Infection caused by various helminths (worms) is among the most widespread of chronic infections and its occurrence is more common in developing regions with poor personal and environmental hygiene. In this article, we will study in detail about the various anthelmintic (anti-parasitic) drugs, mechanism of action, adverse effects/toxicity and drugs of choice. Important therapeutic aspects of individual drugs will also be studied.

Definition of Anthelmintics

Anthelmintic, or antihelminthic, are the drugs that kill or expel parasites and are used for the treatment of various diseases caused by parasites. Helminths are categorized as follow:

- **Nematodes** or roundworms.
- **Platyhelminthes** or flatworms.
- **Trematodes** or flukes.
- **Cestodes** or tapeworms.

Overview of Helminthiasis

Helminths have a complex life cycle, involving various host species and vectors in different stages of their life cycle. In most of the parasitic infections, a human acts as host of the parasites.

There are several major causes of helminthiasis:

- Poor hygiene.
- Infection occurs due to consumption of water and food contaminated with
human or animal feces or under-cooked flesh (pork and fish).
- Some parasites enter the human body through skin and insect bites
  (onchocerca volvulus, Wuchereria bancrofti).

**Various Types of Helminths**

![Image: “Taenia Solium Scolex (x400)” by Îä½ð– Own work. License: CC BY-SA 3.0]

**Tapeworms**

*Taenia saginata, Taenia solium, Hymenolepis nana*

The intermediate hosts of the tapeworms (*T. saginata and T. solium*) are cattle and pigs.

**Taenia solium** (pork tapeworm) is most commonly found in Asia and Latin America. In the US, it is present in patients migrated from these countries. It causes **neurocysticercosis**. Its host is pig and it can be acquired by a human by eating poorly cooked pork. Its eggs are generally ingested by oral-fecal contamination.

**Taenia saginata**, also called beef tapeworm, does not cause neurocysticercosis. Usually, humans get infected with *T. saginata* after consumption of under-cooked beef. It causes **taeniasis** in the intestine and it is harmless. It mostly remains **asymptomatic**.

**Echinococcus Species**
Echinococcus Granulosus

The intermediate hosts for this infection is sheep and the primary host are dogs. Under certain conditions, humans can function as intermediate host. As a consequence, the larvae develop into hydatid cysts within the tissues. They cause the hydatid cysts; the most affected part is the liver (two thirds of the patients).

Flukes

Schistosoma haematobium, Schistosoma mansoni, Schistosoma japonicum

Flukes of genus schistosoma cause schistosomiasis. It is also called snail fever. Different types of snails act as hosts of the genus schistosoma. Complications arise due to immunological reactions towards trapped eggs of schistosoma parasite in various tissues. Eggs reach skin, brain, muscle, adrenal glands and eyes. Eventually, excessive inflammatory process causes organ damage.

Tissue roundworms

Trichinella spiralis, Dracunculus medinensis (guinea worm), Wuchereria bancrofti, Loa loa, Onchocerca volvulus, Brugia malayi

The adult filariae of these types of worms reside mainly in the lymphatic system,
connective tissues or mesentery of the host and produce live embryos or microfilariae, which travel in the bloodstream through transmission from mosquitoes or similar insects when they feed.

After development within the secondary host, the larvae pass to the mouth parts of the insect and are re-injected into humans.

Common filarial diseases are onchocerciasis (the presence of microfilariae in the eye causing 'river blindness'), loiasis (the microfilariae causing inflammation in the skin and other tissues), trichinosis (the larvae from the viviparous female in the intestine migrate to the skeletal muscle, where they become encysted).

Roundworms

*Ascaris Lumbricoides, Toxocara canis*

*Ascariasis* is the most common intestinal nematodal infection. It remains asymptomatic in most of the patients. However, it can cause pulmonary complications (cough, wheezing) and intestinal obstruction when a person is heavily infected. It is usually prevalent in the areas of poor sanitation and hygiene.

Hookworm

*Ancylostoma duodenale, Necator americanus*

The reason for the infection is larval penetration through the skin. After reaching the lung, the larvae migrate to the oral cavity and are swallowed, the hookworm attaches to the intestinal mucosa and feeds through the host.

Anthelmintic Drugs
Albendazole

The drug has a broad range of activity in **neurocysticercosis, echinococcosis, ascariasis, hookworm, and trichuriasis**. The drug acts by inhibiting the **polymerization of helminth β-tubulin**, thus interfering with microtubule-dependent functions such as glucose uptake in the helminths.

Bioavailability of albendazole is less than 5% when taken on an empty stomach. Absorption of the drug is enhanced by administering it with **fatty foods**.

**Side effects** include abdominal pain, nausea, vomiting and increased hepatic **transaminases**; these are generally transient and usually do not require discontinuation of the drug. **LFT’s** should be monitored during therapy with albendazole.

Mebendazole

The drug is effective against a spectrum of intestinal and tissue nematode infections, including **ascariasis, hookworm, enterobiasis** and **trichuriasis**. Mebendazole is the preferred drug for the treatment of multiple infestations and is more efficacious than albendazole in trichuriasis.

The site of action of the drug is the **microtubular protein β-tubulin** of the parasite. It binds to β-tubulin of the worm with high affinity and inhibits its polymerization. It also blocks glucose uptake in the helminths.

Albendazole and mebendazole are effective against the following parasites:

- Ascaris lumbricoides
- Necator americanus
- Trichinella spiralis
- Enterobius vermicularis
- Trichuris trichiuria
- Echinococcus
- Strongyloides stercoralis
- Taenia solium
- Microsporidia
Thiabendazole

Thiabendazole is an older benzimidazole derivative and, apart from the therapeutic response against various helminthes, it has symptomatic relief in cutaneous larva migrans and skeletal muscle symptoms produced by the migration of Trichinella spiralis larvae to muscles.

The mechanism of action of thiabendazole is similar to albendazole. Thiabendazole has anti-inflammatory, analgesic and antipyretic actions. Adverse reactions include dizziness, nausea, vomiting, drowsiness, pruritus, headache, neuropsychiatric disturbances, hepatitis and hypersensitivity reactions including Stevens Johnson syndrome. A topical suspension of thiabendazole is used for cutaneous larva migrans.

Diethylcarbamazine (DEC)

It is a piperazine derivative that is effective against lymphatic filariasis, loiasis, and visceral larva migrans. Diethylcarbamazine is only effective on microfilaria (larvae) stage of various parasites. It does not kill the adult parasite (microfilaria).

It may act by changing the parasite such that it becomes susceptible to the host's normal immune responses (phagocytosis). However, the exact mechanism of action is unclear. It may also interfere with helminth arachidonate metabolism.

It is a drug of choice for loiasis. It is also the drug of choice for filariasis caused by Wuchereria bancrofti and Brugia malayi. Nausea, loss of appetite, headache, weakness and dizziness are common side effects.

Praziquantel

It has activity against schistosomes, cestodes and their larval forms, but not nematodes. It acts by causing leakage of intracellular calcium from the cell membranes of parasites producing contracture and paralysis. The paralyzed tapeworms are dislodged from the attached intestinal mucosa and are expelled from the intestine. Flukes and schistosomes are also cleared in tissues and veins.

Common side-effects are appetite loss, dizziness, drowsiness, headache, malaise, abdominal pain, nausea, vomiting and diaphoresis. Undesirable effects are usually transitory and rarely of clinical importance.

It is a drug of choice to treat the cysticercosis caused by T. solium. Side effects are prominent in patients with a heavy parasite load because of products released from the dead worms.

Praziquantel is contraindicated in the treatment of ocular cysticercosis, as destruction of the organism can cause permanent damage to the eyes. Praziquantel is considered safe for pregnant and lactating women (category B drug).

Piperazine

It is highly active against Ascaris and Enterobius infections with cure rates of 90-100%. It causes hyperpolarization of worm muscle by opening chloride channels that causes relaxation and depresses responsiveness to contractile action of ACh. Flaccid paralysis occurs and worms are expelled alive. Piperazine is safe and well tolerated. Nausea, vomiting, abdominal discomfort and urticaria are occasional.
Py rantel pamoate

It is effective against the following helminthes:

- Ascaris lumbricoides
- Necator americanus
- Enterobius vermicularis

It is a depolarizing neuromuscular blocking agent and it causes paralysis in the parasite. It also inhibits the cholinesterase. It is poorly absorbed from the GI tract.

**Important:** It is mostly effective against intestinal parasites. Caution should be taken while treating the patient with liver dysfunctions.

Niclosamide

It is active against *T. saginata, T. solium, Diphyllobothrium latum* and *Hymenolepis nana,* as well as threadworm. The drug acts by inhibiting oxidative phosphorylation in mitochondria and interfering with the anaerobic generation of ATP in the tapeworm; thus, organisms are killed due to the unavailability of ATP. It does not kill ova/larva.

It is minimally absorbed from the GI tract and no systemic toxicity occurs. It is well tolerated; **minor abdominal symptoms** are produced occasionally. Malaise, pruritus and light headedness are rare. Niclosamide is safe during pregnancy and in patients with poor health.

Levamisole

Levamisole is effective in common roundworm (*A. lumbricoides*). It has a nicotine-like action stimulating and blocking the **neuromuscular junctions.** Consequently, it causes the paralysis of parasites and they are expelled from the body through feces. Low incidences of side effects are nausea, abdominal pain, giddiness, fatigue, drowsiness or insomnia.

Ivermectin

It is obtained from *Streptomyces avermitilis.* Ivermectin acts on the glutamate gated chloride channels (**GluCls**) present in the prostome invertebrates. They control the locomotion and feeding in the parasites. Ivermectin causes the hyperpolarization of the **GluCls,** resulting in the paralysis and death of the parasite.

**Important:** Ivermectin is only effective on the **larvae** stage of various parasites. It does not kill the adult parasite.
Ivermectin is active on the following parasites:

- Onchocerca volvulus
- Strongyloides stercolais
- Ascaris lumbricoides
- Trichuris trichiura
- Enterobius vermicularis
- Filariasis

Onchocerciasis is caused by **Onchocerca volvulus** - the vector is **black fly** (simulium genus). Humans are the hosts of Onchocerca volvulus. The disease is also called **river blindness**. It is most common in **West African savanna** areas and it usually causes blindness by the age of 40 to 50 years in the affected individuals.

Ivermectin (150 mcg/kg, OD oral route) kills 90% of the **microfilaria** within 1 week of treatment. However, the therapy needs to be continued for **10-12 years** (throughout the life span of the parasite) to kill the parasite. It has a long half-life of 48-60 hours.

Adverse effects are usually the result of death of the parasites. These include fever, headache, mild-pruritus, giddiness, weakness, rash, nausea, abdominal pain, constipation, lethargy joint/muscle pain, **hypotension**, **tachycardia** and **edema**. These reactions are mild and last for two days after treatment.

In some patients (1-3%), the reaction could be severe due to high fever, hypotension and **bronchospasm**. **Corticosteroids** are given in such cases for the management of adverse effects. Ivermectin is contraindicated in pregnant and lactating women.

**Bithionol**

It is given with triclabendazole to treat the infections (**fascioliasis**) caused by sheep fluke. Mechanism of action is unknown. Fascioliasis is caused by **Fasciola hepatica**.
Drug of Choice for the Treatment of Helminthic Infections

Roundworms (Nematodes)
- **Ascaris lumbricoides**: (mnemonics: PAM) Pyrantel palmoate, Albendazole, Mebendazole
- **Necator americanus**: (PAM) Pyrantel palmoate, Albendazole, Mebendazole
- **Trichuris trichiura**: Albendazole, Mebendazole
- **Strongyloides stercoralis**: Ivermectin
- **Enterobius vermicularis**: Pyrantel palmoate, Mebendazole
- **Trichinella spiralis**: Mebendazole or Albendazole
- **Cutaneous larva migrans**: Albendazole, Ivermectin
- **Wuchereria bancrofti and Brugia malayi**: DEC (Diethylcarbamazine)
- **Onchocerca volvulus**: Ivermectin

Flukes (Trematodes)
- **Schistosoma haematobium**: Praziquantel
- **Schistosoma mansoni**: Praziquantel
- **Schistosoma japonicum**: Praziquantel
- **Paragonimus westermani**: Praziquantel
- **Fasciola hepatica**: Bithionol or Triclabendazole
- **Fasciolopsis buski**: Praziquantel or Niclosamide

Tapeworms (Cestodes)
- **Taenia saginata**: Praziquantel or Niclosamide
- **Taenia solium**: Praziquantel or Niclosamide
- **Cysticercosis**: Albendazole
- **Diphyllobothrium latum**: Praziquantel or Niclosamide
- **Echinococcus granulosus**: Albendazole
- **Loa loa**: DEC

Review Questions on Anthelmintic Drugs
The correct answers can be found below the references.

1. **Which of the following is the drug of choice for the treatment of loiasis?**
   - A. Albendazole
   - B. Diethylcarbamazine (DEC)
   - C. Praziquantel
   - D. Ivermectin
   - E. Levamisole

2. **Which of the following is the drug of choice for the treatment of filariasis?**
   - A. Pyrantel pamoate
   - B. Diethylcarbamazine (DEC)
   - C. Praziquantel
   - D. Ivermectin
E. Levamisole

3. Which of the following parasites cause neurocysticercosis?

A. Taenia saginata
B. Taenia solium
C. Echinococcus granulosus
D. Wuchereria bancrofti
E. Onchocerca volvulus

References


Antihelminthic therapies via uptodate.com
Albendazole via medscape.com
Diethylcarbamazine via drugbank.ca


Glutamate-gated chloride channel - Mechanism of Action via stanford.edu
Schistosomiasis via medscape.com
Ascariasis via medscape.com


Correct answers: 1B, 2B, 3B

Legal Note: Unless otherwise stated, all rights reserved by Lecturio GmbH. For further legal regulations see our legal information page.