



Tikrit University
College of Veterinary Medicine

Pharmacology

Subject name: **Antiparasitic drugs**
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Lecturer name: **Dr. Buthinah Abulhameed**
Academic

Email: buthinahamee@tu.du.iq

Lecturers link

Antiparasitic drugs

Drugs used to treat infections caused by:

1. Helminthes (anthelmintic drugs). Three major groups of helminths (worms) the nematodes, trematod, and cestodes (flatworms).
2. Arthropods (tick fleas & mites).
3. Protozoa (antiprotozoal drugs).

Some popular parasitic diseases can cause a large number of animals to die. Chronic diseases could block the development of young animals.

The ideal (characteristics) chemotherapeutic drugs

1. Get to site of infection.
2. Destroy pathogenic organisms/cells.
3. Stay at the target site long enough to be effective.
4. Must be eliminated from the body without affecting the structure or function of host cells.
5. High safety.

Antiparasitic drugs divided into:

1. Endoparasitocidal drugs

Anthelmintic drugs mostly broad spectrum. There are many of the drugs that can control/treat majority of helminth infections.

Drugs for the Treatment of Nematodes:

Nematodes are elongated roundworms that possess a complete digestive system, including both a mouth and an anus.

1. Benzimidazoles

This kind of drugs are anthelmintics with broad-spectrum, high performance and low poison, have strong killing effects to nematodes, and some have effects to larva, some even can kill eggs. Several benzimidazoles are in use for the treatment of helminthic infections. Three of these, mebendazole, thiabendazole and albendazole.

A. Mebendazole:

Mebendazole a synthetic benzimidazole compound is effective against a wide spectrum of nematodes. It is a drug of choice in the treatment of infections by whipworm (*Trichuris trichiura*), pinworm (*Enterobius vermicularis*), hookworms (*Necator americanus* and *Ancylostoma duodenale*), and roundworm (*Ascariasis lumbricoides*).

Mechanism of action:

1. *Mebendazole* acts by binding to and interfering with the parasites' microtubules lead to decreasing glucose uptake.
2. Inhibits protein function.

Side effects:

Mebendazole is relatively free of toxic effects, although patients may complain of abdominal pain and diarrhea. It is contraindicated in pregnancy, because it has been shown to be embryotoxic and teratogenic in experimental animals.

B. Thiabendazole

Thiabendazole another synthetic benzimidazole is effective against strongyloidiasis caused by *Strongyloides stercoralis* (threadworm), and early stages of trichinosis (caused by *Trichinella spiralis*). *Thiabendazole*, like the other benzimidazoles, affects microtubular aggregation.

Side effects:

The adverse are dizziness, anorexia, nausea, and vomiting. There have been reports of central nervous system (CNS) signs. Its use is contraindicated during pregnancy.

C. Albendazole

❖ Albendazole appears to cause cytoplasmic microtubular degeneration, which in turn impairs vital cellular processes and leads to parasite death.

❖ Albendazole is given orally and is poorly and because of its poor water solubility.

❖ When the drug is given with a fatty meal instead of on an empty stomach Oral bioavailability is increased as much as five times.

❖ Albendazole has a broad spectrum of activity against intestinal nematodes and cestodes, as well as the liver flukes. It also has been used successfully against *Giardia lamblia*.

❖ Albendazole is an effective treatment of hydatid cyst disease (echinococcosis), especially when accompanied with praziquantel. It also is effective in treating cerebral and spinal neurocysticercosis, particularly when given with dexamethasone.

Adverse effects:

Mild and transient and include headache and nausea. Treatment of hydatid disease (3 months) has a risk of hepatotoxicity.

2. Ivermectin

Ivermectin is the drug of choice for the treatment of onchocerciasis (river blindness) caused by *Onchocerca volvulus* and is a drug of first choice for strongyloides.

Mechanism of action:

Ivermectin targets the parasite's glutamate-gated Cl⁻ channel receptors. Chloride influx is enhanced, and hyperpolarization occurs, resulting in paralysis of the worm. The drug is given orally or S/C. It does not cross the blood-brain barrier and, thus, has no pharmacologic effects in the CNS. However, it is contraindicated in patients with meningitis, because their blood-brain barrier is more permeable and CNS effects might be expected. ***Ivermectin*** is also contraindicated in pregnancy.

3. Piperazine

Mechanism of action:

❖Piperazine acts on the musculature of the helminths to cause paralysis mediated by chloride-dependent hyperpolarization of the muscle membrane. This results in expulsion of the worm.

❖Piperazine acts as an agonist at gated chloride channels on the parasite muscle.

❖Piperazine is an alternative to mebendazole for the treatment of ascariasis, especially in the presence of intestinal or biliary obstruction.

Side effects:

Occasionally include gastrointestinal distress, urticaria, and dizziness. Neurological symptoms of ataxia, hypotonia and visual disturbances.

It should not be used in pregnancy because of the formation of a potentially carcinogenic and teratogenic nitrosamine metabolite.

4. Diethylcarbamazine

Mechanism of action:

Diethylcarbamazine is used in the treatment of filariasis because of its ability to immobilize microfilariae and adult filarial worms. Enhances phagocytosis and killing of parasites.

Side effects:

Adverse effects are primarily caused by host reactions to the killed organisms. The severity of symptoms includes fever, malaise, rash, myalgias, arthralgias, and headache.

5. Pyrantel pamoate

Pyrantel pamoate is effective in the treatment of infections caused by roundworms, pinworms, and hookworms.

Mechanism of action:

It acts as a depolarizing, neuromuscular-blocking agent, causing persistent activation of the parasite's nicotinic receptors. The paralyzed worm is then expelled from the host's intestinal tract. **Adverse effects** are mild and include nausea, vomiting, and diarrhea.

Drugs for the Treatment of Trematodes:

The trematodes (flukes) are leaf-shaped flatworms that are generally characterized by the tissues they infect. For example, they may be categorized as liver, lung,

intestinal, or blood flukes. The *schistosomes* (blood flukes) are a group of trematodes.

Praziquantel

Trematode infections are generally treated with *praziquantel* this drug is an agent of choice for the treatment of all forms of schistosomiasis and other trematode infections and for cestode infections like cysticercosis.

Mechanism of action:

Permeability of the cell membrane to calcium is increased, causing and paralysis of the parasite.

Side effects:

Common adverse effects include drowsiness, dizziness, malaise, and anorexia, as well as gastrointestinal upsets. The drug is not recommended for pregnancy.

Praziquantel is contraindicated for the treatment of ocular cysticercosis, because destruction of the organism in the eye may damage the organ.

Drugs for the Treatment of Cestodes:

The cestodes, or a true tapeworm, typically have a flat, segmented body and attach to the host's intestine. The tapeworm has a head with round suckers. Some tapeworms have a projection (*rostellum*) that bears hooks. This head or *scolex* is used by the worm to attach to tissues.

Niclosamide

Niclosamide has been used extensively in the treatment of tapeworm infections caused by *Taenia saginata*, *Taenia solium*, *Diphyllobothrium latum*, *Fasciolopsis buski*.

Mechanism of Action:

Niclosamide was widely used to treat infestations of cestodes. Niclosamide inhibits the production of energy derived from anaerobic metabolism.

Adverse Effects:

No serious side effects are associated with Niclosamide use, although some patients report abdominal discomfort and loose stools.

2. Ectoparasitocidal drugs:

Ectoparasites are live outside of the body and in the environment as fleas, ticks, mite and flies (arthropods).

Formulations of Ectoparasites Drugs:

❖Dips/sprays

Products for use as immersion dips usually require dilution in water prior to use and are available as emusifiable concentrates.

Amitraz:

Amitraz is applied externally and has broad-spectrum activity against all mites and ticks.

Adverse effects:

Amitraz may cause a transient sedative effect.

At high exposures the following adverse effects may occur:

1. Severe signs of depression and reluctance to move
2. Increased glucose concentrations.
3. Polyuria

4. Bradycardia.

ANTICHOLINESTERASE PARASITICIDES

Organophosphates:

These compounds are broad-spectrum Anthelmintic or insecticides. Examples of available organophosphate preparations

Diazinon, Haloxon, Malathion, Dichorvos, coumaphos and Cypermethrin.

Mechanism of Action:

Inhibition of cholinesterase and parasite unable to move by stopping nerve transmission (parasitic paralysis).

Side effects:

Salivation, Lacrimation, urination, Defication and GI upset.

Pyrethrins:

Treatment of ectoparasites by using insecticides:

1. Extracted from pyrethrum flowers.
2. Generally safe for most mammals.
3. Quick kill effect with low residues

❖Spot-on:

Topical high-concentration, low-volume preparations have been designed to increase both the convenience of treatment and compliance. Topical spot-on products are

either absorbed systemically or distribute laterally and remain within the skin.

Systemically active products include:

1. Selamectin

2. Fenthion.