Phenolphthalein *(BAN, rINN)*

Dihydroxyphthalophenone; Fenolftalein; Fenolftaleína; Fenolftaleinas; Fenoliftaleiini; Fenoloftaleina; Phénolphtaléine; Phenolphtaleinum; Phenolphthaleinum. 3,3-Bis(4-hydroxyphenyl)-phthalide.

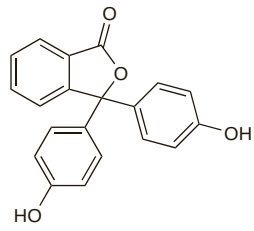
Фенолфталеин

$C_{20}H_{14}O_4$ = 318.3.

CAS — 77-09-8.

ATC — A06AB04.

ATC Vet — QA06AB04.



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

Ph. Eur. 6.2 (Phenolphthalein). A white or almost white powder. Practically insoluble in water; soluble in alcohol. Protect from light.

Adverse Effects and Precautions

As for Bisacodyl, p.1710. Hypersensitivity reactions, usually as skin rashes or eruptions, have occurred with phenolphthalein. Phenolphthalein may cause pink discoloration of alkaline urine.

Tumours have occurred in *rats* and *mice* given very high doses of phenolphthalein; there does not appear to be evidence of carcinogenicity in humans, but phenolphthalein-containing products have been withdrawn in many countries because of concerns about long-term safety.

Effects on the skin. Reports of skin reactions associated with phenolphthalein include fixed drug eruptions,[1,2] erythema multiforme reactions,[1,3] and toxic epidermal necrolysis.[4,5]

1. Baer RL, Harris H. Types of cutaneous reactions to drugs. *JAMA* 1967; **202:** 710–13.
2. Savin JA. Current causes of fixed drug eruptions. *Br J Dermatol* 1970; **83:** 546–9.
3. Shelley WB, *et al.* Demonstration of intercellular immunofluorescence and epidermal hysteresis in bullous fixed drug eruption due to phenolphthalein. *Br J Dermatol* 1972; **86:** 118–25.
4. Kar PK, *et al.* Toxic epidermal necrolysis in a patient induced by phenolphthalein. *J Indian Med Assoc* 1986; **84:** 189–93.
5. Artymowicz RJ, *et al.* Phenolphthalein-induced toxic epidermal necrolysis. *Ann Pharmacother* 1997; **31:** 1157–9.

Overdosage. The most likely consequence of phenolphthalein overdosage is excessive purgation, which may require fluid and electrolyte replacement. However, a possible association with acute pancreatitis occurred in a 34-year-old man who inadvertently ingested phenolphthalein 2 g. There was complete recovery with no sequelae from the pancreatitis.[1] Widespread organ failure with disseminated intravascular coagulation, massive liver damage, pulmonary oedema, renal failure, and myocardial damage in a second patient[2] were attributed to self-poisoning with an unknown quantity of phenolphthalein-containing laxative, although the diagnosis was problematic. The patient died despite intensive support.

1. Lambrianides AL, Rosin RD. Acute pancreatitis complicating excessive intake of phenolphthalein. *Postgrad Med J* 1984; **60:** 491–2.
2. Sidhu PS, *et al.* Fatal phenolphthalein poisoning with fulminant hepatic failure and disseminated intravascular coagulation. *Hum Toxicol* 1989; **8:** 381–4.

Pharmacokinetics

Up to 15% of phenolphthalein given orally is subsequently excreted in the urine. Enterohepatic circulation occurs and the glucuronide is excreted in the bile. Elimination may take several days.

Uses and Administration

Phenolphthalein is a diphenylmethane stimulant laxative that has been used for the treatment of constipation (p.1693) and for bowel evacuation before investigational procedures or surgery. It has been withdrawn in many countries because of concern over its carcinogenic potential after reports of tumours in *rodents*.

It has been given in pills or tablets, and as an emulsion with liquid paraffin. Yellow phenolphthalein, an impure form, has been used similarly.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Fructines; ***Chile:*** Felaxen†; ***Cz.:*** Confetto Falqui†; ***Israel:*** Easylax; ***S.Afr.:*** Brooklax; Dr Mackenzies Veinoids; Laxador; Laxene; Laxicaps P†; SB Strong-Lax; Super-Tabs; Surge; ***Singapore:*** Regulim†; ***Switz.:*** Reguletts; ***Thai.:*** Purmolax†; Regulim; ***Turk.:*** Alin; Laksafenol; ***Venez.:*** Agarolax†.

Multi-ingredient: ***Arg.:*** Cascara Sagrada Bouzen†; Cascara Sagrada Puler†; Genolaxante; Veracolate; ***Austral.:*** Ford Pills; ***Austria:*** Waldheim Abfuhrdragees forte; ***Belg.:*** Grains de Vals; ***Braz.:*** Emagrex†; Fenogar†; Manolio†; Obesidex†; Obesifran†; Prisoventril†; ***Chile:*** Agarol; Bulgarolax; Fenokomp 39; Fenolftaleina Compuesta†; Oblax A-1-1; ***Ger.:*** Vencipon N†; ***Hung.:*** Artin†; Bilagit†; ***India:*** Agarol†; Jetomisol-P; ***Indon.:*** Laxadine; ***Israel:*** Laxative; Laxative Comp; ***Port.:*** Byl†; Caroid†; ***S.Afr.:*** Brooklax Pills; Redupon†; SB 3 Triple Action Pills; Veracolate†; ***Spain:*** Laxante Bescansa Aloico; Mahiou†; ***Switz.:*** Paragar; ***Thai.:*** Emulax; Veracolate; Zenda†; ***Turk.:*** Karboseptin; Musilaks; ***UK:*** Fam-Lax; ***USA:*** Agoral; Doxidan†; ***Venez.:*** Agarol†.

Pipenzolate Bromide *(BAN, rINN)*

Bromuro de pipenzolato; Pipenzolat Bromür; Pipenzolate, Bromure de; Pipenzolate Methylbromide; Pipenzolati Bromidum. 3-Benziloyloxy-1-ethyl-1-methylpiperidinium bromide.

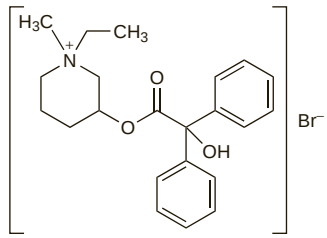
Пипензолата Бромид

$C_{22}H_{28}BrNO_3$ = 434.4.

CAS — 13473-38-6 (pipenzolate); 125-51-9 (pipenzolate bromide).

ATC — A03AB14.

ATC Vet — QA03AB14.



Profile

Pipenzolate bromide is a quaternary ammonium antimuscarinic with peripheral actions similar to those of atropine (p.1219). It has been used as an adjunct in the treatment of gastrointestinal disorders characterised by smooth muscle spasm.

Preparations

Proprietary Preparations (details are given in Part 3)
Ger.: Ila-med m; ***Mex.:*** Expal; Pipzen; ***Turk.:*** Piptalin.

Multi-ingredient: ***Chile:*** Baldmin; Gasorbol; Sinpasmon; ***Indon.:*** Piptal; ***Mex.:*** Espasal; Espasin†; Expal Compuesto; Finprob; ***Turk.:*** Asilon; Libkol; ***UAE:*** Alinal†.

Piperidolate Hydrochloride *(BANM, rINNM)*

Hidrocloruro de piperidolato; Pipéridolate, Chlorhydrate de; Piperidolati Hydrochloridum. 1-Ethyl-3-piperidyl diphenylacetate hydrochloride.

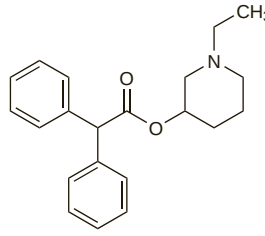
Пиперидолата Гидрохлорид

$C_{21}H_{25}NO_2$,HCl = 359.9.

CAS — 82-98-4 (piperidolate); 129-77-1 (piperidolate hydrochloride).

ATC — A03AA30.

ATC Vet — QA03AA30.



(piperidolate)

Profile

Piperidolate hydrochloride is a tertiary amine antimuscarinic with effects similar to those of atropine (p.1219). It has been given in the symptomatic treatment of smooth muscle spasm associated with gastrointestinal disorders.

Preparations

Proprietary Preparations (details are given in Part 3)
Mex.: Dactil OB.

Multi-ingredient: ***Braz.:*** Dactil OB.

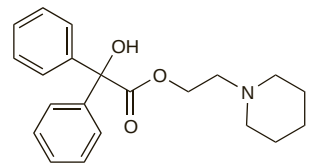
Pipethanate Ethobromide *(rINNM)*

Ethylpipethanate Bromide; Etobromuro de pipetanato; Piperilate Ethobromide; Pipéthanate, Ethobromure de; Pipethanati Ethobromidum. 1-(2-Benziloyloxyethyl)-1-ethylpiperidinium bromide.

Пипетаната Этобромид

$C_{23}H_{30}BrNO_3$ = 448.4.

CAS — 4546-39-8 (pipethanate); 23182-46-9 (pipethanate ethobromide).



(pipethanate)

Profile

Pipethanate ethobromide is an antimuscarinic with actions similar to those of atropine (p.1219). It has been used in the symptomatic treatment of visceral spasms in oral doses of up to 160 mg daily in divided doses. Pipethanate ethobromide has also been given intramuscularly or intravenously in doses of 10 to 20 mg daily and rectally in doses of 60 or 120 mg daily.

Preparations

Proprietary Preparations (details are given in Part 3)
Chile: Nospasmin; ***Ital.:*** Spasmodil; ***Jpn:*** Panpurol†.

Multi-ingredient: ***Chile:*** Nospasmin Compuesto.

Pirenzepine Hydrochloride *(BANM, USAN, rINNM)*

Hidrocloruro de pirenzepina; LS-519 (pirenzepine); LS-519-Cl2; Pirentsepiinidihydrokloridimonohydraatti; Pirenzepin-dihidrokloridmonohidrát; Pirenzepin-dihydrochlorid monohydrát; Pirenzepindihydrokloridmonohydrat; Pirenzépine, Chlorhydrate de; Pirenzépine (dichlorhydrate de) monohydraté; Pirenzepini dihydrochloridum monohydricum; Pirenzepini Hydrochloridum; Pirenzepino dihidrochloridas monohidratas. 5,11-Dihydro-11-(4-methylpiperazin-1-ylacetyl)pyrido[2,3-*b*][1,4]benzodiazepin-6-one dihydrochloride monohydrate.

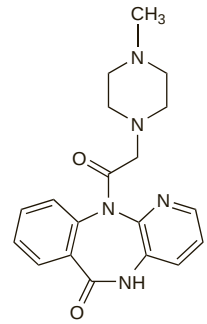
Пирензепина Гидрохлорид

$C_{19}H_{21}N_5O_2$,2HCl,H_2O = 442.3.

CAS — 28797-61-7 (pirenzepine); 29868-97-1 (pirenzepine hydrochloride).

ATC — A02BX03.

ATC Vet — QA02BX03.



(pirenzepine)

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

Ph. Eur. 6.2 (Pirenzepine Dihydrochloride Monohydrate; Pirenzepine Hydrochloride BP 2008). A white or yellowish crystalline powder. Freely soluble in water; very slightly soluble in dehydrated alcohol; practically insoluble in dichloromethane; slightly soluble in methyl alcohol. A 10% solution in water has a pH of 1.0 to 2.0. Protect from light.

Adverse Effects and Precautions

Dry mouth and blurred vision have been reported but the risk of antimuscarinic effects (see Atropine Sulfate, p.1219) may be reduced. Pirenzepine should be used with caution in patients with renal impairment, particularly those with end-stage renal failure.

Effects on the blood. Thrombocytopenia in one patient and agranulocytosis in another was probably associated with the use of pirenzepine.[1]

1. Stricker BHC, *et al.* Blood disorders associated with pirenzepine. *BMJ* 1986; **293:** 1074.

Interactions

As for antimuscarinics in general (see Atropine Sulfate, p.1220).

Pharmacokinetics

Pirenzepine is absorbed from the gastrointestinal tract but the bioavailability is reported to be only about 20 to 30%, and is decreased to about 10 to 20% when taken with food. Very little pirenzepine is metabolised. About 10% of an oral dose is excreted unchanged in the urine, the remainder being excreted in the faeces.

Pirenzepine has an elimination half-life of about 12 hours and is about 12% bound to plasma proteins. Diffusion across the blood-brain barrier is poor and only minimal amounts are present in breast milk.

Renal impairment. The renal clearance and total plasma clearance of pirenzepine may be significantly reduced in patients with renal impairment,[1,2] with clearance decreasing proportionately with the degree of renal impairment. The half-life of pirenzepine is increased with reported values ranging from 14 to 20 hours.[1-3] Plasma concentrations of pirenzepine may be reduced by up to about 50% during haemodialysis.[2,3]

1. Krakamp B, *et al.* Steady-state intravenous pharmacokinetics of pirenzepine in patients with hepatic insufficiency and combined renal- and hepatic insufficiency. *Eur J Clin Pharmacol* 1989; **36:** 71–3.
2. Krakamp B, *et al.* Steady-state intravenous pharmacokinetics of pirenzepine in patients with differing degrees of renal dysfunction. *Eur J Clin Pharmacol* 1989; **36:** 75–8.
3. MacGregor T, *et al.* Oral pharmacokinetics of pirenzepine in patients with chronic renal insufficiency, failure, and maintenance haemodialysis. *Eur J Clin Pharmacol* 1990; **38:** 405–6.

Uses and Administration

Pirenzepine is a selective M_1 tertiary amine antimuscarinic that displays a preferential action on the gastric mucosa thus causing a reduction in the secretion of gastric acid; it also reduces the secretion of pepsin. At therapeutic doses it has few other antimuscarinic actions.

Pirenzepine hydrochloride has been used in the management of peptic ulcer disease (p.1702) in a usual oral dose of 50 mg two or three times daily for 4 to 6 weeks. It has also been given by slow intravenous injection in doses of up to 60 mg daily.

Myopia. Pirenzepine ophthalmic gel has been investigated[1-3] in children for its potential in slowing the progression of myopia. In a study[3] involving 353 children with myopia, pirenzepine 2% gel given once or twice daily into the lower eyelid for 1 year was associated with reduced progression: at 12 months myopia had progressed by a mean of 0.7 and 0.47 dioptres in children assigned to once and twice daily dosage respectively, compared with 0.84 dioptres in those given placebo. The gel was generally well tolerated, the most frequent adverse effects being development of papillae or follicles, or abnormalities of accommodation such as mydriasis or cycloplegia. Of 55 patients who failed to complete the study, 31 did so as a result of adverse effects.

1. Bartlett JD, *et al.* A tolerability study of pirenzepine ophthalmic gel in myopic children. *J Ocul Pharmacol Ther* 2003; **19:** 271–9.
2. Siatkowski RM, *et al.* US Pirenzepine Study Group. Safety and efficacy of 2% pirenzepine ophthalmic gel in children with myopia: a 1-year, multicenter, double-masked, placebo-controlled parallel study. *Arch Ophthalmol* 2004; **122:** 1667–74.
3. Tan DTH, *et al.* Asian Pirenzepine Study Group. One-year multicenter, double-masked, placebo-controlled, parallel safety and efficacy study of 2% pirenzepine ophthalmic gel in children with myopia. *Ophthalmology* 2005; **112:** 84–91.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Droxol†; ***Austria:*** Gastrozepin; ***Cz.:*** Gastrozepin†; ***Ger.:*** Gastricur†; Gastrozepin; Ulcoprotect†; ***Gr.:*** Gastrozepin†; ***Ital.:*** Frazim†; Gastropiren; ***Jpn:*** Gastrozepin; ***Neth.:*** Gastrozepin†; ***Port.:*** Gastrozepina†; ***Rus.:*** Gastrozepin (Гастроцепин); ***Switz.:*** piren-basan†; ***Thai.:*** Cevanil†; ***Venez.:*** Ligeral†.

Multi-ingredient: ***Arg.:*** Duo Vizerul†.

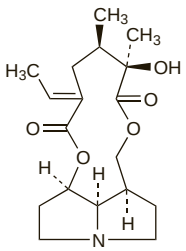
Platyphylline Acid Tartrate

Platyphylline Bitartrate; Platyphyllini Hydrotartras. 1,2-Dihydro-12-hydroxysenecionan-11,16-dione hydrogen tartrate.

Платифиллина Битартрат

$C_{18}H_{27}NO_5,C_4H_6O_6$ = 487.5.

CAS — 480-78-4 (platyphylline); 1257-59-6 (platyphylline acid tartrate).



(platyphylline)

Profile

Platyphylline acid tartrate is a pyrrolizidine alkaloid occurring in *Senecio platyphyllus* and other *Senecio* spp. It has antimuscarinic actions and has been given with papaverine in antispasmodic preparations.

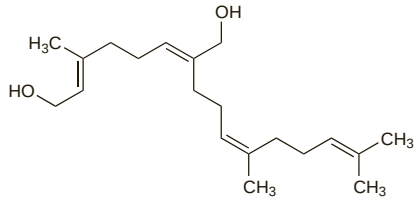
Plaunotol *(rINN)*

CS-684; Plaunotolum. (2*Z*,6*E*)-2-[(3*E*)-4,8-Dimethyl-3,7-nonadienyl]-6-methyl-2,6-octadiene-1,8-diol.

Плаунотол

$C_{20}H_{34}O_2$ = 306.5.

CAS — 64218-02-6.



Profile

Plaunotol is a complex aliphatic alcohol extracted from the Thai medicinal plant plau-noi (*Croton sublyratus* (Euphorbiaceae)). It is reported to possess cytoprotective properties and has been used in the treatment of gastritis and peptic ulcer disease in an oral dose of 80 mg three times daily.

Preparations

Proprietary Preparations (details are given in Part 3)

Jpn: Kelnac; ***Thai.:*** Kelnac.

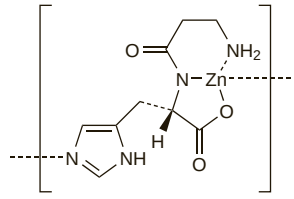
Polaprezinc *(rINN)*

Polaprézinc; Polaprezincum; Z-103; Zinc-L-carnosine. *catena*-Poly{zinc-μ-[β-alanyl-L-histidinato(2-)-*N*,N^N,*O*:N^τ]}.

Полапрезинк

$(C_9H_{12}N_4O_3Zn)_n$.

CAS — 107667-60-7.



Profile

Polaprezinc is a cytoprotective agent used in the treatment of peptic ulcer disease.

Poldine Metilsulfate *(BAN, pINN)*

IS-499; McN-R-726-47; Metilsulfato de poldina; Poldine Methosulphate; Poldine Methylsulfate *(USAN)*; Poldine Methylsulphate; Poldine, Métilsulfate de; Poldini Metilsulfas. (*RS*)-2-Benziloyloxymethyl-1,1-dimethylpyrrolidinium methylsulphate.

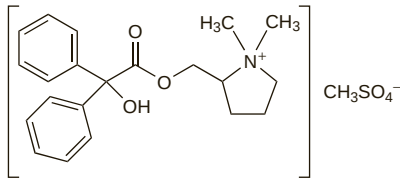
Польдина Метилсульфат

$C_{21}H_{26}NO_3,CH_3O_4S$ = 451.5.

CAS — 596-50-9 (poldine); 545-80-2 (poldine metilsulfate).

ATC — A03AB11.

ATC Vet — QA03AB11.



Pharmacopoeias. In *Br.*

BP 2008 (Poldine Metilsulfate). A white odourless or almost odourless crystalline powder. Freely soluble in water; soluble in alcohol; slightly soluble in chloroform. A 1% solution in water has a pH of 5.0 to 7.0.

Profile

Poldine metilsulfate is a quaternary ammonium antimuscarinic with peripheral actions similar to those of atropine (p.1219) and has been used in the management of gastrointestinal disorders, including peptic ulcer disease.

Preparations

BP 2008: Poldine Tablets.

Polycarbophil *(BAN, rINN)*

Policarbofilo; Polycarbophile; Polycarbophilum.

Поликарбофил

CAS — 9003-97-8.

Pharmacopoeias. In *US.*

USP 31 (Polycarbophil). It is polyacrylic acid cross-linked with divinyl glycol. White to creamy-white granules, with a characteristic, ester-like odour. Swells in water to a range of volumes, depending primarily on the pH. Insoluble in water, in common organic solvents, and in dilute acids and alkalis. A 1% mixture in water has a pH of not more than 4.0. Store in airtight containers.

Polycarbophil Calcium *(BANM, rINNM)*

AHR-3260B; Calcii Polycarbophilum; Calcium Polycarbophil *(USAN)*; Policarbofilo cálcico; Polycarbophile Calcique; Polycarbophilum Calcii; Polykarbofiilikalsium; Polykarbofilkalcium; Polykarbophilum Calcicum; WI-140.

Кальций Поликарбофил

CAS — 126040-58-2.

ATC — A06AC08.

ATC Vet — QA06AC08.

Pharmacopoeias. In *US.*

USP 31 (Calcium Polycarbophil). A white to creamy-white powder. Insoluble in water, in common organic solvents, and in dilute acids and alkalis. It loses not more than 10% of its weight on drying and contains not less than 18% and not more than 22% of calcium, calculated on the dried basis. Store in airtight containers.

Adverse Effects and Precautions

As for Ispaghula, p.1737. Polycarbophil calcium releases calcium ions in the gastrointestinal tract and should be avoided by patients who must restrict their calcium intake.

There is a risk of intestinal or oesophageal obstruction and faecal impaction, especially if such bulk laxatives are swallowed dry. Therefore, they should always be taken with sufficient fluid and should not be taken immediately before going to bed. They should be avoided by patients who have difficulty swallowing.

Interactions

The calcium component of polycarbophil calcium may produce interactions typical of calcium salts (p.1677), such as reducing the absorption of tetracyclines from the gastrointestinal tract; it should not be taken within 2 hours of the antibacterial. Polycarbophil calcium has also been reported to decrease the absorption of ciprofloxacin and mycophenolate mofetil.

Uses and Administration

Polycarbophil calcium has similar properties to ispaghula (p.1737) and is used as a bulk laxative and for adjusting faecal consistency. After ingestion calcium ions are replaced by hydrogen ions from gastric acid and the resultant polycarbophil exerts a hydrophilic effect in the intestines.

It is given orally in a usual dose equivalent to 1 g of polycarbophil up to four times daily, as necessary. Doses should be taken with at least 250 mL of water.

Polycarbophil is used topically as a vaginal moisturiser and as an ocular lubricant.

◊ References.

1. Danhof IE. Pharmacology, toxicology, clinical efficacy, and adverse effects of calcium polycarbophil, an enteral hydrosorptive agent. *Pharmacotherapy* 1982; **2:** 18–28.
2. Toskes PP, *et al.* Calcium polycarbophil compared with placebo in irritable bowel syndrome. *Aliment Pharmacol Ther* 1993; **7:** 87–92.
3. Chiba T, *et al.* Colonic transit, bowel movements, stool form, and abdominal pain in irritable bowel syndrome by treatments with calcium polycarbophil. *Hepatogastroenterology* 2005; **52:** 1416–20.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Fibercon†; ***Austral.:*** Replens; ***Austria:*** Fibercon†; ***Belg.:*** Replens†; ***Braz.:*** Muvinor; ***Canad.:*** Replens; ***Gr.:*** Fibercon†; ***Israel:*** Fibercon†; ***Ital.:*** Modula; Replens; ***Jpn:*** Colonel; ***Mex.:*** Fibercon†; ***Neth.:*** Fibercon†; ***Spain:*** Replens†; ***Swed.:*** Replens; ***Thai.:*** Fibercon†; ***USA:*** Equalactin; Fiber-Lax; Fibercon; FiberNorm; Replens.

Multi-ingredient: ***Ital.:*** Ormobyl CM†; ***USA:*** Aquasite†.