; Dang Qui; Danggui.

Pharmacopoeias. In *Chin.*, which specifies the root.
Br. includes separate monographs for Angelica Sinensis Root for use in Traditional Herbal Medicine, and Processed Angelica Sinensis Root for use in Traditional Herbal Medicinal Product.
BP 2008 (Angelica Sinensis Root for use in THM). The dried whole root of *Angelica sinensis* (*A. polymorpha* var. *sinensis*). It contains not less than 0.1% of *Z*-ligustilide ($C_{12}H_{14}O_2$ = 190.2), calculated with reference to the dried material. Protect from moisture.
BP 2008 (Processed Angelica Sinensis Root for use in THMP). The smoked, sliced, and dried root of Angelica Sinensis Root for use in THM. It contains not less than 0.1% of *Z*-ligustilide, calculated with reference to the dried material. Protect from moisture.

Profile

Dong quai is the dried root of Chinese angelica, *Angelica sinensis* (*A. polymorpha* var. *sinensis*) (Apiaceae). It is used in traditional Chinese medicine in the treatment of menstrual and menopausal disorders, respiratory disorders, and herpes zoster infections.

Other *Angelica* spp. employed in herbal medicine are described on p.2258.

Preparations

Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Austral.:*** Capsella Complex; Dong Quai Complex; Extralife Meno-Care; Feminine Herbal Complex; ***Canad.:*** Natural HRT; ***Hong Kong:*** Phytoestrin†; ***Singapore:*** Phytoestrin.

Drosera

Droséra; Droserae herba; Herba Rorellae; Rorela; Ros Solis; Rossolis; Sonnentau; Sundew.

Profile

Drosera consists of the air-dried entire plant *Drosera rotundifolia* (Droseraceae) and other *Drosera* spp. Preparations of drosera have been used for its reputed value in respiratory disorders.

Homoeopathy. Drosera has been used in homoeopathic medicines under the following names: Drosera rotundifolia; Dros rot.

Preparations

Proprietary Preparations (details are given in Part 3)
Ger.: Makatussin Saft Drosera†; Makatussin Tropfen Drosera†.

Multi-ingredient: ***Austral.:*** Asa Tones; ***Austria:*** Pilka; Pilka Forte; ***Belg.:*** Saintbois; ***Chile:*** Fitotos; Gotas Nican†; Notosil†; Pectoral Pasteur; Pulmagol; Ramistos; Sedotus†; ***Cz.:*** Bronchicum Pflanzlicher Hustenstiller†; Stodal; Tussilen; ***Fr.:*** Pastilles Monleon; Tussidoron; ***Ger.:*** Bronchicum Pflanzlicher†; Drosithym-N; Lomal†; Makatussin Tropfen forte†; Tussiflorin Hustenstiller†; ***Indon.:*** Silex; ***Israel:*** Pilka; ***Mex.:*** Citos; Fen-y-Tos; ***Port.:*** Broncodiazina; Pilka F†; ***S.Afr.:*** Cough Elixir; ***Spain:*** Broncovital†; Pazbronquial; Pilka; ***Switz.:*** Bromocod N; Bronchofluid N†; Demo Elixir pectoral N; DemoTussil; Dragees S contre la toux†; Drosinula†; Escotussin; Famel; Gouttes contre la toux "S"; Makaphyt Gouttes antitussives; Makaphyt Sirop; Nican; Pastilles bronchiques S nouvelle formule; Pastilles pectorales Demo N; Pilka†; Sirop pectoral contre la toux S; Sirop S contre la toux et la bronchite; Thymodrosin N†; Tussanil Compositum†; ***Venez.:*** Codebromil; Dromil Sauco; Pi-Fedrin.

Drotaverine *(rINN)*

Drotaverina; Drotavérine; Drotaverinum. 1-(3,4-Diethoxybenzylidene)-6,7-diethoxy-1,2,3,4-tetrahydroisoquinoline.

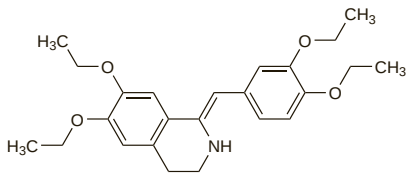
Дротаверин

$C_{24}H_{31}NO_4$ = 397.5.

CAS — 14009-24-6 (drotaverine); 985-12-6 (drotaverine hydrochloride).

ATC — A03AD02.

ATC Vet — QA03AD02.



Pharmacopoeias. *Pol.* includes Drotaverine Hydrochloride.

Profile
Drotaverine is used as an antispasmodic in the management of biliary-tract, urinary-tract, and gastrointestinal spasm, in usual oral doses of 120 to 240 mg daily in divided doses. It has also been given by intramuscular or intravenous injection.

◊ References.

1. Bolaji OO, *et al.* Pharmacokinetics and bioavailability of drotaverine in humans. *Eur J Drug Metab Pharmacokinet* 1996; **21:** 217–21.
2. Romics I, *et al.* The effect of drotaverine hydrochloride in acute colicky pain caused by renal and ureteric stones. *BJU Int* 2003; **92:** 92–6.
3. Singh KC, *et al.* Drotaverine hydrochloride for augmentation of labor. *Int J Gynaecol Obstet* 2004; **84:** 17–22.

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

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Proconfial†; ***Cz.:*** No-Spa; ***Hung.:*** No-Spa; ***India:*** Drotin; Drovera†; DVN; ***Malaysia:*** No-Spa; ***Philipp.:*** No-Spa; ***Pol.:*** Galospa; No-Spa; ***Rus.:*** Bezpa (Беспа); No-Spa (Но-Шпа); Spacovin (Спаковин); Spasmol (Спазмол); Spazoverin (Спазоверин); ***Thai.:*** D-Tarine†; Deolin; No-Spa; Spablock; Spacovin; Sparax; Sparta; Toverine.

Multi-ingredient: ***Cz.:*** Quarelin†; ***Hung.:*** Algoflex-M; Algopyrin Complex; No-Spalgin; Paniverin; Quarelin; ***Rus.:*** No-Spalgin (Но-Шпалгин).

Dulcamara

Bittersüss; Bittersweet; Douce-Amère; Dulcamarae Caulis; Woody Nightshade.

Profile
Dulcamara consists of the dried stems and branches of *Solanum dulcamara* (Solanaceae). It was formerly a popular remedy for chronic rheumatism and skin eruptions and was given as an infusion.

All parts of the plant are poisonous due to the presence of solanaceous alkaloids. The berries have caused poisoning in children. Adverse effects are treated as described under Atropine, p.1220.

Homoeopathy. Dulcamara has been used in homoeopathic medicines under the following names: Solanum dulcamara; Dulc.

Preparations

Proprietary Preparations (details are given in Part 3)
Ger.: Cefabene; Solapsor†.

Multi-ingredient: ***Austria:*** Dermatodoron; ***Ger.:*** Dermatodoron; ***S.Afr.:*** Cough Elixir; Dermatodoron.

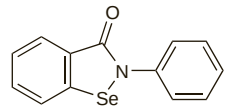
Ebselen *(rINN)*

DR-3305; Ebsélène; Ebseleno; Ebselenum; PZ-51. 2-Phenyl-1,2-benzisoselenazolin-3-one.

Эбселен

$C_{13}H_9NOSe$ = 274.2.

CAS — 60940-34-3.



Profile
Ebselen has antoxidant activity and inhibits lipid peroxidation. It has been investigated as a neuroprotectant in stroke.

◊ References.

1. Yamaguchi T, *et al.* Ebselen in acute ischemic stroke: a placebo-controlled, double-blind clinical trial. *Stroke* 1998; **29:** 12–17.
2. Saito I, *et al.* Neuroprotective effect of an antioxidant, ebselen, in patients with delayed neurological deficits after aneurysmal subarachnoid hemorrhage. *Neurosurgery* 1998; **42:** 269–78.

Echinacea

Black Sampson; Blyškiųjų ežiuolių šaknys (pale coneflower root); Brauneria; Coneflower; Echinacea angustifolia, racine d' (narrow-leaved coneflower root); Echinacea pallida, racine d' (pale coneflower root); Echinacea purpurea, parties aériennes fleuries d' (purple coneflower herb); Echinacea purpurea, racine d' (purple coneflower root); Echinaceae angustifoliae radix (narrow-leaved coneflower root); Echinaceae pallidae radix (pale coneflower root); Echinaceae purpureae herba (purple coneflower herb); Echinaceae purpureae radix (purple coneflower root); Equinácea; Kaitapäivänhatunjuuri (narrow-leaved coneflower root); Kořen třapatky bledé (pale coneflower root); Kořen třapatky úzkolisté (narrow-leaved coneflower root); Läkerudbeckiarot (pale coneflower root); Liten läkerudbeckiarot (narrow-leaved coneflower root); Rohtopäivänhatunjuuri (pale coneflower root); Rudbeckia; Siauralapių ežiuolių šaknys (narrow-leaved coneflower root); Sonnenhutkraut.

Pharmacopoeias. In *Eur.* (see p.vii) and *US*.
Ph. Eur. 6.2 (Narrow-Leaved Coneflower Root; Echinaceae Angustifoliae Radix). The dried, whole, or cut underground parts of *Echinacea angustifolia*. It contains a minimum 0.5% of echinacoside ($C_{35}H_{46}O_{20}$ = 786.7), calculated with reference to the dried drug. Store uncomminuted. Protect from light.
Ph. Eur. 6.2 (Pale Coneflower Root; Echinaceae Pallidae Radix). The dried, whole, or cut underground parts of *Echinacea pallida*. It contains a minimum 0.2% of echinacoside calculated with reference to the dried drug. Store uncomminuted. Protect from light.
Ph. Eur. 6.2 (Purple Coneflower Herb; Echinaceae Purpureae Herba). The dried, whole or cut flowering aerial parts of *Echinacea purpurea*. It contains a minimum of 0.1% of the sum of caftaric acid ($C_{13}H_{12}O_9$ = 312.2) and cichoric acid ($C_{22}H_{18}O_{12}$ = 474.4). Store uncomminuted.
Ph. Eur. 6.2 (Purple Coneflower Root; Echinaceae Purpureae Radix). The dried, whole or cut underground parts of *Echinacea purpurea*. It contains a minimum of 0.5% of the sum of caftaric acid ($C_{13}H_{12}O_9$ = 312.2) and cichoric acid ($C_{22}H_{18}O_{12}$ = 474.4). Store uncomminuted.
USP 31 (Echinacea Angustifolia). It consists of the dried rhizome and roots of *Echinacea angustifolia* (Asteraceae), harvested in the autumn after 1 or more years of growth. It contains not less than 0.5% of total phenols. Protect from light.
USP 31 (Echinacea Pallida). It consists of the dried rhizome and roots of *Echinacea pallida* (Asteraceae), harvested in the autumn after 3 or more years of growth. It contains not less than 0.5% of total phenols. Protect from light.
USP 31 (Echinacea Purpurea Root). It consists of the dried rhizome and roots of *Echinacea purpurea* (Asteraceae), harvested in the autumn after 3 or more years of growth. It contains not less than 0.5% of total phenols. Protect from light.
USP 31 (Echinacea Purpurea Aerial Parts). The aerial parts of *Echinacea purpurea* (Asteraceae) harvested during the flowering stage. It contains not less than 1.0% of chicoric acid, and not less than 0.01% of dodecatetraenoic acid isobutylamides ($C_{16}H_{25}NO$), calculated on the dried basis. Store in airtight containers. Protect from light.

Profile
Echinacea, the dried, whole, or cut underground parts of *Echinacea angustifolia* (*Brauneria angustifolia*), *E. pallida* (*B. pallida*), or *E. purpurea*, or the aerial parts of *E. purpurea*, is reported to have immunostimulant properties. It is used in herbal preparations for the prophylaxis of bacterial and viral infections.

Homoeopathy. Echinacea has been used in homoeopathic medicines under the following names: Echinacea purpurea; Echinacea purpurea ex planta tota; Echinacea purpurea, Planta tota; Echinacea angustifolia; Echin. an.

Adverse effects. The most common adverse effects reported on short-term use of echinacea were gastrointestinal and skin-related; these were generally transient and reversible.[1] Hypersensitivity reactions including anaphylaxis have been reported.[1-4]

1. Huntley AL, *et al.* The safety of herbal medicinal products derived from Echinacea species. *Drug Safety* 2005; **28:** 387–400.
2. Mullins RJ, Heddle R. Adverse reactions associated with echinacea: the Australian experience. *Ann Allergy Asthma Immunol* 2002; **88:** 42–51.
3. Health Canada. Natural health products and adverse reactions. *Can Adverse React News* 2004; **14** (1): 2. Also available at: http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/medeff/carn-bcei_v14n1_e.pdf (accessed 11/08/05)
4. Adverse Drug Reactions Advisory Committee (ADRAC). Adverse reactions to complementary medicines. *Aust Adverse Drug React Bull* 2005; **24:** 2. Also available at: http://www.tga.health.gov.au/adr/aadrb/aadr0502.htm (accessed 11/08/05)

Pharmacokinetics. The pharmacokinetics of alkamides extracted from *Echinacea angustifolia* roots have been studied[1] in human subjects. Fast absorption of some alkamides was shown after oral use; highly lipophilic alkamides could not be detected in plasma.

1. Woelkart K, *et al.* Bioavailability and pharmacokinetics of alkamides from the roots of Echinacea angustifolia in humans. *J Clin Pharmacol* 2005; **45:** 683–9.

Use in respiratory disorders. Echinacea is widely used in herbal preparations to treat upper respiratory-tract infections such as the common cold. Studies[1-3] have produced conflicting results, but systematic reviews suggest that most have methodological flaws[4] rendering evidence of efficacy unconvincing.[4,5] A meta-analysis[6] of 14 randomised controlled studies suggested that echinacea does have a benefit in decreasing the incidence and duration of the common cold, although it was acknowledged that larger prospective studies controlling for several variables (e.g. species) are needed before it can be routinely recommended. Comparative evaluation of specific preparations is also difficult because of varying composition. Evaluation of the effect of 3 extracts of *Echinacea angustifolia* root, each produced by a different extraction method and with defined phytochemical profiles, demonstrated no clinically significant effects by any of them on experimental rhinovirus infection or ensuing illness compared with placebo.[7] Alkamides, polysaccharides, and caffeic acid derivatives, which have been proposed as the active components of echinacea preparations, were present in varying amounts in the extracts.

1. Turner RB, *et al.* Ineffectiveness of echinacea for prevention of experimental rhinovirus colds. *Antimicrob Agents Chemother* 2000; **44:** 1708–9.
2. Barrett BP, *et al.* Treatment of the common cold with unrefined echinacea: a randomized, double-blind, placebo-controlled trial. *Ann Intern Med* 2002; **137:** 939–46.
3. Taylor JA, *et al.* Efficacy and safety of echinacea in treating upper respiratory tract infections in children: a randomized controlled trial. *JAMA* 2003; **290:** 2824–30.
4. Caruso TJ, Gwaltney JM. Treatment of the common cold with echinacea. *Clin Infect Dis* 2005; **40:** 807–10.
5. Linde K, *et al.* Echinacea for preventing and treating the common cold. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2006 (accessed 31/07/08).
6. Shah SA, *et al.* Evaluation of echinacea for the prevention and treatment of the common cold: a meta-analysis. *Lancet Infect Dis* 2007; **7:** 473–80.
7. Turner RB,*et al.* An evaluation of Echinacea angustifolia in experimental rhinovirus infections. *N Engl J Med* 2005; **353:** 341–8.

Preparations

Proprietary Preparations (details are given in Part 3)
Austral.: Echinacin; ***Austria:*** Echinacin; Echinaforce; Sanvita Immun; ***Belg.:*** Echinacin; ***Braz.:*** Enax; Equinacea†; Imunnal; Imunocel†; Imunogreen; ***Canad.:*** Citranacea†; Triple Blend Echinacea; ***Cz.:*** Echinacin; Immunal; ***Ger.:*** aar vir; Cefatox†; Echan; Echifit†; Echiherb†; Echinacin; Echinaforce; Echinapur; Echinatur; Episcorit; Esberitox mono; Lymphozil; Pascotox forte-Injektopas†; Pascotox mono†; Pascotox Purpurea; Resistan mono; Resplant†; toxi-loges; Wiedimmun†; ***Gr.:*** Echinacin; ***Hung.:*** Echinacin; ***Ital.:*** EuMunil; ***Mex.:*** Inmune Booster†; Regripax; ***Pol.:*** Echinapur; Echinerba; Immunal; Lymphozil; Purex; ***Rus.:*** Immunal (Иммунал); Immunorm (Иммунорм); ***Spain:*** Echinacin; Ekian; Revitonil; ***Switz.:*** Echinacin; Echinaforce; EchinaMed; Echiplant†; ***UK:*** Benylin Active Response†; Echinacea; Echinaforce; Phytocold; Skin Clear; ***Venez.:*** Flucaps.

Multi-ingredient: ***Arg.:*** Parodontax Fluor; SX-22; ***Austral.:*** Andrographis Complex; Andrographis Compound; Astragalus Complex; Broncafect; Cats Claw Complex; Cold and Flu Relief†; Cough Relief†; Diaco; Digest; Echinacea 4000; Echinacea ACE + Zinc; Echinacea Complex; Echinacea Lozenge; Euphrasia Complex; Flavons; Galium Complex†; Gartech; Herbal Cleanse†; Herbal Cold & Flu Relief†; Lifesystem Herbal Plus Formula 8 Echinacea†; Logicin Natural Lozenges†; Odourless Garlic†; Proyeast†; Sambucus Complex†; Urgenin†; Urinase†; ***Austria:*** Esberitox; Parodontax; Spasmo-Urgenin; Urgenin; ***Belg.:*** Medica Junior; Urgenin; ***Braz.:*** Infantoss†; Malvatricin Natural; Malvatricin Natural Organic; Malvatricin Natural Soft; Parodontax; ***Canad.:*** Bentasil Licorice with Echinacea†; Benylin First Defense†; Echinacea Goldenseal Formula†; ***Chile:*** Citro-C; Paltomiel Plus; ***Ger.:*** Ermsech†; Esberitox N; Hewenephron duo†; ***Hong Kong:*** Urgenin; ***Indon.:*** Biofos; Curmunos; Ekinase; Flavin; Hepasil; Hepatin; Imboost; Imboost Force; Imudator; Norflam; Primunox; Proimbus; Proza; Stamino; StarMuno; Stimox; Tribost; ***Israel:*** Parodontax†; Urgenin; ***Ital.:*** Bodyguard; Dermilia Flebozin; Golatux; Immumil Plus; Immumil†; Immun-up; Influ-Zinc; Nepiros; Probigol; Promix 3†; Promix†; Ribovir; Sclerovis H; ***Malaysia:*** Echinacea Plus†; Esberitox N; Total Man†; ***Mex.:*** Gripaleta†; ***NZ:*** Lice Blaster; Strepsils Echinacea Defence; ***Pol.:*** Cardiobonisol; Echinasal; Esberitox N; Immunofort; Pectobonisol; Plantifort; Reumaherb; ***Port.:*** Neo Urgenin; Spasmo-Urgenin†; Vitace; ***Rus.:*** Prostanorm (Простанорм); ***S.Afr.:*** Spasmo-Urgenin†; Wecesin; ***Singapore:*** Noricaven†; Proza; ***Spain:*** Neo Ur-