Pharmacokinetics

Bethanechol chloride is poorly absorbed from the gastrointestinal tract. It is not hydrolysed by cholinesterases. At standard doses bethanechol does not cross the blood-brain barrier.

Uses and Administration

Bethanechol chloride, a choline ester, is a quaternary ammonium parasympathomimetic that mainly exhibits the muscarinic actions of acetylcholine (p.1877). It is not inactivated by cholinesterases so its actions are more prolonged than those of acetylcholine. Bethanechol chloride has little if any nicotinic activity and is used for its actions on the bladder and gastrointestinal tract. It has been used as an alternative to catheterisation in the treatment of urinary retention and has also been used for gastric atony and retention, abdominal distension following surgery, congenital megacolon, and gastro-oesophageal reflux disease. Bethanechol chloride is given in usual doses of 5.15 mg subcutaneously or 10 to 50 mg orally, both up to 4 times daily, but dosage must be adjusted individually. Oral doses should be taken on an empty stomach. The effects usually occur within 5 to 15 minutes of a subcutaneous dose, or 30 to 90 minutes of an oral dose, and disappear within about 1 to 2 hours depending on the dose and route. However, large oral doses (300 to 400 mg) may produce effects for up to 6 hours. For a warning to avoid intravenous or intramuscular use, see under Precautions, above.

Decreased gastrointestinal motility. Parasympathomimetics such as bethanechol enhance gastric contractions and increase intestinal motility and form just one of many treatment that have been used in conditions associated with decreased gastrointestinal motility (p.1694).

Gastro-oesophageal reflux disease. Prokinetic drugs such as bethanechol have been tried in gastro-oesophageal reflux disease (p.1696).

References.

- Thanick KD, et al. Reflux esophagitis: effect of oral bethanechol on symptoms and endoscopic findings. Ann Intern Med 1980; 93: 805–8.
- Saco LS, et al. Double-blind controlled trial of bethanechol and antacid versus placebo and antacid in the treatment of erosive esophagitis. Gastroenterology 1982; 82: 1369–73.
- Thanick K, et al. Bethanechol or cimetidine in the treatment of symptomatic reflux esophagitis: a double-blind control study. Arch Intern Med 1982; 142: 1479–81.
- Strickland AD, Chang JHT. Results of treatment of gastroesophageal reflux with bethanechol. J Pediatr 1983; 103: 311–15.

Stuttering. A double-blind placebo-controlled study¹ in 10 patients with stuttering (p.1001) on the whole failed to confirm an earlier report² of benefit using bethanechol although 2 patients who did respond elected to continue treatment after the study.

- Kampman K, Brady JP. Bethanechol in the treatment of stuttering. J Clin Psychopharmacol 1993; 13: 284–5.
- 2. Hays P. Bethanechol chloride in treatment of stuttering. *Lancet* 1987: i. 271

Urinary incontinence and retention. Bethanechol is one of the parasympathomimetics that have been given to increase detrusor activity in patients with overflow incontinence, but there have been doubts about the effectiveness of such treatment (see p.2180). Bethanechol was also one of the parasympathomimetics used in the management of postoperative urinary retention but they have generally been superseded by catheterisation.

References.

- Finkbeiner AE. Is bethanechol chloride clinically effective in promoting bladder emptying: a literature review. J Urol (Baltimore) 1985; 134: 443–9.
- Kemp B, et al. Prophylaxis and treatment of bladder dysfunction after Wertheim-Meigs operation: the positive effect of early postoperative detrusor stimulation using the cholinergic drug betanecholchloride. Int Urogynecol J Pelvic Floor Dysfunct 1997; 8: 138-41.
- Riedl CR, et al. Electromotive administration of intravesical bethanechol and the clinical impact on acontractile detrusor management: introduction of a new test. J Urol (Baltimore) 2000; 164: 2108–11.

Preparations

USP 31: Bethanechol Chloride Injection; Bethanechol Chloride Oral Solution; Bethanechol Chloride Oral Suspension; Bethanechol Chloride Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Miotonachol; Austral.: Urocarb; Austria: Myocholine; Belg.: Myocholine; Braz.: Liberar; Canad.: Duvoid; Myotonachol†, Ger.: Myocholine; India: Urotone; Urotonine†: Israel: Urecholine†; Switz.: Myocholine; Thai.: Ucholine; Urecholine†; UK: Myotonine; USA: Myotonachol; Urecholine

Bibrocathol (rINN)

Bibrocathin; Bibrocatholum; Bibrocatol; Bibrokatol; Bibrokatol; Bismuth Tetrabrompyrocatechinate; Tetrabromopyrocatechol Bismuth. 4,5,6,7-Tetrabromo-2-hydroxy-1,3,2-benzodioxabismole

Биброкатол C_6 HBiBr $_4$ O $_3$ = 649.7. CAS — 6915-57-7. ATC — S01AX05. ATC Vet — QS01AX05.

Profile

Bibrocathol is a bismuth-containing compound that has been applied topically in the treatment of eye disorders, wounds, and burns

Preparations

Proprietary Preparations (details are given in Part 3)
Gen.: Noviform; Posiformin; Swed.: Noviform; Switz.: Noviform†.
Multi-ingredient: Gen.: Novifort†.

Bicyclol

4,4'-Dimethoxy-5,6,5',6'-bis(methylene-dioxy)-2-hydroxymethyl-2'methoxycarbonyl biphenyl.

Бициклол

 $C_{19}H_{18}O_9 = 390.3.$

Profile

Bicyclol has been used as a hepatoprotectant in the management of hepatitis. It has been given orally in a dose of 25 or 50 mg three times daily for at least 6 months.

♦ References.

- Liu Q, et al. A useful agent for chemoprevention of hepatocellular carcinoma? Cancer Biol Ther 2006; 5: 1674–6.
- Wu T, et al. Bicyclol for chronic hepatitis B. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2006 (accessed 01/05/08).
 Yang XY, et al. Bicyclol for chronic hepatitis C. Available in The
- Yang XY, et al. Bicyclol for chronic hepatitis C. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2007 (accessed 01/05/08).

Bifendate

Dimethyl 7,7'-dimethoxy-(4,4'-bi-I ,3-benzodioxole)-5,5'-dicarboxylate.

 $C_{20}H_{18}O_{10} = 418.4.$ CAS — 73536-69-3.

Pharmacopoeias. In Chin.

Profile

Bifendate is derived from schisandra (see p.2384). It is used in Chinese medicine for chronic hepatitis.

Bifendate has been reported to reduce blood concentrations of ciclosporin (see p.1826).

Bile Acids and Salts

Biliares, ácidos y sales.

CAS — 81-25-4 (cholic acid); 11006-55-6 (sodium tauro-glycocholate); 361-09-1 (sodium cholate).

Pharmacopoeias. Jpn includes bear bile.

Profile

The principal primary bile acids, cholic acid and chenodeoxycholic acid (p.2280), are produced in the liver from cholesterol and are conjugated with glycine or taurine to give glycocholic acid, taurocholic acid, glycochenodeoxycholic acid, and taurochenodeoxycholic acid, before being secreted into the bile where they are present as the sodium or potassium salts (bile salts). Secondary bile acids are formed in the colon by bacterial deconjugation and 7a-dehydroxylation of cholic acid and chenodeoxycholic acid, producing deoxycholic acid and lithocholic acid, respectively. Ursodeoxycholic acid (p.2408) is a minor bile acid in man although it is the principal bile acid in bears. Dehydrocholic acid (p.2292) is a semisynthetic bile acid.

The total body pool of bile salts is about 3 g, and most of the secreted bile salts are reabsorbed in a process of enterohepatic recycling, so that only a small fraction of this amount must be synthesised *de novo* each day.

Bile salts are strongly amphiphilic; with the aid of phospholipids they form micelles and emulsify cholesterol and other lipids in bile. Oral administration of chenodeoxycholic acid also reduces the synthesis of cholesterol in the liver, while ursodeoxycholic acid reduces biliary cholesterol to other bile acids. The bile acids (but not the bile salts) also have a choleretic action, increasing the secretion of bile, when given by mouth.

Chenodeoxycholic acid and ursodeoxycholic acid are given by mouth in the management of cholesterol-rich gallstones (p.2409) in patients unsuited to, or unwilling to undergo, surgery. Ursodeoxycholic acid is also being studied in some liver disorders.

Preparations containing bile salts have been used to assist the emulsification of fats and absorption of fat-soluble vitamins in conditions in which there is a deficiency of bile in the gastroinestinal tract. Ox bile has also been used in the treatment of chronic constipation. Cholic acid is used for the treatment of inborn errors in primary bile synthesis.

Sodium cholate has been used for its spermicidal properties in barrier contraceptives.

Preparations

Proprietary Preparations (details are given in Part 3)

Chile: Desicol; Ger.: Cholecysmon†; Mex.: Virulizin; Rus.: Festal (Фестал); S.Afr.: Bilron†; Venez.: Hepa-Desicol.

Multi-ingredient: Arg. Bibol Leloup; Bil 13; Bilagol; Bilidren; Biliosan Compuesto†; Carbogasol Digestivo; Cascara Sagrada Bouzen†; Digesplen; Gastron Fuerte; Hepatalgina; Nilflux, Opobyl; Pankreon Compuesto†; Veracolate; Zimerol; Austral.: Digestaid: Enzyme; Lexat†; Austria: Arca-Enzym; Buccalin; Combizym Compositum; Dragees Neunzehn†; Helopanzym; intestinol; Silberne; Belg: Buccaline; Grains de Vals; Braz.: B-Vesli; Dasc; Emagrex†; Figatli; Jurubileno†; Nutrizim†; Canda.: Bicholate; Herbalax†; Laxative†; Protectaid; Chile: Combizym Compositum; Finz; Cambizym Compositum; Finz; Combizym Compositum; Finz; Combizym Compositum; Finz; Betopanbiline; Ger.: Combizym Compositum; Finz; Planga Compositum; Finz; Despetal; Planga: Combizym Compositum; India: Digeplex-T; Dispeptal†; Parizym; Ipental†; Merckenzyme; Panolase†; Papytazyme; Indon.: Benozym; Berzymplex; Cotazym Forte; Enzymfort; Enzyplex; Enzyplex; Mex.: Dirfaben†; Dixiflen; Espaven Enzimatico; Ochozim; Onoton; Zimeton; NZ; Buccaline; Port.: Byl†; Caroid†; Combizym Compositum; Fremetone Composto; Rus.: Ipental (Илентал); Singapore: Enzyplex; Spain: Menabil Compolex†; Swed.: Combizym Compositum; Swed.: Combizym Compositum; Enzyplex; Papytazyme; Veracolate; Turk.: Flaton; Intestinol; Multanzim; Pankrodigest; UK: Protectaid; USA: Digespespin; Venze.: Combizym Forte; Nutizym Compositum; Pankreon Compositum; Stamyl.

Birch Leaf

Abedul, hojas de; Beržų lapai; Betulae folium; Birkenblätter; Björkblad; Bouleau; Bouleau, feuille de; Březový list; Koivunlehti; Liść brzozy; Nyírfalevél; Silver Birch Leaf.

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

Ph. Eur. 6.2 (Birch Leaf). The whole or fragmented dried leaves of *Betula pendula* and/or *B. pubescens* as well as hybrids of both species. It contains not less than 1.5% of flavonoids, calculated as hyperoside ($C_{21}H_{20}O_{12}=464.4$), with reference to the dried drug. Protect from light.

Profile

Birch leaf is used in herbal medicine, particularly for urinary-tract disorders. Birch leaf oil has also been used.

Preparations

Proprietary Preparations (details are given in Part 3) **Ger.:** Urorenal†.

Multi-ingredient: Arg.: Sequals G; Austral.: Guaiacum Complext; Austria: Blasentee St. Sevenn; Heumann's Blasen- und Nierentee; Rheuma; Sobitat; Cz.: Abfuhr-Heilkrautertee†; Blasen- und Nierentee†; Cajova Smes pri Redukcni Diete†; Fytokliman Planta; Nephrosal†; Reduktan; Senalax; Species Dirueticae Planta†; Species Unologicae Planta; Stoffwechseltee N†; Urologicka Cajova Smes; Fr.: B.O.P.; Depuratum; Drainactil; Mediflor no II Draineur Renal et Digestif†; Mediflor Tisane Antirhumatismale No 2; Ger.: Antihypertonicum S; BioCyst, Canephron novo†; Cystinol N; Dr Wiemanns Rheumatonikum; Dr. Scheffler Bergischer Krautertee Blasen- und Nierentee Heumann Blasen- und Nierentee Solubitrat S†; Heumann Blasen- und Nierentee Solubitrat uro; Hevert-Blasen-Nieren-Tee N; Heweberberol-Tee; Nephron-Rasc;†; Nephronom med†; Nephropur tri†; Nephroselect M; Nephrubin-N†; Nierentee 2000†; Nieron Blasen- und Nierentee; Urodi phyto†; Nach: Betulla (Specie Composta)†; Gramigna (Specie Composta)†; Lipaver, Listerine Fresh Citrus; Listerine Tartar Control; Pol.: Betasol; Diabetofort; Herbaton; Nefrobonisoi; NeoFitolizyna; Urosept, Rus.: Herbion Urological