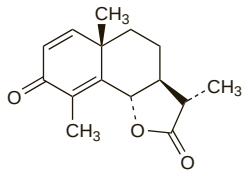
Santonin

Santoniini; Santonina; Santoninum. (3*S*,3a*S*,5a*S*,9b*S*)-3a,5,5a,9b-Tetrahydro-3,5a,9-trimethylnaphtho[1,2-*b*]furan-2,8(3*H*,4*H*)-dione.

Сантонин

$C_{15}H_{18}O_3$ = 246.3.

CAS — 481-06-1.



Pharmacopoeias. In *Jpn*.

Profile

Santonin is a crystalline lactone obtained from the dried unexpanded flowerheads of *Artemisia cina* (santonica, wormwood) and other species of *Artemisia* (Compositae). It was formerly used as an anthelmintic in the treatment of roundworm (*Ascaris*) infection, but has been superseded by other less toxic anthelmintics.

It is used as a flavour in food.

Selamectin *(USAN, rINN)*

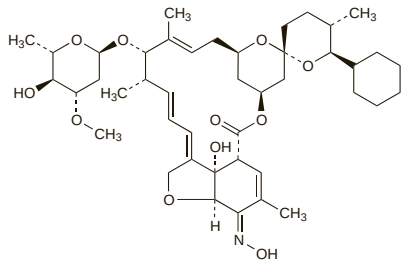
Selamectina; Sélamectine; Selamectinum; Selamektiini; Selamektin; UK-124114. (2a*E*,4*E*,5′*S*,6*S*,6′*S*,7*S*,8*E*,11*R*,13*R*,15*S*,17a*R*,20a*R*,20b*S*)-6′-Cyclohexyl-7-[(2,6-dideoxy-3-*O*-methyl-α-L-*arabino*-hexopyranosyl)oxy]-3′,4′,5′,6,6′,7,10,11,14,15,20a,20b-dodecahydro-20b-hydroxy-5′,6,8,19-tetramethylspiro(11,15-methano-2*H*,13*H*,17*H*-furo[4,3,2-*p*,*q*][2,6]benzodioxacyclooctadecin-13,2′-[2*H*]pyran)-17,20(17a*H*)-dione 20-oxime.

Селамектин

$C_{43}H_{63}NO_{11}$ = 770.0.

CAS — 165108-07-6.

ATC Vet — QP54AA05.



Pharmacopoeias. In *Eur.* (see p.vii) for veterinary use only.

Ph. Eur. 6.2 (Selamectin for Veterinary Use). A semi-synthetic product derived from a fermentation product. A white or almost white, hygroscopic powder. Practically insoluble in water; soluble in acetone and in dichloromethane; freely soluble in isopropyl alcohol; sparingly soluble in methyl alcohol. Store in airtight containers.

Profile

Selamectin is an avermectin anthelmintic and ectoparasiticide used in veterinary medicine.

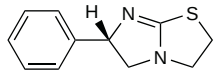
Tetramisole Hydrochloride *(BANM, USAN, rINNM)*

Hidrocloruro de tetramisol; ICI-50627; McN-JR-8299-11; R-8299; Tétramisole, Chlorhydrate de; Tetramisoli Hydrochloridum. (±)-2,3,5,6-Tetrahydro-6-phenylimidazo[2,1-*b*]thiazole hydrochloride.

Тетрамизола Гидрохлорид

$C_{11}H_{12}N_2S,HCl$ = 240.8.

CAS — 5036-02-2 (tetramisole); 5086-74-8 (tetramisole hydrochloride).



(tetramisole)

Pharmacopoeias. In *Fr.* for veterinary use only.

Profile

Tetramisole hydrochloride is an anthelmintic used in veterinary medicine for the control of nematode infections. It is a racemic mixture and the laevo-isomer, levamisole hydrochloride (p.147), accounts for most of its activity.

Preparations

Proprietary Preparations (details are given in Part 3)
Braz.: Ascarizole†; Tetramizotil†.

Multi-ingredient: ***India:*** Jetomisol-P.

Thiacetarsamide *(rINNM)*

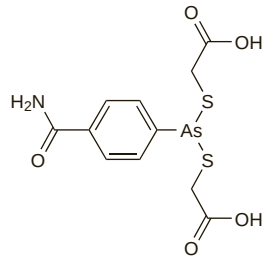
Thiacétarsamide; Thiacetarsamidum; Tiacetarsamida. *p*-[Bis(carboxymethylmercapto)arsino]benzamide; 4-Carbamylphenyl bis[carboxymethylthio]arsenite.

Тиацетарсамид

$C_{11}H_{12}AsNO_5S_2$ = 377.3.

CAS — 531-72-6.

ATC Vet — QP52AX08.



Profile

Thiacetarsamide is an anthelmintic used in veterinary medicine.

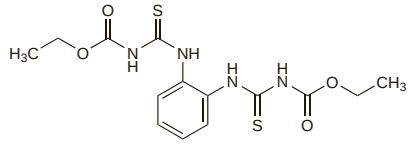
Thiophanate *(BAN)*

Tiofanato. 4,4′-*o*-Phenylenebis(ethyl 3-thioallophanate).

$C_{14}H_{18}N_4O_4S_2$ = 370.4.

CAS — 23564-06-9.

ATC Vet — QP52AC04.



Profile

Thiophanate is an anthelmintic used in veterinary medicine for the control of nematode infections.

Tiabendazole *(BAN, rINN)*

E233; MK-360; Thiabendazole *(USAN)*; Tiabendatsoli; Tiabendazol; Tiabendazolas; Tiabendazolum. 2-(Thiazol-4-yl)-1*H*-benzimidazole.

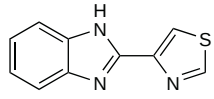
Тиабендазол

$C_{10}H_7N_3S$ = 201.2.

CAS — 148-79-8.

ATC — D01AC06; P02CA02.

ATC Vet — QD01AC06; QP52AC10.



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

Ph. Eur. 6.2 (Tiabendazole). A white or almost white crystalline powder. Practically insoluble in water; slightly soluble in alcohol and in dichloromethane; it dissolves in dilute mineral acids. Protect from light.

USP 31 (Thiabendazole). A white to practically white, odourless or practically odourless, powder. Practically insoluble in water; slightly soluble in alcohol and in acetone; very slightly soluble in chloroform and in ether.

Adverse Effects

Dizziness and gastrointestinal disturbances, especially anorexia, nausea and vomiting, diarrhoea, and abdominal pain are common during treatment with tiabendazole. Other adverse effects occurring occasionally include pruritus, skin rashes, headache, fatigue, drowsiness, drying of mucous membranes, hyperglycaemia, disturbance of vision including colour vision, leucopenia, tinnitus, effects on the liver including cholestasis and parenchymal damage (in some cases severe and irreversible), enuresis, crystalluria, and bradycardia and hypotension. There have also been reports of erythema multiforme, fatal Stevens-Johnson syndrome, toxic epidermal necrolysis, convulsions, and effects on mental state.

Fever, chills, angioedema, and lymphadenopathy have been reported, but may represent allergic response to dead parasites rather than to tiabendazole.

The urine of some patients taking tiabendazole may have a characteristic odour similar to that after eating asparagus; it is attributed to the presence of a tiabendazole metabolite.

Effects on the salivary glands. Dry mouth with swollen parotid and salivary glands suggestive of the sicca complex preceded the development of cholestatic jaundice in a 17-year-old boy given tiabendazole.[1]

1. Davidson RN, *et al.* Intrahepatic cholestasis after thiabendazole. *Trans R Soc Trop Med Hyg* 1988; **82:** 620.

Hypersensitivity. Severe erythema multiforme developed in a patient 16 days after a course of tiabendazole.[1] Many of the lesions encircled pre-existing melanocytic naevi.

1. Humphreys F, Cox NH. Thiabendazole-induced erythema multiforme with lesions around melanocytic naevi. *Br J Dermatol* 1988; **118:** 855–6.

Precautions

Tiabendazole should be used with caution in patients with hepatic or renal impairment. Tiabendazole causes drowsiness in some patients and those affected should not drive or operate machinery.

Tiabendazole should not be used in mixed worm infections involving *Ascaris lumbricoides* as it can cause these roundworms to migrate; live roundworms have emerged through the mouth or nose.

Pregnancy. Tiabendazole is teratogenic in *mice* although there are no adequate and well controlled studies in human pregnancy.

Renal impairment. Tiabendazole and its 5-hydroxy metabolite did not accumulate in an anephric patient on haemodialysis and haemoperfusion who was treated for severe strongyloidiasis.[1] However, the potentially toxic conjugated glucuronide and sulfate metabolites did accumulate. The clearance of all 3 metabolites was poor by haemodialysis; haemoperfusion was much more efficient, although for rapid removal the haemoperfusion columns should be changed every hour.

1. Bauer L, *et al.* The pharmacokinetics of thiabendazole and its metabolites in an anephric patient undergoing hemodialysis and hemoperfusion. *J Clin Pharmacol* 1982; **22:** 276–80.

Interactions

Xanthines. For the effect of tiabendazole on serum concentrations of *theophylline*, see p.1145.

Pharmacokinetics

Tiabendazole is readily absorbed from the gastrointestinal tract and reaches peak concentrations in the plasma after 1 to 2 hours. It is metabolised to 5-hydroxythiabendazole and excreted principally in the urine as glucuronide or sulfate conjugates; about 90% is recovered in the urine within 48 hours of ingestion, but only 5% in the faeces. Absorption may occur from preparations applied to the skin or eyes.

◊ References.

1. Tocco DJ, *et al.* Absorption, metabolism, and excretion of thiabendazole in man and laboratory animals. *Toxicol Appl Pharmacol* 1966; **9:** 31–9.

Uses and Administration

Tiabendazole, a benzimidazole derivative, is an anthelmintic with activity against most nematode worms; activity against some larval stages and ova has also been demonstrated. The mode of action is not certain, but tiabendazole may inhibit the fumarate-reductase system of worms thereby interfering with their source of energy.

Tiabendazole is used in the treatment of cutaneous larva migrans, dracunculiasis (guinea worm infection),

and toxocariasis. It may also be used in the treatment of strongyloidiasis, and can provide symptomatic relief during the larval invasion stage of trichinosis. Tiabendazole is also active against some intestinal nematodes, but should not be used as primary therapy; the treatment of mixed infections including ascariasis is not recommended since tiabendazole may cause the worms to migrate to other body organs causing serious complications. For discussions of the treatment of the above infections see under Choice of Anthelmintic, p.134, and under the individual headings below.

Tiabendazole is given orally, with meals, usually in a dose of 25 mg/kg twice daily for 2 or more days, the duration depending on the type of infection; the daily dose should not exceed 3 g. For those unable to tolerate 2 doses daily, 25 mg/kg may be given after the largest meal on day 1 and repeated 24 hours later after a similar meal on day 2. For mass treatment, a single dose of 50 mg/kg after the evening meal is suggested although the incidence of adverse effects may be higher than with 2 doses of 25 mg/kg.

In cutaneous larva migrans, 25 mg/kg may be given twice daily for 2 days, repeated after 2 days if necessary; topical treatment with a 10 to 15% suspension intended for oral use has also been advocated as an alternative or adjunct to oral treatment.

In dracunculiasis, 25 to 50 mg/kg may be given twice daily for one day; in massive infection a further 50 mg/kg may be given after 5 to 8 days.

In strongyloidiasis, 25 mg/kg may be given twice daily for 2 or 3 days or 50 mg/kg as a single dose; when the infection is disseminated treatment for at least 5 days may be necessary.

In trichinosis, 25 mg/kg may be given twice daily for 2 to 4 successive days.

In toxocariasis, 25 mg/kg may be given twice daily for 5 to 7 days.

Tiabendazole also has some antifungal activity. It is used as a fungicidal preservative for certain foods.

Dracunculiasis. Tiabendazole[1,2] may be used for symptomatic treatment of dracunculiasis (p.136), although it has no direct anthelmintic effect. It is used to facilitate removal of the worm from subcutaneous tissues.

1. Muller R. Guinea worm disease: epidemiology, control, and treatment. *Bull WHO* 1979; **57:** 683–9.
2. Kale OO, *et al.* Controlled comparative trial of thiabendazole and metronidazole in the treatment of dracontiasis. *Ann Trop Med Parasitol* 1983; **77:** 151–7.

Strongyloidiasis. Tiabendazole may be used in the treatment of strongyloidiasis (p.138), but albendazole or ivermectin are generally preferred.

References.

1. Grove DI. Treatment of strongyloidiasis with thiabendazole: an analysis of toxicity and effectiveness. *Trans R Soc Trop Med Hyg* 1982; **76:** 114–18.
2. Barnish G, Barker J. An intervention study using thiabendazole suspension against strongyloides fuelleborni-like infections in Papua New Guinea. *Trans R Soc Trop Med Hyg* 1987; **81:** 60–3.
3. Boken DJ, *et al.* Treatment of Strongyloides stercoralis hyperinfection syndrome with thiabendazole administered per rectum. *Clin Infect Dis* 1993; **16:** 123–6.
4. Gann PH, *et al.* A randomized trial of single- and two-dose ivermectin versus thiabendazole for treatment of strongyloidiasis. *J Infect Dis* 1994; **169:** 1076–9.
5. Pitisuttithum P, *et al.* A randomized comparative study of albendazole and thiabendazole in chronic strongyloidiasis. *Southeast Asian J Trop Med Public Health* 1995; **26:** 735–8.
6. Schaffel R, *et al.* Thiabendazole for the treatment of strongyloidiasis in patients with hematologic malignancies. *Clin Infect Dis* 2000; **31:** 821–2.

Syngamosis. Tiabendazole has been used successfully[1,2] to treat syngamosis (p.138) when it has occurred in man.

1. Grell GAC, *et al.* Syngamus in a West Indian. *BMJ* 1978; **2:** 1464.
2. Leers W-D, *et al.* Syngamosis, an unusual case of asthma: the first reported case in Canada. *Can Med Assoc J* 1985; **132:** 269–70.

Preparations

BP 2008: Tiabendazole Tablets;
USP 31: Thiabendazole Oral Suspension; Thiabendazole Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Foldan; ***Austral.:*** Mintezol; ***Braz.:*** Benzol†; Foldan; Thiaben†; Thianax; Tiabenzol†; Tiadol; Tiaplex; ***Chile:*** Soldrin; ***Gr.:*** Mintezol; ***Mex.:*** Eprofil; ***Spain:*** Triasox†; ***USA:*** Mintezol; ***Venez.:*** Drofen†.

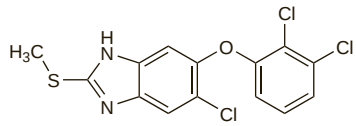
Multi-ingredient: ***Braz.:*** Derms; Eraverm-T†; Folderm Pomada; Forverm; Helmi-Ped†; Helmib†; Helmiben; Helmidrax†; Josverm†; Metiaben†; Micoplex; Neovermin; Octelmin†; Poliben†; Profium; Prohelmin†; Thiabena†; Vermilen Composto†; Vermol†; Zoles†.

Triclabendazole *(BAN, rINN)*

Triclabendazol; Triclabendazolum. 5-Chloro-6-(2,3-dichlorophenoxy)-2-(methylthio)benzimidazole.

Триклабендазол

$C_{14}H_9Cl_3N_2OS$ = 359.7.
CAS — 68786-66-3.
ATC — P02BX04.
ATC Vet — QP52AC01.



Profile

Triclabendazole is a benzimidazole anthelmintic used in veterinary medicine for the treatment of fascioliasis. It is also increasingly being used in the treatment of human fascioliasis, and is under investigation for the treatment of human paragonimiasis.

Liver fluke infections. Although bithionol or praziquantel are used to treat fascioliasis (p.137), some consider triclabendazole to be the drug of choice.[1] A suggested oral dose is 10 mg/kg, given as a single dose after food; the dose may be repeated once.[1] Several studies[2-7] have demonstrated the efficacy of triclabendazole in fascioliasis.

1. Abramowicz M, ed. *Drugs for parasitic infections.* 1st ed. New Rochelle NY: The Medical Letter, 2007.
2. Apt W, *et al.* Treatment of human chronic fascioliasis with triclabendazole: drug efficacy and serologic response. *Am J Trop Med Hyg* 1995; **52:** 532–5.
3. El-Karaksy H, *et al.* Human fascioliasis in Egyptian children: successful treatment with triclabendazole. *J Trop Pediatr* 1999; **45:** 135–8.
4. Millán JC, *et al.* The efficacy and tolerability of triclabendazole in Cuban patients with latent and chronic Fasciola hepatica infection. *Am J Trop Med Hyg* 2000; **63:** 264–9.
5. Graham CS, *et al.* Imported Fasciola hepatica infection in the United States and treatment with triclabendazole. *Clin Infect Dis* 2001; **33:** 1–5.
6. Talaie H, *et al.* Randomized trial of a single, double and triple dose of 10 mg/kg of a human formulation of triclabendazole in patients with fascioliasis. *Clin Exp Pharmacol Physiol* 2004; **31:** 777–82.
7. Marcos LA, *et al.* Natural history, clinicoradiologic correlates, and response to triclabendazole in acute massive fascioliasis. *Am J Trop Med Hyg* 2008; **78:** 222–7.

Lung fluke infections. Encouraging results were reported from a pilot study of triclabendazole[1] in the treatment of paragonimiasis (p.137). In an open comparative study[2] in 62 patients, a more rapid parasitological response was obtained with triclabendazole in oral doses of 5 mg/kg once daily for 3 days, 10 mg/kg twice on one day, or 10 mg/kg as a single dose, than with praziquantel. Clinical symptoms resolved at a comparable rate in all groups. A later study compared the two one-day regimens in 154 patients.[3] After 3 months, the cure rates (assessed by clearance of eggs from sputum) were 84.4% in those given a single dose of 10 mg/kg, and 90.9% in those given two such doses on the same day. In those who were still infected at 3 months, a second two-dose course resulted in complete parasitological clearance at 1 year.

1. Ripert C, *et al.* Therapeutic effect of triclabendazole in patients with paragonimiasis in Cameroon: a pilot study. *Trans R Soc Trop Med Hyg* 1992; **86:** 417.
2. Calvopiña M, *et al.* Treatment of human pulmonary paragonimiasis with triclabendazole: clinical tolerance and drug efficacy. *Trans R Soc Trop Med Hyg* 1998; **92:** 566–9.
3. Calvopiña M, *et al.* Comparison of two single-day regimens of triclabendazole for the treatment of human pulmonary paragonimiasis. *Trans R Soc Trop Med Hyg* 2003; **97:** 451–4.

Preparations

Proprietary Preparations (details are given in Part 3)
Fr.: Egaten.
