in the liver; the principal metabolite, dihydrolevobunolol, is reported to possess beta-blocking activity. The metabolites and some unchanged drug are excreted in the urine.

Uses and Administration

Levobunolol is a non-cardioselective beta blocker (p.1225). It is reported to lack intrinsic sympathomimetic activity and membrane-stabilising properties.

Levobunolol is used as the hydrochloride to reduce raised intra-ocular pressure in open-angle glaucoma and ocular hypertension (p.1873). It begins to act 1 hour after instillation with maximal effect seen between 2 and 6 hours; the effect may be maintained for up to 24 hours. Levobunolol hydrochloride is usually used as a 0.5% ophthalmic solution instilled once or twice daily; alternatively a 0.25% solution may be instilled twice daily.

Preparations

BP 2008: Levobunolol Eye Drops;
USP 31: Levobunolol Hydrochloride Ophthalmic Solution.

Proprietary Preparations (details are given in Part 3)
Arg.: Betagan; Levunolol; ***Austral.:*** Betagan; ***Austria:*** Vistagan; ***Belg.:*** Betagan; ***Braz.:*** B-Tablock; Betagan; ***Canad.:*** Betagan; Ophtho-Bunolol†; ***Chile:*** Betagen; ***Cz.:*** Vistagan; ***Denm.:*** Betagan; ***Fr.:*** Betagan; ***Ger.:*** Vistagan; ***Gr.:*** Pentila†; Vistagan; ***Hong Kong:*** Betagan; ***Hung.:*** Vistagan; ***Irl.:*** Betagan; ***Israel:*** Betagan; ***Ital.:*** Vistagan; ***Malaysia:*** Betagan†; ***Mex.:*** Betagan; ***Neth.:*** Betagan; ***NZ:*** Betagan; ***Port.:*** Betagan; ***S.Afr.:*** Betagan; ***Singapore:*** Betagan; ***Spain:*** Betagan; ***Switz.:*** Vistagan; ***Thai.:*** Betagan; ***Turk.:*** Betagan; ***UK:*** Betagan; ***USA:*** Ak-Beta; Betagan; ***Venez.:*** Vistagan.

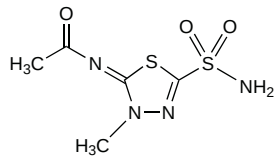
Multi-ingredient: ***Canad.:*** Probeta†.

Methazolamide *(BAN, rINN)* ⊗

Metazolamida; Méthazolamide; Methazolamidum. *N*-(4-Methyl-2-sulphamoyl-Δ^2-1,3,4-thiadiazolin-5-ylidene)acetamide.

Метазоламид

$C_5H_8N_4O_3S_2$ = 236.3.
CAS — 554-57-4.
ATC — S01EC05.
ATC Vet — QS01EC05.



Pharmacopoeias. In *US*.
USP 31 (Methazolamide). A white or faintly yellow crystalline powder with a slight odour. Very slightly soluble in water and in alcohol; slightly soluble in acetone; soluble in dimethylformamide. Protect from light.

Adverse Effects and Precautions

As for Acetazolamide, p.1875.

Hypersensitivity. Cholestatic hepatitis with jaundice, rash, and subsequent pure red cell aplasia was associated with methazolamide in a patient.[1] Drug-induced hypersensitivity was suspected as the cause of the reaction.

1. Krivoy N, *et al*. Methazolamide-induced hepatitis and pure RBC aplasia. *Arch Intern Med* 1981; **141:** 1229–30.

Pharmacokinetics

Methazolamide is absorbed from the gastrointestinal tract more slowly than acetazolamide. It has been reported not to be extensively bound to plasma protein, and to have a half-life of about 14 hours. About 15 to 30% of the dose is excreted in the urine; the fate of the remainder is unknown.

Uses and Administration

Methazolamide is an inhibitor of carbonic anhydrase with actions similar to those of acetazolamide (p.1876). It is used in the treatment of glaucoma (p.1873) in oral doses of 50 to 100 mg two or three times daily. Its action is less prompt but of longer duration than that of acetazolamide, lasting for 10 to 18 hours.

The diuretic activity of methazolamide is less pronounced than that of acetazolamide.

Preparations

USP 31: Methazolamide Tablets.

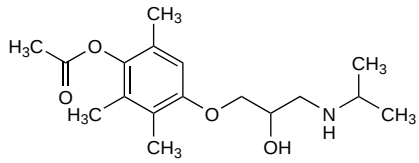
Proprietary Preparations (details are given in Part 3)
Arg.: Glaumetax†; ***Canad.:*** Neptazane†; ***Israel:*** Neptazane†; ***Thai.:*** Neptazane†; ***USA:*** GlaucTabs†; MZM†.

Metipranolol *(BAN, USAN, rINN)* ⊗

BMOI-004; Methypranolol; Métipranolol; Metipranololum; VUAB-6453 (SPOFA); VUFB-6453. 1-(4-Acetoxy-2,3,5-trimethylphenoxy)-3-isopropylaminopropan-2-ol; 4-(2-Hydroxy-3-isopropylaminopropoxy)-2,3,6-trimethylphenyl acetate.

Метипранолол

$C_{17}H_{27}NO_4$ = 309.4.
CAS — 22664-55-7.
ATC — S01ED04.
ATC Vet — QS01ED04.



NOTE. MPR is a code approved by the BP 2008 for use on single unit doses of eye drops containing metipranolol where the individual container may be too small to bear all the appropriate labelling information.

Pharmacopoeias. In *Br*.
BP 2008 (Metipranolol). A white crystalline powder. Practically insoluble in water; soluble in alcohol, in acetone, and in methyl alcohol; dissolves in dilute mineral acids. The filtrate of a 2.5% suspension in water has a pH of 9.0 to 10.0. Protect from light.

Adverse Effects, Treatment, and Precautions

As for Beta Blockers, p.1226.

Conjunctivitis, conjunctival leucoplakia, transient stinging, as well as other ocular adverse effects have been reported with metipranolol eye drops. Granulomatous anterior uveitis has been reported rarely; a high incidence reported in the UK may have been associated with changes induced by radiation sterilisation of metipranolol eye drops in their final container, but this preparation is no longer available.

Interactions

The interactions associated with beta blockers are discussed on p.1228.

Uses and Administration

Metipranolol is a non-cardioselective beta blocker (p.1225). It is reported to be largely lacking in intrinsic sympathomimetic activity and membrane-stabilising properties.

Metipranolol is used to reduce raised intra-ocular pressure in the management of open-angle glaucoma and ocular hypertension (p.1873). Eye drops usually containing metipranolol 0.1 or 0.3% are used twice daily.

Metipranolol has also been used by mouth in the management of cardiovascular disorders.

Preparations

BP 2008: Metipranolol Eye Drops.

Proprietary Preparations (details are given in Part 3)
Austria: Beta-Ophtiole; ***Belg.:*** Beta-Ophtiole; ***Cz.:*** Trimepranol; ***Ger.:*** Betamann; ***Ital.:*** Turoptin; ***Malaysia:*** Beta-Ophtiole†; ***Neth.:*** Beta-Ophtiole; ***Philipp.:*** Beta-Ophtiole; ***Pol.:*** Betamann; ***Port.:*** Beta-Ophtiole; ***S.Afr.:*** Beta-Ophtiole; ***Singapore:*** Beta-Ophtiole†; ***Switz.:*** Turoptin†; ***Thai.:*** Beta-Ophtiole†; ***Turk.:*** Turoptin; ***USA:*** OptiPranolol.

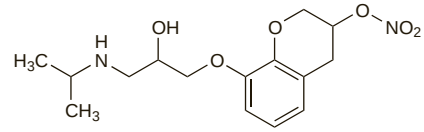
Multi-ingredient: ***Austria:*** Betacarpin; ***Belg.:*** Normoglaucon; ***Cz.:*** Trimecryton†; ***Ger.:*** Normoglaucon; Torrat†; Tri-Torrat†; ***Gr.:*** Beta Opthiole; Ripix†; ***Hong Kong:*** Torrat†; ***Ital.:*** Ripix; ***Malaysia:*** Normoglaucon†; ***Neth.:*** Normoglaucon; ***Pol.:*** Normoglaucon; ***Port.:*** Normoglaucon; ***Singapore:*** Normoglaucon†; ***Switz.:*** Ripix; ***Thai.:*** Normoglaucon†.

Nipradilol *(rINN)* ⊗

K-351; Nipradilolum; Nipradolol. 8-[2-Hydroxy-3-(isopropylamino)propoxy]-3-chromanol 3-nitrate.

Нипрадилол

$C_{15}H_{22}N_2O_6$ = 326.3.
CAS — 81486-22-8.



Profile

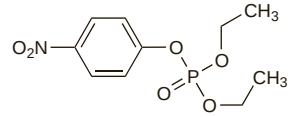
Nipradilol is a non-cardioselective beta blocker (p.1225). It is also reported to have direct vasodilating activity. It is used in the management of glaucoma and ocular hypertension (p.1873); eye drops containing nipradilol 0.05% are instilled twice daily.

Preparations

Proprietary Preparations (details are given in Part 3)
Jpn: Hypadil.

Paraoxon

E-600. Diethyl *p*-nitrophenyl phosphate.
$C_{10}H_{14}NO_6P$ = 275.2.
CAS — 311-45-5.
ATC — S01EB10.
ATC Vet — QS01EB10.



Profile

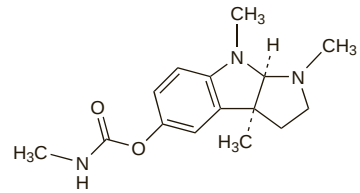
Paraoxon is a potent inhibitor of cholinesterase activity that has been used with other miotics in the treatment of glaucoma. It is the active metabolite of the organophosphorus insecticide parathion (p.2048) and therefore produces similar toxicity but with a faster onset.

Preparations

Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Ital.:*** Mios.

Physostigmine *(BAN)*

Eserine; Fisostigmina; Fysostigmiini; Fysostigmin; Physostigminum. (3a*S*,8a*R*)-1,2,3,3a,8,8a-Hexahydro-1,3a,8-trimethylpyrrolo[2,3-*b*]indol-5-yl methylcarbamate.
$C_{15}H_{21}N_3O_2$ = 275.3.
CAS — 57-47-6.
ATC — S01EB05; V03AB19.
ATC Vet — QA03AX90; QA03FA90; QS01EB05; QV03AB19.



Description. An alkaloid obtained from the calabar bean (ordeal bean; chopnut), the seed of *Physostigma venenosum* (Leguminosae).

Pharmacopoeias. In *US*.
USP 31 (Physostigmine). An alkaloid usually obtained from the dried ripe seed of *Physostigma venenosum* (Leguminosae). It is a white, odourless, microcrystalline powder which acquires a red tint on exposure to heat, light, or air, or on contact with traces of metals. M.p. not lower than 103°. Slightly soluble in water; freely soluble in alcohol; very soluble in chloroform and in dichloromethane; soluble in fixed oils and in benzene. Store in airtight containers. Protect from light.

Physostigmine Salicylate *(BANM)*

Eserine Salicylate; Ésérine, salicylate d'; Eserini salicylas; Ezerino salicilatas; Fisostigmina, salicilato de; Fizostigmino salicilatas; Fizostygminy salicylan; Fizosztigmin-szalicilát; Fysostigmiinisalisylaatti; Fysostigminsalicylat; Fysostigmin-salicylát; Physostig. Sal.; Physostigmine Monosalicylate; Physostigmini salicylas.
$C_{15}H_{21}N_3O_2,C_7H_6O_3$ = 413.5.
CAS — 57-64-7.
ATC — S01EB05; V03AB19.
ATC Vet — QS01EB05; QV03AB19.