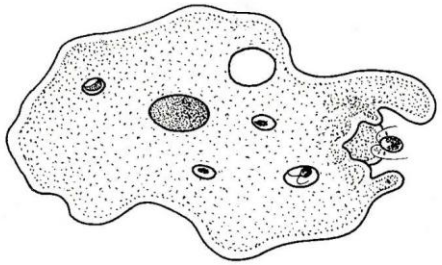
Amebiasis

Amebiasis is infection with ***Entamoeba histolytica***.



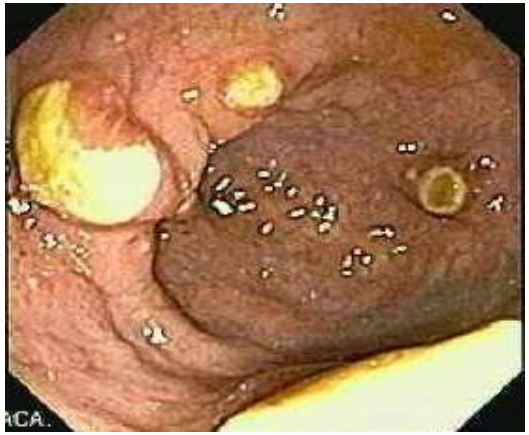
This organism can cause:

Asymptomatic intestinal infection.

Mild to moderate colitis.

Severe intestinal infection (dysentery).

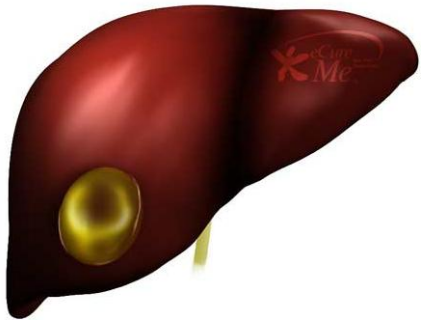
Ameboma (a tumor-like mass in the intestines in amebiasis which results in a large local lesion of the bowel).



Ameboma

Liver abscess and other extraintestinal infection.

The choice of drugs for amebiasis depends on the clinical presentation.



Treatment of Specific Forms of Amebiasis

Asymptomatic Intestinal Infection

Asymptomatic carriers are treated with a **luminal amebicide**.

Standard luminal amebicides are:

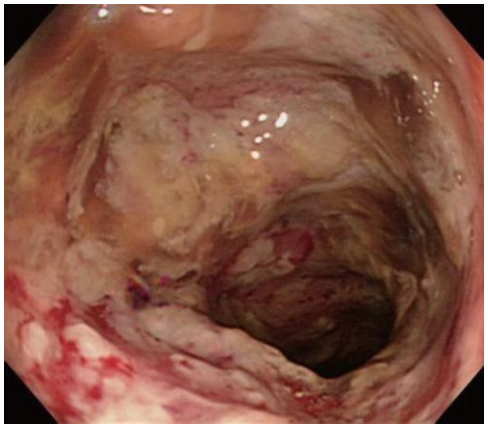
Diloxanide furoate, Iodoquinol, and Paromomycin.

Therapy with a luminal amebicide is also required in the treatment of all other forms of amebiasis.

Amebic Colitis

Metronidazole + a luminal amebicide is the treatment of choice.

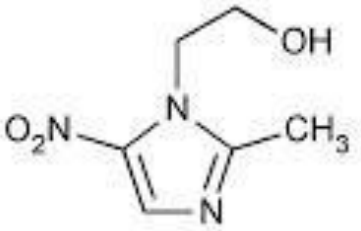
Tetracyclines and **erythromycin** are alternative drugs for moderate colitis but are not effective against extraintestinal disease.



Amebic Colitis

Dehydroemetine or emetine can also be used, but are best avoided because of toxicity.

Metronidazole

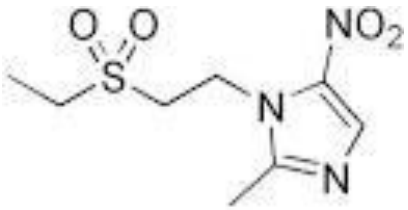


Drug of choice in the treatment of extraluminal amebiasis.

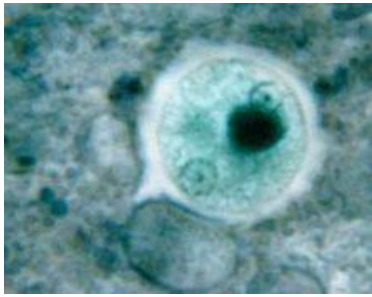
It kills trophozoites but not cysts of *E histolytica* and effectively eradicates intestinal & extraintestinal tissue infections.

Trophozoite of Entamoeba histolytica in intestine.

Tinidazole



Similar activity & better toxicity profile than metronidazole.



cysts of *E histolytica*

Pharmacokinetics & Mechanism of Action

Oral metronidazole and tinidazole are readily absorbed.

The half-life:

Metronidazole 7.5 hours

Tinidazole 12–14 hours.

The nitro group of metronidazole is chemically reduced in anaerobic bacteria and sensitive protozoans.

Reactive reduction products are responsible for antimicrobial activity.

The mechanism of tinidazole is assumed to be the same

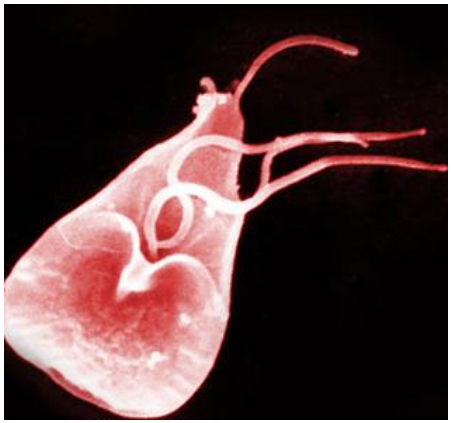
Clinical Uses

Amebiasis

Metronidazole or tinidazole

The drug of choice in the treatment of all tissue infections with *E histolytica*.

Neither drug is effective against luminal parasites and so **must be used with a luminal amebicide to ensure eradication of the infection**.



Giardiasis

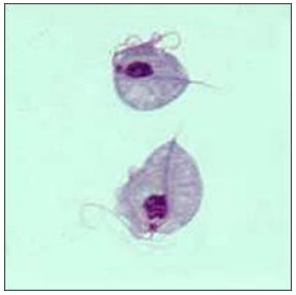
Metronidazole is the treatment of choice for giardiasis. Efficacy after a single treatment is about 90%.

Tinidazole is equally effective.

Trichomoniasis

Metronidazole is the treatment of choice.

A single dose of 2 g is effective.



Trichomonas vaginalis

Adverse Effects & Cautions

Common:

Nausea, headache, dry mouth, a metallic taste in the mouth occurs commonly.

Infrequent adverse effects:

vomiting, diarrhea, insomnia, weakness, dizziness, thrush, rash, dysuria, dark urine, vertigo, paresthesias, and neutropenia.

Rare:

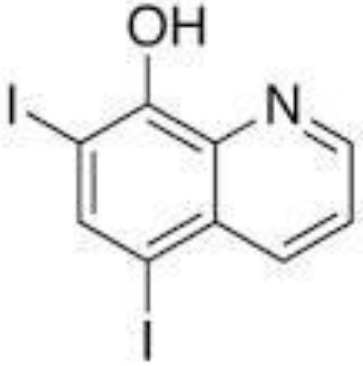
Pancreatitis and severe central nervous system toxicity (ataxia, encephalopathy, seizures)

Metronidazole has a disulfiram -like effect.

Tinidazole is better tolerated.

Metronidazole is best avoided in pregnant or nursing women, although congenital abnormalities have not clearly been associated with use in humans.

Iodoquinol



Luminal amebicide, but not against **trophozoites** in the intestinal wall or extraintestinal tissues.

90% is excreted in the feces.

<u>Infrequent adverse effects:</u>

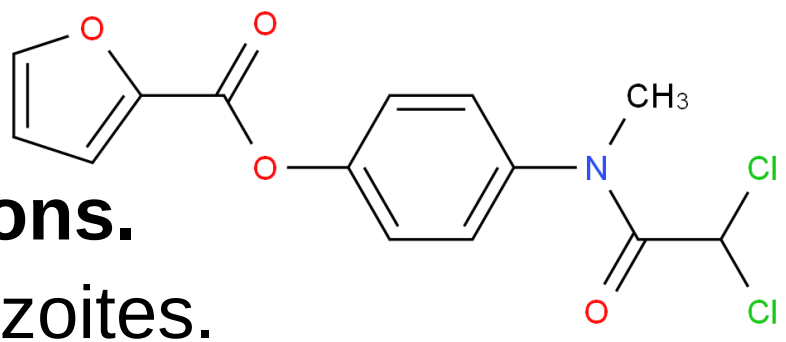
Diarrhea , anorexia, nausea, vomiting, abdominal pain, headache, rash, and pruritus.

Taken with meals to limit gastrointestinal toxicity.

Used with **caution** in patients with optic neuropathy, renal or thyroid disease, or nonamebic hepatic disease.

Should be discontinued if it produces persistent diarrhea or signs of iodine toxicity (dermatitis, urticaria, pruritus, fever).

Diloxanide Furoate

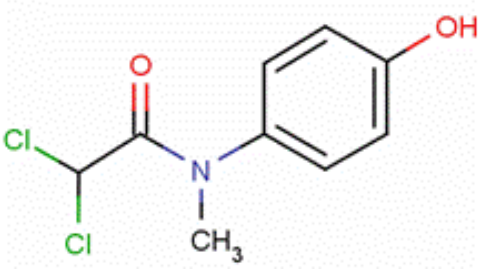


Drug of choice for

asymptomatic luminal infections.

Not active against tissue trophozoites.

In the gut, it splits into **diloxanide** and **furoic acid**; about 90% of the **diloxanide** is rapidly absorbed.



The **unabsorbed diloxanide** is the **active antiamebic**

The mechanism of action is unknown.

Used with a tissue amebicide, usually **metronidazole**, to treat serious intestinal & extraintestinal infections.

Adverse effects:

Flatulence is common, but nausea and abdominal cramps are infrequent and rashes are rare.

The drug is not recommended in pregnancy

Paromomycin Sulfate

Aminoglycoside antibiotic that is not absorbed from the gastrointestinal tract.

It is used only as a luminal amebicide and has no effect against extraintestinal amebic infections.

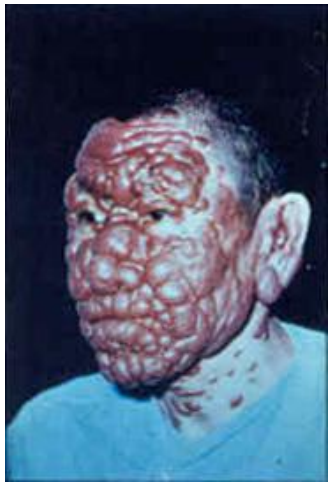
Adverse effects

Occasional abdominal distress & diarrhea.

Parenteral paromomycin is now used

to treat visceral leishmaniasis.

a sand fly



Post-kala-azar dermal leishmaniasis ,
a complication of visceral leishmaniasis.

Emetine & Dehydroemetine

Emetine, an alkaloid derived from **ipecac.**

Dehydroemetine, a synthetic analog.

Effective against **tissue trophozoites** of *E histolytica,*

Their use is limited to **severe amebiasis when metronidazole cannot be used.**

Used for the minimum period needed to relieve severe symptoms (3–5 days) and should be administered S.C. (preferred) or I.M.

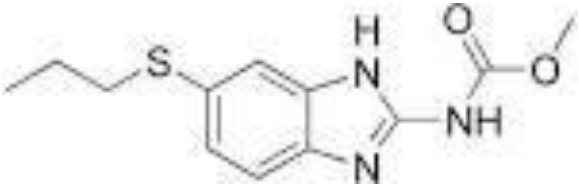
Adverse effects

Pain, tenderness, and sterile abscesses at the injection site; diarrhea, nausea, and vomiting; muscle weakness and discomfort.

Serious toxicities include cardiac arrhythmias, heart failure, and hypotension.

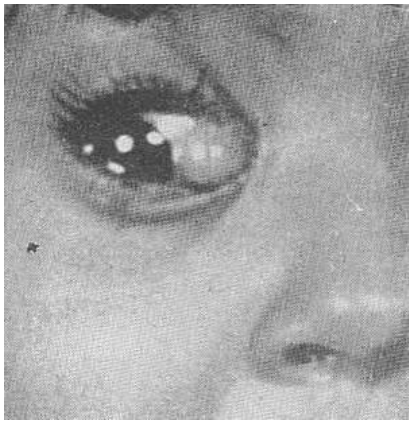
Antihelminthic Drugs

Albendazole



A broad-spectrum oral antihelminthic.

The drug of choice for **hydatid disease** (tapeworm cysts in vital organs) and **cysticercosis** (a tissue infection with the larval stage of the pork tapeworm).



Usually given with **corticosteroids** to decrease inflammation caused by dying organisms.

Erratically absorbed, first-pass metabolism in the liver to the **active metabolite albendazole sulfoxide.**

Acts by inhibiting microtubule synthesis.

Clinical Uses

Administered on an **empty stomach** when used against intraluminal parasites but **with a fatty meal** when used against tissue parasites.

It is also effective against: **Pinworm, Hookworm, Ascariasis, Trichuriasis, and Strongyloidiasis.**

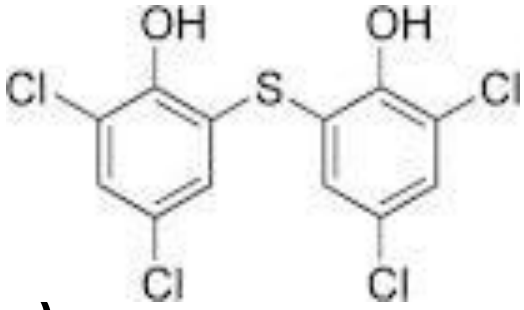
Adverse Reactions

When used for 1–3 days, free of adverse effects.

Mild and transient epigastric distress, diarrhea, headache, nausea, dizziness, lassitude, and insomnia can occur.

In long-term use for hydatid disease, albendazole can cause abdominal distress, headaches, fever, fatigue, alopecia, increases in liver enzymes, and **pancytopenia** (low level of all blood cells produced by the bone marrow).

Bithionol



An alternative drug for the

treatment of **fascioliasis** (sheep liver fluke)

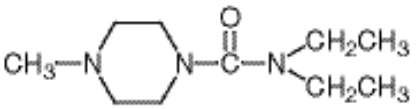
& **pulmonary paragonimiasis** (Lung Fluke).

Adverse Reactions:

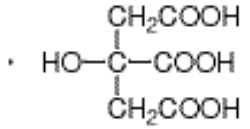
generally mild (40% of patients) and include:

diarrhea, abdominal cramps, anorexia, nausea, vomiting, dizziness, and headache.

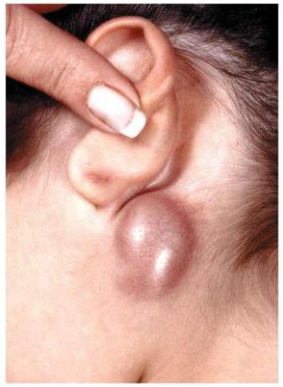
Skin rashes may occur, a reaction to antigens released from dying worms.

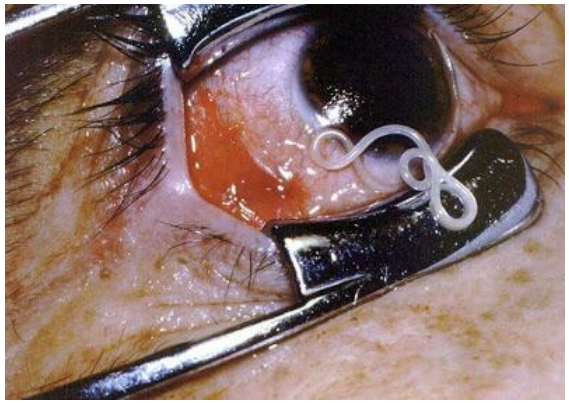


Diethylcarbamazine Citrate



Drug of choice in the treatment of **filariasis, loiasis** (Loa loa), and **tropical eosinophilia** (*Monsonella streptoceca*).





Mechanism:

Immobilizes microfilariae and displacing them from tissues and making them more susceptible to destruction by host defense mechanisms.

The mode of action against adult worms is unknown.

Adverse Reactions

generally mild and transient, include headache, malaise, anorexia, weakness, nausea, vomiting, and dizziness.

Adverse effects also occur as a result of the release of proteins from dying microfilariae or adult worms. Reactions include fever, malaise, papular rash, headache, gastrointestinal symptoms, cough, chest pain, and muscle or joint pain.

Leukocytosis is common (white blood cell count above the normal range in the blood).

Eosinophilia (abnormally high amounts of eosinophils).

Proteinuria may also occur.

Caution when using diethylcarbamazine in patients with hypertension or renal disease.

Doxycycline

Has **macrofilaricidal** activity against ***W bancrofti***, and better activity than any other available drug against **adult worms**.

Active also against **onchocerciasis**

(river blindness caused by

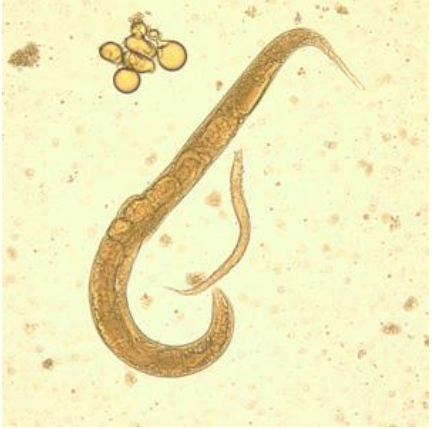
Onchocerca volvulus infection

a roundworm).

Doxycycline acts indirectly, by killing ***Wolbachia***, an intracellular bacterial symbiont of filarial parasites.

It may be used for **filariasis**, both for treatment of active disease and in mass chemotherapy campaigns.

Ivermectin



Strongyloides stercoralis

Drug of choice in:

Strongyloidiasis:

Paralyzes nematodes by intensifying GABA–mediated transmission in peripheral nerves.

Onchocerciasis:

Microfilaricidal.

It does not kill adult worms but blocks the release of microfilariae.

After a single dose, microfilariae in the skin diminish rapidly within 2–3 days .

Microfilariae in the anterior chamber of the eye decrease slowly over months, eventually clear & gradually return.

Repeated doses have a low macrofilaricidal action and permanently reduce microfilarial production.

Adverse Reactions:

In strongyloidiasis:

fatigue, dizziness, nausea, vomiting, abdominal pain, and rashes.

In onchocerciasis

Occurs in 5–30% ,generally mild due to the killing of microfilariae.

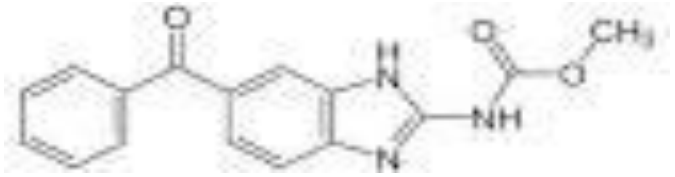
A more intense reaction in **1–3%**

A severe reaction in **0.1%,** including high fever, hypotension, and bronchospasm.

Swellings and abscesses occasionally occur at 1–3 weeks at sites of adult worms.

Corneal opacities & eye lesions may develop several days after treatment.

Mebendazol



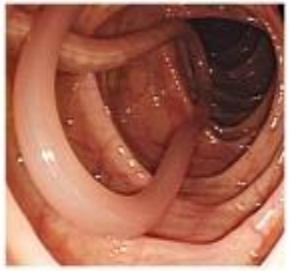
Wide spectrum of antihelminthic activity &a low incidence of adverse effects.

Less than 10% of the oral dose is absorbed. Absorption is increased with a fatty meal.

Acts by inhibiting microtubule synthesis.

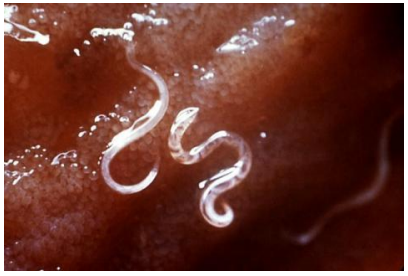
Mebendazole is indicated for use in:

Ascariasis,

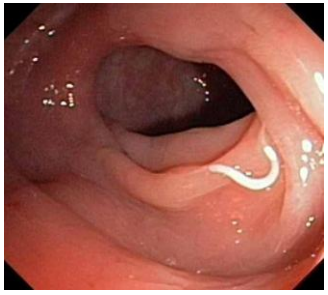


trichuriasis

hookworm

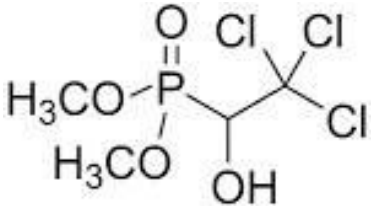


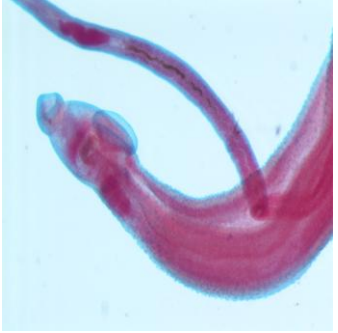
pinworm



and certain other helminthic infections.

Metrifonate





Safe, low-cost alternative drug for ***Schistosoma haematobium*** infections.

Not active against *S mansoni* or *S japonicum*.

Organophosphate cholinesterase inhibitor temporarily paralyzes the adult worms, resulting in their shift from the bladder venous plexus to small arterioles of the lungs, where they are trapped, encased by the immune system, and die.

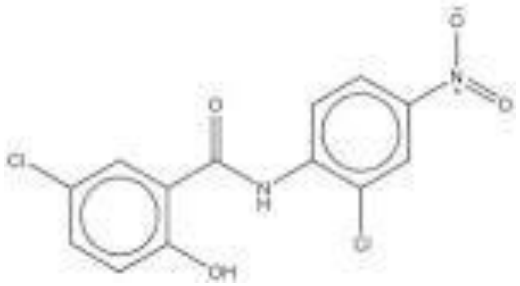
Given three times orally at 14-day intervals.

A prophylactic agent when given monthly to children

Used in mass treatment programs.

trypanosomiasis in infected blood

Niclosamide



Second-line drug for the treatment of most tapeworm infections.

Niclosamide is a **salicylamide derivative**.

Minimally absorbed from the GIT.

Adult worms (but not ova) are rapidly killed, due to inhibition of oxidative phosphorylation or stimulation of ATPase activity.

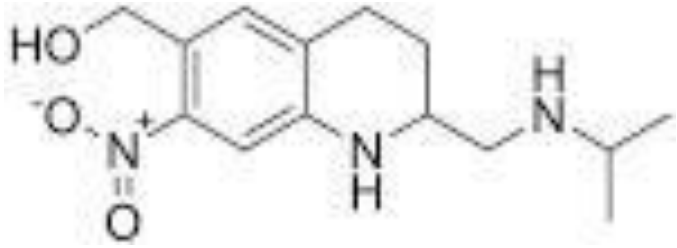
Clinical Uses

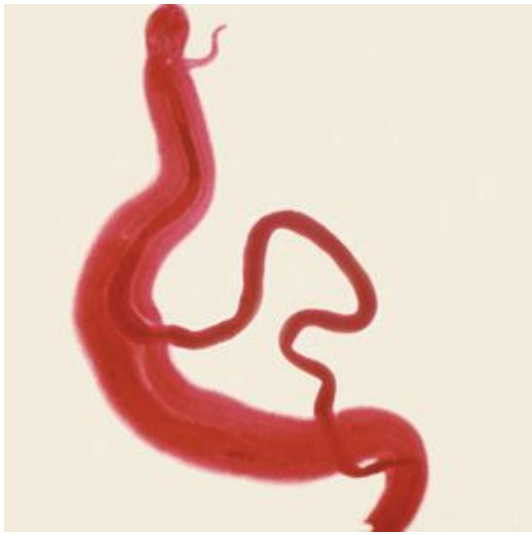
2 g once, given in the morning on an empty stomach.

The tablets must be chewed thoroughly and then swallowed with water.

Purgative needed.

Oxamniquine





Alternative to praziquantel for the treatment of ***S mansoni*** infections.

Used extensively for mass treatment.

Not effective against *S haematobium* or *S japonicum*.

Active against both mature and immature stages.

The mechanism of action is unknown.

Contraction and paralysis of the worms results in detachment from terminal venules in the mesentery and transit to the liver, where many die.

Surviving females return to the mesenteric vessels but cease to lay eggs.

In mixed schistosome infections, it has been used in combination with metrifonate.

Piperazine

An alternative for the treatment of **ascariasis**.

Causes paralysis of ascaris by blocking ACh at the myoneural junction.

This action is mediated by its agonist effect on the inhibitory GABA receptors. Its selectivity for helminthes is because vertebrates only use GABA in the CNS & the helminthes' GABA receptor is a different isoform to the vertebrates' one.

live worms are expelled by normal peristalsis.

75 mg/kg orally once daily for 2 days.

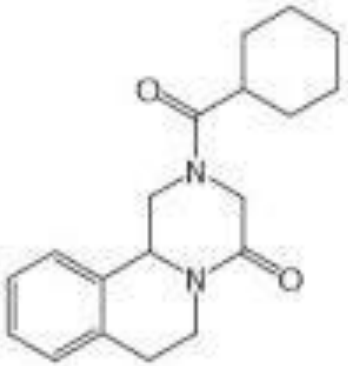
For heavy infections treatment is repeated after 1 wk.

Adverse effects: generally mild (5–30%)

nausea, vomiting, diarrhea, abdominal pain, dizziness, & headache.

Neurotoxicity & allergic reactions are rare.

Praziquantel



Effective in **schistosome infections** of all species & most other trematode & cestode infections, including cysticercosis.

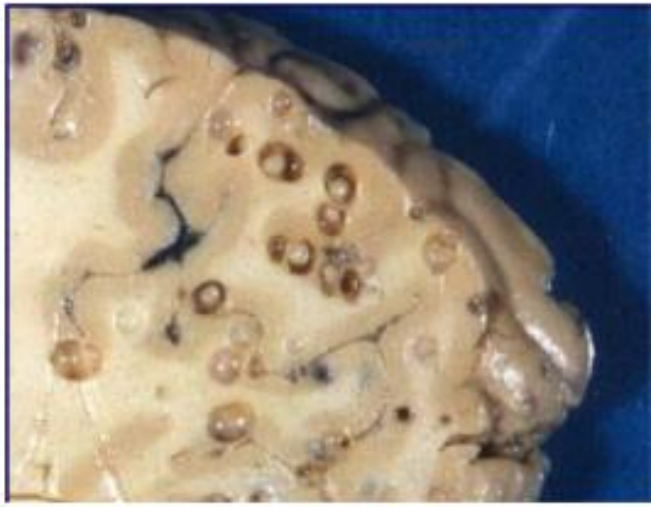
safe and effective as a single oral dose,

Useful in mass treatment of several infections.

Plasma concentrations of praziquantel increase when the drug is taken with **a high-carbohydrate meal**.

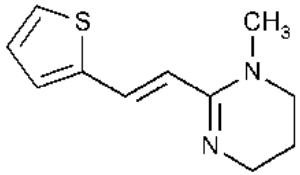
It increases the permeability of cell membranes to calcium, resulting in paralysis, dislodgement, and death.

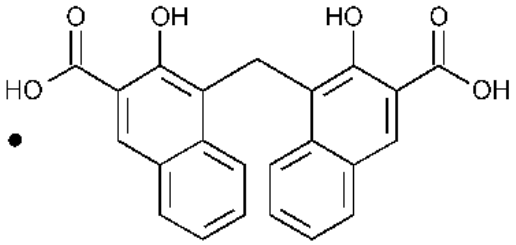
Mild and transient adverse effects, except for **Neurocysticercosis** due to inflammatory reactions around dying parasites.



Brain parenchymal cysticercosis.

Pyrantel Pamoate





Broad-spectrum antihelminthic.

highly effective for **pinworm, ascaris** & ***Trichostrongylus orientalis*** infections and moderately effective against **hookworm**.

A neuromuscular blocker, causes paralysis of worms, which is followed by expulsion.

Effective in intestinal tract, not **in the tissues or the ova**

Given orally once with or without food.

For **pinworm**, the dose is repeated in 2 weeks.

For **ascariasis**, a single dose be repeated if eggs are found 2 weeks after treatment.

For **hookworm**, a single dose is effective against light infections. In heavy infections, a 3-day course.

A course of treatment can be repeated in 2 weeks.