4. Akpolat I, *et al.* Acute renal failure due to overdose of colloidal bismuth. *Nephrol Dial Transplant* 1996; **11:** 1890–8.
5. İşlek İ, *et al.* Reversible nephrotoxicity after overdose of colloidal bismuth subcitrate. *Pediatr Nephrol* 2001; **16:** 510–14.
6. Hruz P, *et al.* Fanconi's syndrome, acute renal failure, and tonsil ulcerations after colloidal bismuth subcitrate intoxication. *Am J Kidney Dis* 2002; **39:** E18.
7. Playford RJ, *et al.* Bismuth induced encephalopathy caused by tri potassium dicitrato bismuthate in a patient with chronic renal failure. *Gut* 1990; **31:** 359–60.
8. Hasking GJ, Duggan JM. Encephalopathy from bismuth subsalicylate. *Med J Aust* 1982; **2:** 167.
9. Mendelowitz PC, *et al.* Bismuth absorption and myoclonic encephalopathy during bismuth subsalicylate therapy. *Ann Intern Med* 1990; **112:** 140–1.
10. Vernace MA, *et al.* Chronic salicylate toxicity due to consumption of over-the-counter bismuth subsalicylate. *Am J Med* 1994; **97:** 308–9.

Toxicity from non-conventional use. The FDA has warned against use of an injectable product called bismacine or chromacine, which contains large amounts of bismuth. There are reports of death or serious adverse effects associated with its use. Although unlicensed for any use, bismacine has apparently been used in alternative medicine to treat Lyme disease.[1]

1. FDA. FDA warns consumers and health care providers not to use bismacine, also known as chromacine (issued 21st July 2006). Available at: http://www.fda.gov/bbs/topics/NEWS/2006/NEW01415.html (accessed 28/01/08)

Interactions

Bismuth salts given orally reduce the absorption of tetracyclines, possibly by chelation or by reducing tetracycline solubility as a result of increasing the gastric pH. This interaction can be minimised by separating doses of the two drugs by a couple of hours. The clinical significance of this interaction to the use of bismuth salts for peptic ulcer disease is unclear; tripotassium dicitratobismuthate or bismuth salicylate have been given at the same time as tetracycline as part of triple therapy for the eradication of *Helicobacter pylori*.

Antisecretory drugs. Pretreatment with *omeprazole* resulted in about a threefold increase in absorption of bismuth from tripotassium dicitratobismuthate in 6 healthy subjects.[1] The mean peak plasma concentration of bismuth after a single dose of 240 mg of tripotassium dicitratobismuthate was increased from 36.7 to 86.7 nanograms/mL after omeprazole suggesting an increased risk of toxicity from combined therapy. The mechanism was thought to be the increase in gastric pH produced by the antisecretory drug as similar results had been reported with *ranitidine*.[2] However, the clinical significance of these interactions to the use of antisecretory drugs with bismuth compounds for eradication of *Helicobacter pylori* is unclear; bismuth compounds have been combined with proton pump inhibitors or H_2 antagonists in short-term regimens as part of triple or quadruple therapy.

1. Treiber G, *et al.* Omeprazole-induced increase in the absorption of bismuth from tripotassium dicitrato bismuthate. *Clin Pharmacol Ther* 1994; **55:** 486–91.
2. Nwokolo CU, *et al.* The effect of histamine H -receptor blockade on bismuth absorption from three ulcer-healing compounds. *Gastroenterology* 1991; **101:** 889–94.

Pharmacokinetics

Poorly soluble bismuth compounds are largely converted to insoluble bismuth oxide, hydroxide, and oxychloride in the acidic environment of the stomach. Most of the bismuth compounds included in this monograph are thus only slightly absorbed. Increased gastric pH may increase bismuth absorption—see Antisecretory Drugs, above. Unabsorbed bismuth is excreted in the faeces. Absorbed bismuth is distributed throughout body tissues, including bone, and is slowly excreted in the urine and bile. It has a plasma half-life of about 5 days and continues to be excreted for about 12 weeks after stopping therapy.

◊ References.

1. Nwokolo CU, *et al.* The absorption of bismuth from oral doses of tripotassium dicitrato bismuthate. *Aliment Pharmacol Ther* 1989; **3:** 29–39.
2. Froomes PRA, *et al.* Absorption and elimination of bismuth from oral doses of tripotassium dicitrato bismuthate. *Eur J Clin Pharmacol* 1989; **37:** 533–6.
3. Lacey LF, *et al.* Comparative pharmacokinetics of bismuth from ranitidine bismuth citrate (GR122311X), a novel anti-ulcerant and tripotassium dicitrato bismuthate (TDB). *Eur J Clin Pharmacol* 1994; **47:** 177–80.

Uses and Administration

Some insoluble salts of bismuth are given orally for their supposed antacid action and for their mildly astringent action in various gastrointestinal disorders, including diarrhoea (p.1694) and dyspepsia (p.1695). Such salts include the aluminate, salicylate, subcarbonate, and subnitrate. Bismuth salicylate, which is given as an antidiarrhoeal and weak antacid in doses up to about 4 g daily in divided doses, possesses in addition the properties of the salicylates.

Tripotassium dicitratobismuthate is active against *Helicobacter pylori* and has been used as triple therapy (with metronidazole and either tetracycline or amoxicillin) to eradicate this organism and thereby prevent relapse of duodenal ulcer. It is also used as a mucosal protectant for the treatment of peptic ulcer disease (p.1702). Bismuth subcitrate potassium and bismuth salicylate are also active against *H. pylori* and have been used similarly in eradication regimens.

The usual oral dose of tripotassium dicitratobismuthate in benign gastric and duodenal ulceration is 240 mg twice daily, or 120 mg four times daily before food. Treatment is for a period of 4 weeks, extended to 8 weeks if necessary. Maintenance therapy with tripotassium dicitratobismuthate is not recommended although treatment may be repeated after a drug-free interval of one month. When used as part of triple therapy the usual dose of tripotassium dicitratobismuthate has been 120 mg four times daily for 2 weeks. The usual dose of bismuth salicylate as part of triple therapy is 525 mg four times daily for 2 weeks. Appropriate antisecretory treatment with a histamine H_2-antagonist or a proton pump inhibitor is usually added to these regimens.

A complex of bismuth citrate with ranitidine, ranitidine bismuth citrate (p.1768), is also used in the treatment of peptic ulcer disease.

Some insoluble salts of bismuth have been used topically in the treatment of skin disorders, wounds, and burns. Some have been used as ingredients of ointments or suppositories (sometimes containing more than one bismuth salt) in the treatment of haemorrhoids and other anorectal disorders (p.1697). Bismuth compounds that have been used topically and/or rectally include the oxide, subgallate, and subnitrate; bismuth resorcinol compounds have also been used. For the use of bismuth subnitrate and iodoform paste as a wound dressing, see Iodoform, p.1650.

Numerous other salts and compounds of bismuth have been promoted for various therapeutic purposes. Glycobiarsol was formerly given orally as an amoebicide.

Homoeopathy. Bismuth has been used in homoeopathic medicines under the following names: Bismuthum; Bismutum metallicum.

Bismuth oxide has been used in homoeopathic medicines under the following names: Bismuthum oxydatum; Bis. ox.

Bismuth subnitrate has been used in homoeopathic medicines under the following names: Heavy bismuth subnitrate; Bismuthi subnitras ponderosus; Bismutum subnitricum; Bism. sub.

Preparations

BPC 1954: Bismuth Subnitrate and Iodoform Paste;
USP 31: Bismuth Subsalicylate Magma; Bismuth Subsalicylate Oral Suspension; Bismuth Subsalicylate Tablets; Compound Resorcinol Ointment; Milk of Bismuth.

Proprietary Preparations (details are given in Part 3)
Arg.: Re-Dux; Sesamoil; ***Braz.:*** Pepto-Bismol; Peptosan†; Peptulan; Senophile†; ***Canad.:*** Bismed†; Maalox Multi-action; Neo-Laryngobis; Pepto-Bismol; Personnel; ***Cz.:*** De-Nol†; Jatrox†; ***Fr.:*** Amygdorectol†; ***Ger.:*** Angass S†; Dermatol†; Haemo-Exhirud Bufexamac; Katulcin-R†; Stryphnasal N; Telen†; Ulkowis†; ***Gr.:*** De-Nol; ***Hong Kong:*** De-Nol; ***Hung.:*** De-Nol†; ***India:*** Trymo; ***Indon.:*** Scantoma; ***Irl.:*** De-Noltab†; ***Israel:*** Kalbeten; Pink Bismuth; ***Ital.:*** De-Nol; ***Mex.:*** Biselic†; Bismed; Bismofarma; Bisval; Facidmol; Itamol; Pepto-Bismol; Siparox; Sucrato; ***Neth.:*** De-Nol; ***NZ:*** De-Nol; ***Port.:*** De-Nol†; ***Rus.:*** De-Nol (Де-Нол); ***S.Afr.:*** De-Nol; ***Singapore:*** De-Nol; ***Spain:*** Gastrodenol; Rectamigdol; ***Switz.:*** Amygdorectol; ***Thai.:*** Gastro-Bismol; ***Turk.:*** De-Nol; Dermatol; ***UK:*** De-Noltab; Pepto-Bismol; ***USA:*** Bismatrol; Children's Kaopectate; Devrom; K-Pek†; Kao-Tin; Kaopectate; Kapectolin; Maalox Total Stomach Relief; Peptic Relief; Pepto-Bismol; ***Venez.:*** Pepto-Bismol†.

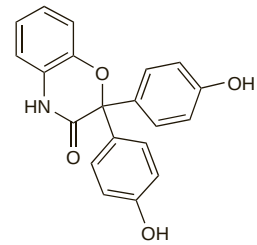
Multi-ingredient: ***Arg.:*** Anusol; Anusol Duo S; Benitol; Bismuto con Pectina; Colistop; Colistoral†; Crema De Bismuto; Cutidermin†; Gastop; Gastranil†; Gastricur; Histidanol†; Lemil; Mabis; ***Belg.:*** Gastrofilm†; Procto-Synalar; Rectovasol; ***Braz.:*** Aftine; Anusol-HC; Bismu-Jet; Bisuisan†; Claudemor; Colutoide; Cutisanol; Magnesia Bisurada; Neoseptil†; Salicilato de Bismuto Composto†; Senophile†; ***Canad.:*** Bismutal; Onrectal; Pepto-Bismol; Thunas Pile†; ***Cz.:*** Carbocit; Mastu S; Sagittaproct†; Spofax; Suspensio Visnevski cum Pice Liquida Herbacos; ***Fin.:*** Tannopon; ***Fr.:*** Anoreine; Anusol; Cutiphile†; Paps; Pholcones Bismuth; ***Ger.:*** Angass; Anisan†; Bismolan H Corti; Bismolan N†; Bismolan†; Combustin Heilsalbe; Duoventrin; Eulatin N; Eulatin NN; Faktu akut; Friosmin N†; Hamo-ratiopharm N; Hamoagil plus; Mastu S; Nervogastrol N†; Pascomag†; Spasmo-Nervogastrol†; Tamposit N†; Ventricon N; Vit-u-pept†; Wismut comp†; ***Hong Kong:*** Anusol; Anusol-HC†; Haemoral; Mastu S; Rowatanal; ***Hung.:*** Bolus Adstringens; Dermaforine†; Mastu S; Nilacid; ***Indon.:*** Anusol; Anusol-HC; ***Irl.:*** Anugesic-HC; Anusol; Anusol-HC; Rowatanal; ***Israel:*** Anusol†; Hemo; Rectozorin; Rekiv; ***Ital.:*** Antiemorroidali; Anusol; ***Malaysia:*** Rowatanal; ***Mex.:*** Estomacurol; Heliton; ***Neth.:*** Anaesthetica; Roteroblong Maagtabletten; Theranal; ***Pol.:*** Gastro; Hemorectal; ***Port.:*** Claudemor†; Servetinal†; Synalar Rectal; ***Rus.:*** Anaesthesol (Анестезол); Anusol (Анузол); Neo-Anusol (Нео-анузол); Proctosan (Проктозан); Simetrid (Симетрид); ***S.Afr.:*** Anugesic; Anusol; Arola Rosebalm; Biskapect; Bisma Rex†; Chloropect; Enterodyne; Kantrexil; Sentinel Ulcer Mixture; ***Singapore:*** Rowatanal; ***Spain:*** Grietalgen; Grietalgen Hidrocort†; Hemodren Compuesto†; Nasopomada; Pomada Infantil Vera†; Sabanotropico; Synalar Rectal; ***Switz.:*** Bismorectal; Cicafissan; Euproctol N; Fissan†; Furodermal; Haemocortin; Haemolan; La pommade du Dr Brand; Leucen; Magenpulver Hafter†; Magentabletten Hafter†; Rectoseptal-Neo bismuthe; ***Thai.:*** Anusol; Biodan†; Mastu S; Ulgastrin; ***Turk.:*** Dermikolin; Hemoralgine; Kortos; Metamorfoz; ***UK:*** Anugesic-HC; Anusol; Anusol-HC, Plus HC; Bisma-Rex; Hemocane; Moorland; OxBipp; Stomach Mixture; ***USA:*** Anumed; Anumed HC; BFI; Calmol; Heliadc; Hem-Prep; Hemril; K-C; Kao-Paverin; Kaodene Non-Narcotic; Mammol; Pylera; Rectagene Medicated Rectal Balm; ***Venez.:*** Claudemor†; Klincosal; Polantac.

Bisoxatin Acetate *(BANM, USAN, rINNM)*

Acetato de bisoxatina; Bisoxatin Diacetate; Bisoxatine, Acétate de; Bisoxatini Acetas; Wy-8138. 2,2-Bis(4-hydroxyphenyl)-1,4-benzoxazin-3(2*H*,4*H*)-one diacetate.

Бизоксатина Ацетат

$C_{24}H_{19}NO_6$ = 417.4.
CAS — 17692-24-9 (bisoxatin); 14008-48-1 (bisoxatin acetate).
ATC — A06AB09.
ATC Vet — QA06AB09.



(bisoxatin)

Profile

Bisoxatin acetate is a stimulant laxative that has been used in the treatment of constipation (p.1693).

Preparations

Proprietary Preparations (details are given in Part 3)
Belg.: Wylaxine; ***Venez.:*** Regoxal.

Bran

Crusca; Farelo; Kleie; Salvado; Son.

Отруби

Description. Bran consists of the fibrous outer layers of cereal grains. It contains celluloses, polysaccharides or hemicelluloses, protein, fat, minerals, and moisture and may contain part of the germ or embryo. Bran provides water-insoluble fibre and, depending on the source, may also provide water-soluble fibre (see also Dietary Role, below). It comprises about 12% of the weight of the grain and is a byproduct of flour milling. It is available in various grades.

Pharmacopoeias. *US* includes wheat bran.
USP 31 (Wheat Bran). The outer fraction of the cereal grain (comprising the pericarp, seed coat (testa), nucellar tissue, and aleurone layer) derived from *Triticum aestivum*, *T. compactum*, *T. durum*, or other common einkorn and emmer wheat cultivars. It is obtained by milling and processing the whole wheat grain, and is available in a variety of particle sizes depending on the degree of milling. It contains not less than 36% of dietary fibre. It is a light tan powder having a characteristic aroma. Practically insoluble in cold water and in alcohol.

Adverse Effects

Large quantities of bran may temporarily increase flatulence and abdominal distension, and intestinal obstruction may occur rarely.

Colonic atony. Colonic atony has been reported in patients who had increased their intake of dietary fibre to relieve constipation associated with systemic sclerosis.[1]

1. Gough A, *et al.* Dietary advice in systemic sclerosis: the dangers of a high fibre diet. *Ann Rheum Dis* 1998; **57:** 641–2.