2. British Association for Emergency Medicine. Clinical Effectiveness Committee guideline for the management of pain in children (2004). Available at: http://www.emergencymed.org.uk/BAEM/CEC/assets/cec_pain_in_children.pdf (accessed 26/06/08)
3. Marsh DF, *et al.* Opioid systems and the newborn. *Br J Anaesth* 1997; **79:** 787–95.
4. Anonymous. Drugs in the management of acute diarrhoea in infants and young children. *Bull WHO* 1989; **67:** 94–6.
5. Cimolai N, Carter JE. Antimotility agents for paediatric use. *Lancet* 1990; **336:** 874.

Administration in renal impairment. See under Precautions, above.

Cough. A systematic review[1] of over-the-counter preparations for acute cough concluded that codeine appeared no more effective than placebo in reducing cough symptoms in adults or children, although the number of patients in the studies considered was small.

See also Administration in Children, above.

1. Smith SM, *et al.* Over-the-counter medications for acute cough in children and adults in ambulatory settings. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2008 (accessed 26/06/08).

Pain. Systematic reviews[1,2] comparing paracetamol-codeine combinations versus paracetamol alone concluded that in single-dose studies addition of codeine to paracetamol produced a comparatively small but statistically significant increase in analgesic effect; however, there was an increased incidence of adverse effects with the combination.

1. de Craen AJM, *et al.* Analgesic efficacy and safety of paracetamol-codeine combinations versus paracetamol alone: a systematic review. *BMJ* 1996; **313:** 321–5.
2. Moore A, *et al.* Single dose paracetamol (acetaminophen), with and without codeine, for postoperative pain. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 1998 (accessed 26/06/08).

Preparations

BP 2008: Co-codamol Capsules; Co-codamol Tablets; Co-codaprin Tablets; Codeine Linctus; Codeine Phosphate Injection; Codeine Phosphate Oral Solution; Codeine Phosphate Tablets; Dispersible Co-codaprin Tablets; Effervescent Co-codamol Tablets; Paediatric Codeine Linctus;
USP 31: Acetaminophen and Codeine Phosphate Capsules; Acetaminophen and Codeine Phosphate Oral Solution; Acetaminophen and Codeine Phosphate Oral Suspension; Acetaminophen and Codeine Phosphate Tablets; Aspirin and Codeine Phosphate Tablets; Bromodiphenhydramine Hydrochloride and Codeine Phosphate Oral Solution; Butalbital, Aspirin, Caffeine, and Codeine Phosphate Capsules; Carisoprodol, Aspirin, and Codeine Phosphate Tablets; Codeine Phosphate Injection; Codeine Phosphate Tablets; Codeine Sulfate Tablets; Guaifenesin and Codeine Phosphate Syrup; Terpin Hydrate and Codeine Elixir.

Proprietary Preparations (details are given in Part 3)
Austral.: Actacode; ***Austria:*** Codipertussin; Codipront Mono; Coditard; Makatussin-Hustentropfen; Tricodein; ***Belg.:*** Bromophar; Bronchodine; Bronchosedal; Eulyptan†; Gloceda†; Glottyl; Toularynx; ***Canad.:*** Codeine Contin; ***Fr.:*** Codedrill; Codenfan; Neo-Codion; Paderyl; ***Ger.:*** Antitussivum Burger; Bronchicum Mono Codein; codi OPT; Codicaps mono; Codicaps N†; Codicaps Neo; Codicompren; Codipertussin; Codipront Mono†; Makatussin Codein; Melrosum Codein Hustensirup†; Neo-Codion NN†; Optipect Kodein; Tryasol; Tussoret; ***Gr.:*** Codipront N†; ***Hong Kong:*** Codipront N†; ***India:*** Codifos; ***Irl.:*** Codant; Codinex; ***Israel:*** Codical; Rekod; ***Malaysia:*** Setlinctus†; ***Neth.:*** Bronchicum Extra Sterk; ***Port.:*** Toseina; ***Rus.:*** Neo-Codion (Нео-Кодион); ***Spain:*** Bisoltus; Codeisan; Codulin; Fludan Codeina; Histaverin; Notusin; Perduretas Codeina; Toseina; ***Switz.:*** Makatussin nouvelle formule; Tricodein†; ***UK:*** Bepro; Galcodine; ***Venez.:*** Codipront Mono.

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

Croton Oil

Aceite de crotón; Oleum Crotonis; Oleum Tiglii.

CAS — 8001-28-3.

Pharmacopoeias. *Chin.* includes fruits of *Croton tiglium*.

Profile

Croton oil is an oil expressed from the seeds of *Croton tiglium* (Euphorbiaceae). Externally, it is a powerful counter-irritant and vesicant. Croton oil is also used with phenol in cosmetic chemical peeling of the skin.

Croton oil has such a violent purgative action that it should not be used as a laxative. Croton oil contains phorbol esters, which are carcinogenic.

Homoeopathy. Croton has been used in homoeopathic medicines under the following names: Croton tiglium; Crot. tig.

Preparations

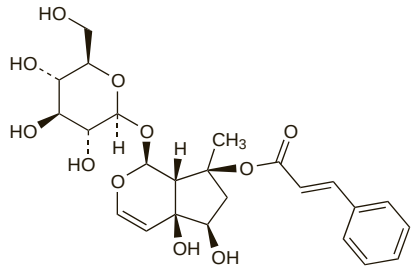
Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Canad.:*** Rheumalan†.

Devil's Claw Root

Djävulsklorot; Harpagofytový kořen; Harpagonjuuri; Harpagophyti radix; Harpagophyton; Harpagophyton, racine d'; Harpagophytum; Inkaruočių šaknys; Ördögcsáklya gyökér; Raíz de harpagofito; Teufelskrallenwurzel.

CAS — 19210-12-9 (harpagoside).



(harpagoside)

Pharmacopoeias. In *Eur.* (see p.vii), which also includes the dry extract.
Ph. Eur. 6.2 (Devil's Claw Root; Devil's Claw BP 2008). The cut and dried tuberous, secondary roots of *Harpagophytum procumbens* and/or *H. zeyheri*. Greyish-brown to dark brown with a bitter taste. Contains not less than 1.2% harpagoside ($C_{24}H_{30}O_{11}$ = 494.5), calculated with reference to the dried drug. Protect from light.

Profile

Devil's claw root is used in herbal remedies for musculoskeletal and joint disorders. Its activity is attributed in part to the plant's content of iridoid glycosides, notably harpagoside.

Pain. Preparations containing devil's claw root have been tried with some success in the treatment of musculoskeletal disorders such as low back pain and osteoarthritis. There is some evidence of efficacy for daily doses standardised to 50 to 100 mg harpagoside but the quality of reporting in trials is generally poor and further studies are needed to establish its place in therapy.[1,2]

1. Gagnier JJ, *et al.* Harpgophytum [sic] procumbens for osteoarthritis and low back pain: a systematic review. *BMC Complement Altern Med* 2004; **4:** 13.
2. Gagnier JJ, *et al.* Herbal medicine for low back pain. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2006 (accessed 05/10/06).

Preparations

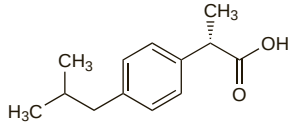
Proprietary Preparations (details are given in Part 3)
Arg.: Herbaccion Flex†; ***Braz.:*** Tenitrat; ***Fr.:*** Elusanes Harpagesic; Harpadol; Harpagocid; ***Ger.:*** Ajuta; Allya; Arthrosetten H; Arthrotabs; Bomarthros; Cefatec; Dolo-Arthrodynat†; Dolo-Arthrosetten H; Doloteffin; flexi-loges; Harpagoforte; HarpagoMega†; Harpagosan†; Herbadon†; Jucurba; Matai†; Pargo†; Rheuferm Phyto; Rheuma-Sern; Rivoltan; Sogoon; Teltonal; Teufelskralle; ***Pol.:*** Reumaphyt; ***Spain:*** Fitokey Harpagophytum; Harpagofito Orto; ***UK:*** Atrosan; Flexiherb.

Multi-ingredient: ***Austral.:*** Arthriforte; Arthritic Pain Herbal Formula 1; Bioglan Arthri Plus; Boswellia Compound; Devils Claw Plus; Extralife Arthri-Care; Guaiacum Complex†; Herbal Arthritis Formula†; Lifesystem Herbal Formula 1 Arthritic Aid†; Prost-1†; ***Belg.:*** Algi-Cool; ***Cz.:*** Antirevmaticky Caj; ***Fr.:*** Arkophytum†; ***Ger.:*** Dr Wiemanns Rheumatonikum; ***Ital.:*** Bodyguard; Cartago; Flodolor; Nevril; Pik Gel; Reumafort; ***Malaysia:*** Celery Plus†; ***Mex.:*** Rodan; ***Pol.:*** Reumaherb; ***Spain:*** Dolosul†; Natusor Harpagosinol†.

Dexibuprofen *(BAN, USAN, rINN)*

Deksibuprofeeni; Dexibuprofène; Dexibuprofeno; Dexibuprofenum; *S*-(+)-Ibuprofen.

Дексибупрофен
CAS — 51146-56-6.
ATC — M01AE14.
ATC Vet — QM01AE14.



Profile

Dexibuprofen is the *S*(+)-enantiomer of ibuprofen (p.64) and is used similarly in the management of mild to moderate pain and inflammation in conditions such as dysmenorrhoea, headache, postoperative pain, dental pain, sprains, and soft-tissue rheumatism. It is also used in musculoskeletal and joint disorders such as ankylosing spondylitis, osteoarthritis, and rheumatoid arthritis. It may be used as an antipyretic to reduce fever.

The usual adult dose is 600 to 900 mg daily by mouth in up to 3 divided doses, adjusted according to response, to a usual maximum of 1.2 g daily. Elderly patients should be started at the lower end of the dose range; dosage may then be increased according to tolerance. Dose reductions are also recommended in patients with hepatic or renal impairment, see below.

For doses in children, see below.

◊ References.

1. Phleps W. Overview on clinical data of dexibuprofen. *Clin Rheumatol* 2001; **20** (suppl 1): S15–S21.
2. Mayrhofer F. Efficacy and long-term safety of dexibuprofen [S(+)-ibuprofen]: a short-term efficacy study in patients with osteoarthritis of the hip and a 1-year tolerability study in patients with rheumatic disorders. *Clin Rheumatol* 2001; **20** (suppl 1): S22–S29.
3. Hawel R, *et al.* Comparison of the efficacy and tolerability of dexibuprofen and celecoxib in the treatment of osteoarthritis of the hip. *Int J Clin Pharmacol Ther* 2003; **41:** 153–64.

Administration in children. Although dexibuprofen is not licensed for use in children under 18 years of age in the UK, some countries permit such use. For example, in Switzerland, dexibuprofen has been given to children aged 6 years and over; usual oral doses are 10 to 15 mg/kg daily in 2 to 4 divided doses. Licensed product information for one preparation recommends a maximum dose of 300 mg daily for those weighing less than 30 kg.

Administration in hepatic and renal impairment. UK licensed product information specifies that the initial dose of dexibuprofen should be reduced in patients with mild to moderate hepatic or renal impairment; it should not be used in those with severe impairment.

Pharmacokinetics. For mention of the metabolism of dexibuprofen, see p.65.

Further references.

1. Eller N, *et al.* Pharmacokinetics of dexibuprofen administered as 200 mg and 400 mg film-coated tablets in healthy volunteers. *Int J Clin Pharmacol Ther* 1998; **36:** 414–17.

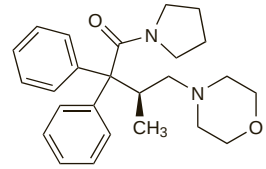
Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Dextropirac†; Dolomin†; ***Austria:*** Actifen; Eu-Med Neu; Monactil; Movone; Seractil; ***Chile:*** Dexelle; ***Cz.:*** Seractil; ***Denm.:*** Seractiv; ***Fin.:*** Dexit; ***Ger.:*** Deltaran; ***Gr.:*** Seractil; ***Hung.:*** Seractil; ***India:*** Sibet; ***Ital.:*** Seractil; ***Neth.:*** Seractil; ***Norw.:*** Seractiv; ***Pol.:*** Dexprofen; Seractil; ***Port.:*** Seractil; ***Spain:*** Atriscal; Seractil; ***Swed.:*** Tradil; ***Switz.:*** DexOptifen; Seractil; ***UK:*** Seractil.

Dextromoramide *(BAN, plNN)* ⊗

Dekstromoramidi; Dextrodiphenopyrine; Dextromoramid; Dextromoramida; Dextromoramidum; *d*-Moramid; Pyrrolamidol. (+)-1-(3-Methyl-4-morpholino-2,2-diphenylbutyryl)pyrrolidine.

Декстроморамид
$C_{25}H_{32}N_2O_2$ = 392.5.
CAS — 357-56-2.
ATC — N02AC01.
ATC Vet — QN02AC01.



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

Dextromoramide Tartrate *(BANM, plNNM)* ⊗

Bitartrate de Dextromoramide; Dekstromoramiditartraatti; Dekstromoramido tartratas; Dextromoramide Acid Tartrate; Dextromoramide Hydrogen Tartrate; Dextromoramide, tartrate de; Dextromoramidi tartras; Dextromoramid-tartarát; Dextromoramidtartrat; Tartrato de dextromoramida.

Декстроморамида Тартрат
$C_{25}H_{32}N_2O_2,C_4H_6O_6$ = 542.6.
CAS — 2922-44-3.

Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Dextromoramide Tartrate). A white or almost white, crystalline or amorphous powder. Soluble in water; sparingly soluble in alcohol. A 1% solution in water has a pH of 3.0 to 4.0.

Profile

Dextromoramide is an opioid analgesic (p.104) structurally related to methadone (p.82). It has been used in the treatment of severe pain although it was not recommended for use in obstetric analgesia because of an increased risk of neonatal depression. Dextromoramide is subject to abuse.

Dextromoramide has been given orally as the tartrate. It has also been given rectally as suppositories and by subcutaneous or intramuscular injection.

Preparations

BP 2008: Dextromoramide Tablets.

Proprietary Preparations (details are given in Part 3)
Irl.: Palfium; ***Neth.:*** Palface; Palfium.

Dextropropoxyphene *(BAN, pINN)*

Dekstropropoksifeeni; Dextropropoxifen; Dextropropoxifeno; Dextropropoxyphène; Dextropropoxyphenum; Propoxyphene. (+)-(1*S*,2*R*)-1-Benzyl-3-dimethylamino-2-methyl-1-phenylpropyl propionate.

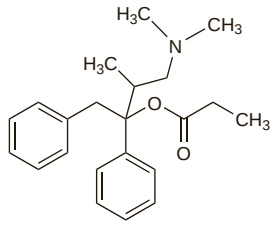
Декстропропоксифен

$C_{22}H_{29}NO_2$ = 339.5.

CAS — 469-62-5.

ATC — N02AC04.

ATC Vet — QN02AC04.



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

Dextropropoxyphene Hydrochloride

(BANM, pINNM)

Dekstropropoksifeenihydrokloridi; Dekstropropoksifeno hidrochloridas; Dextropropoxifén-hidroklorid; Dextropropoxifenhydroklorid; Dextropropoxyfen-hydrochlorid; Dextropropoxyphène, chlorhydrate de; Dextropropoxypheni hydrochloridum; Hidrocloruro de dextropropoxifeno; Propoxyphene Hydrochloride *(USAN)*.

Декстропропоксифена Гидрохлорид

$C_{22}H_{29}NO_2$,HCl = 375.9.

CAS — 1639-60-7.

NOTE. Compounded preparations of dextropropoxyphene hydrochloride may be represented by the following names:

- Co-proxamol (*BAN*)—dextropropoxyphene hydrochloride 1 part and paracetamol 10 parts (w/w).

Pharmacopoeias. In *Eur.* (see p.vii) and *US*.

Ph. Eur. 6.2 (Dextropropoxyphene Hydrochloride). A white or almost white crystalline powder. Very soluble in water; freely soluble in alcohol. Protect from light.

USP 31 (Propoxyphene Hydrochloride). A white odourless crystalline powder. Freely soluble in water; soluble in alcohol, in acetone, and in chloroform; practically insoluble in ether and in benzene. Store in airtight containers.

Dextropropoxyphene Napsilate *(BANM, pINNM)*

Dextropropoxyphène, Napsilate de; Dextropropoxyphene Napsylate; Dextropropoxypheni Napsilas; Napsilato de dextropropoxifeno; Propoxyphene Napsylate *(USAN)*. Dextropropoxyphene naphthalene-2-sulphonate monohydrate.

Декстропропоксифена Напсилат

$C_{22}H_{29}NO_2$,$C_{10}H_8O_3S$,H_2O = 565.7.

CAS — 17140-78-2 (anhydrous dextropropoxyphene napsilate); 26570-10-5 (dextropropoxyphene napsilate monohydrate).

NOTE. Compounded preparations of dextropropoxyphene napsilate may be represented by the following names:

- Co-proxAPAP (*PEN*)—dextropropoxyphene napsilate and paracetamol.

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

BP 2008 (Dextropropoxyphene Napsilate). An odourless or almost odourless white powder. It exhibits polymorphism. Practically insoluble in water; soluble in alcohol; freely soluble in chloroform.

USP 31 (Propoxyphene Napsylate). A white powder having essentially no odour. Very slightly soluble in water; soluble 1 in 15 of alcohol and 1 in 10 of chloroform; soluble in acetone and in methyl alcohol. Store in airtight containers.

Dependence and Withdrawal

As for Opioid Analgesics, p.101.

Dextropropoxyphene has been subject to abuse (see under Precautions, below).

◊ Reports of dextropropoxyphene dependence and its treatment.

1. Wall R, *et al.* Addiction to Distalgesic (dextropropoxyphene). *BMJ* 1980; **280:** 1213–14.
2. D'Abadie NB, Lenton JD. Propoxyphene dependence: problems in management. *South Med J* 1984; **77:** 299–301.

Adverse Effects

As for Opioid Analgesics in general, p.102.

In the recommended dosage the adverse effects of dextropropoxyphene are less marked than those of morphine. Gastrointestinal effects, dizziness, and drowsiness are the most common. Liver impairment, manifest as abnormal liver function tests and, more rarely, as reversible jaundice, has been reported.

There have been a large number of fatalities from either accidental or intentional overdosage with dextropropoxyphene. Many reports emphasise the rapidity with which death ensues; death within an hour of overdosage is not uncommon, and it can occur within 15 minutes. Overdosage is often complicated by patients also taking other CNS depressants such as alcohol and using mixed preparations such as dextropropoxyphene with paracetamol or aspirin.

Symptoms of overdosage are similar to those of opioid poisoning in general, but in addition patients may experience psychotic reactions. There may be cardiac conduction abnormalities and arrhythmias.

Dextropropoxyphene injections are painful and have a very destructive effect on soft tissues and veins when abused in this way.

Anorectal reactions have followed the prolonged use of suppositories containing dextropropoxyphene; the reactions appear to be dose dependent.

Effects on the blood. A 12-year history of haemolysis and subsequent significant haemolytic anaemia in an elderly woman[1] was associated with chronic, periodic, and occasionally excessive intake of co-proxamol.

1. Fulton JD, McGonigal G. Steroid responsive haemolytic anaemia due to dextropropoxyphene paracetamol combination. *J R Soc Med* 1989; **82:** 228.

Effects on the ears. A report of complete nerve deafness associated with chronic abuse of co-proxamol was made to the UK CSM.[1] The CSM had received 2 other reports of permanent hearing loss attributed to co-proxamol abuse; transient hearing loss had also been reported in 2 patients taking usual doses; 7 further reports described tinnitus.

1. Ramsay BC. Complete nerve deafness after abuse of co-proxamol. *Lancet* 1991; **338:** 446–7.

Effects on the liver. There have been occasional reports of jaundice in patients taking dextropropoxyphene alone but many of the 49 suspected hepatic reactions with dextropropoxyphene reported to the UK CSM by 1985[1] had involved use with paracetamol; clinical features including malaise, jaundice, raised serum transaminases, and sometimes fever, were however generally characteristic of dextropropoxyphene alone. Relapsing jaundice mimicking biliary disease was attributable to the dextropropoxyphene component of co-proxamol in 3 patients,[2] whereas there was no abnormality of liver function in 11 patients on long-term co-proxamol analgesia.[3] Another report of 9 cases found that the hepatotoxicity of dextropropoxyphene mimicked symptoms of large bile duct obstruction, and suggested that such toxicity might be misdiagnosed.[4] A more recent review[5] also concluded that hepatotoxicity with dextropropoxyphene might mimic a biliary tract disease, sometimes with few or no symptoms.

1. CSM. Hepatotoxicity with dextropropoxyphene. *Current Problems 17* 1986. Available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2024424&RevisionSelectionMethod=LatestReleased (accessed 26/06/08)
2. Bassendine MF, *et al.* Dextropropoxyphene induced hepatotoxicity mimicking biliary tract disease. *Gut* 1986; **27:** 444–9.
3. Hutchinson DR, *et al.* Liver function in patients on long-term paracetamol (co-proxamol) analgesia. *J Pharm Pharmacol* 1986; **38:** 242–3.
4. Rosenberg WMC, *et al.* Dextropropoxyphene induced hepatotoxicity: a report of nine cases. *J Hepatol* 1993; **19:** 470–4.
5. Bergeron L, *et al.* Dextropropoxyphène et atteintes hépatiques: à propos de 4 cas et revue de littèrature. *Therapie* 2002; **57:** 464–72.

Effects on the lungs. Hypersensitivity pneumonitis and skin rash has been reported in a patient taking co-proxamol.[1] No such reaction occurred when the patient was subsequently given paracetamol alone.

1. Matusiewicz SP, *et al.* Hypersensitivity pneumonitis associated with co-proxamol (paracetamol + dextropropoxyphene) therapy. *Postgrad Med J* 1999; **75:** 475–6.

Hypoglycaemia. Hypoglycaemia has occasionally been reported with the use of dextropropoxyphene.[1-6]

1. Wiederholt IC, *et al.* Recurrent episodes of hypoglycemia induced by propoxyphene. *Neurology* 1967; **17:** 703–4.
2. Almirall J, *et al.* Propoxyphene-induced hypoglycemia in a patient with chronic renal failure. *Nephron* 1989; **53:** 273–5.
3. Laurent M, *et al.* Hypoglycémie sous dextropropoxyphène chez des grands vieillards: 7 cas. *Presse Med* 1991; **20:** 1628.
4. Lowenstein W, *et al.* Hypoglycémie au dextropropoxyphène: une urgence chez le toxicomane. *Presse Med* 1993; **22:** 133.
5. Santos Gil I, *et al.* Hipoglucemia secundaria a ingestión de dextropropoxifeno en un paciente adicto a drogas. *Med Clin (Barc)* 1998; **110:** 475–6.
6. Shah P, *et al.* Propoxyphene-induced hypoglycemia in renal failure. *Endocr Pract* 2006; **12:** 170–3.

Overdosage. There have been several reviews or retrospective studies of acute self-poisoning with dextropropoxyphene.[1-4] At a symposium on the safety and efficacy of dextropropoxyphene[5] many of the participants dealt with the problems of dextropropoxyphene overdosage, often in conjunction with paracetamol and sometimes with alcohol. Profound and even fatal CNS depression can develop rapidly as a result of the dextropropoxyphene content and in many cases death has occurred within an hour;[6] it was suggested that as few as 15 to 20 tablets of co-proxamol may be fatal.[7,8] Analysis of suicides involving drugs in England and Wales between 1997 and 1999 revealed that the odds of dying after overdose with co-proxamol were 2.3 times that for tricyclic antidepressant overdose, and 28.1 times greater than for paracetamol.[9] Another analysis of suicides due to poisoning in 3 areas of the UK between 2000 and 2001 identified 123 cases of fatal overdose with co-proxamol;[10] those who also consumed alcohol had generally taken fewer co-proxamol tablets than those who had not, emphasising the increased toxicity of the combination.

An analysis of overdosage involving combination analgesic preparations prescribed in Scotland between 2000 and 2002 also found that overdoses with co-proxamol were 10 times more likely to be fatal when compared with co-dydramol or co-codamol.[11] In the USA[12] the incidence of dextropropoxyphene-associated deaths reached a peak in 1977 and then fell at a rate that was not matched by a decline in prescribing.

It is not clear whether the metabolite, nordextropropoxyphene, plays an important role in fatalities.[12] However, nordextropropoxyphene, like dextropropoxyphene, is considered to have local anaesthetic activity and the membrane stabilising activity of dextropropoxyphene has been implicated as a major factor responsible for its severe cardiac depressant effect.[13]

In January 2005, the UK CSM found the risk of toxicity of co-proxamol in overdose to be unacceptable;[14] consequently, co-proxamol has been gradually withdrawn from the UK market. Fixed-dose combinations of dextropropoxyphene and paracetamol have also been withdrawn in several other countries including Sweden and Switzerland.

1. Young RJ. Dextropropoxyphene overdosage: pharmacological considerations and clinical management. *Drugs* 1983; **26:** 70–9.
2. Madsen PS, *et al.* Acute propoxyphene self-poisoning in 222 consecutive patients. *Acta Anaesthesiol Scand* 1984; **28:** 661–5.
3. Segest E. Poisoning with dextropropoxyphene in Denmark. *Hum Toxicol* 1987; **6:** 203–7.
4. Jonasson U, *et al.* Correlation between prescription of various dextropropoxyphene preparations and their involvement in fatal poisonings. *Forensic Sci Int* 1999; **103:** 125–32.
5. Bowen D, *et al.* (ed). Distalgesic; safety and efficacy. *Hum Toxicol* 1984; **3** (suppl): 1S–238S.
6. Proudfoot AT. Clinical features and management of Distalgesic overdose. *Hum Toxicol* 1984; **3** (suppl): 85S–94S.
7. Whittington RM. Dextropropoxyphene deaths: coroner's report. *Hum Toxicol* 1984; **3** (suppl): 175S–185S.
8. Young RJ, Lawson AAH. Distalgesic poisoning—cause for concern. *BMJ* 1980; **280:** 1045–7.
9. Hawton K, *et al.* Co-proxamol and suicide: a study of national mortality statistics and local non-fatal self-poisonings. *BMJ* 2003; **326:** 1006–8.
10. Hawton K, *et al.* A multicentre study of coproxamol poisoning suicides based on coroners' records in England. *Br J Clin Pharmacol* 2005; **59:** 207–12.
11. Afshari R, *et al.* Co-proxamol overdose is associated with a 10-fold excess mortality compared with other paracetamol combination analgesics. *Br J Clin Pharmacol* 2005; **60:** 444–7.
12. Finkle BS. Self-poisoning with dextropropoxyphene and dextropropoxyphene compounds: the USA experience. *Hum Toxicol* 1984; **3** (suppl): 115S–34S.
13. Henry JA, Cassidy SL. Membrane stabilising activity: a major cause of fatal poisoning. *Lancet* 1986; **i:** 1414–17.
14. MHRA. Withdrawal of co-proxamol products and interim updated prescribing information. Message from Professor G Duff, Chairman of CSM (issued 31st January, 2005). Available at: http://www.mhra.gov.uk/home/groups/pl-a/documents/websiteresources/con019461.pdf (accessed 28/08/08)

Treatment of Adverse Effects

As for Opioid Analgesics in general, p.102.

Rapid treatment of overdosage with naloxone and assisted respiration is essential. Cardiac effects may not be reversed by naloxone. Gastric lavage and activated charcoal may be of value within 1 hour of ingestion, but dialysis is of little use.

Convulsions may require control with an anticonvulsant, bearing in mind that the CNS depressant effects of dextropropoxyphene can be exacerbated (see also Interactions, below). Stimulants should not be used because of the risk of inducing convulsions.

Patients taking overdoses of dextropropoxyphene with paracetamol will also require treatment for paracetamol poisoning (p.108). Mixtures of dextropropoxyphene and aspirin may be involved; the treatment of aspirin poisoning is described on p.20.