ANTI HELMINTIC

Three major groups of helminths (worms) the nematodes, trematod, and cestodes ”infect humans. As in all antibiotic regimens, the anthelmintic drugs are aimed at metabolic targets that are present in the parasite but are either absent from or have different characteristics than those ofthe host.

II. Drugs for the Treatment of Nematodes

Nematodes are elongated roundworms that possess a complete digestive system, including both a mouth and an anus. They cause infections of the intestine as well as the blood and tissues.

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).

Mebendazole **acts by binding to and interfering with the assembly of the parasites' microtubules and also by decreasing glucose uptake**.

Affected parasites are expelled with the feces. *Mebendazole* is nearly insoluble in aqueoussolution. Little of an oral dose (that is chewed) is absorbed by the body, unless it is taken with a high-fat meal. It undergoes first-pass metabolism to inactive compounds.*Mebendazole* is relatively free of toxic effects,although patients may complain of abdominal pain and diarrhea. It is, however, contraindicatedin pregnant women because it has been shown tobe embryotoxic and teratogenic in experimental animals.

B. Pyrantel pamoate

Pyrantel pamoate along with *mebendazole*, is effective in the treatment of infections caused by roundworms, pinworms, and hookworms. *Pyrantel pamoate* is poorly absorbed orally and exerts its effects in the intestinal tract.

It acts as a depolarizing, neuromuscular-blocking agent, causing persistent activation ofthe 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.

C. Thiabendazole

Thiabendazole, like the other benzimidazoles, affects microtubular aggregation. Although nearly insoluble in water, the drug is readily absorbed on oral administration. It is hydroxylated in the liver and excreted in the urine. The adverse effects most often encountered are dizziness, anorexia, nausea, and vomiting. There have been reports of central nervous system (CNS) symptomatology.

D. Ivermectin

Ivermectin [eye-ver-MEK-tin] is the drug of choice for the treatment of onchocerciasis (river blindness) caused by Onchocerca volvulus and is a drug of first choice for cutaneouslarva migrans and strongyloides. *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. 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.

E. Diethylcarbamazine

Diethylcarbamazine [dye-eth-il-kar-BAM-a-zeen] is used in the treatment of filariasis because of its ability to immobilize microfilariae and render them susceptible to host defense mechanisms. It is rapidly absorbed following oral administration with meals and is excreted primarily in the urine. Urinary alkalosis or renal impairment may require dosage reduction. Adverse effects are primarily caused by host reactions to the killed organisms. The severity of symptoms is related to the parasite load and include fever, malaise, rash, myalgias, arthralgias, and headache.

III. 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

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

Praziquantel is rapidly absorbed after oral administration and distributes into the cerebrospinal fluid. High levels occur in the bile. The drug is extensively metabolized oxidatively, resulting ina short half-life. The metabolites are inactive and are excreted through the urine and bile. Common adverse effects include drowsiness, dizziness, malaise, and anorexia, as well as gastrointestinal upsets.

IV. Drugs for the Treatment of Cestodes

The cestodes, or tapeworms typically have a flat, segmented body and attach to the host's intestine Like the trematodes, the tapeworms lack a mouth and a digestive tract throughout their life cycle.

A. Niclosamide

Niclosamide is the drug of choice for most cestode (tapeworm) infections. Its action has been ascribed to inhibition of the parasite's mitochondrial phosphorylation of adenosine diphospate, which produces usable energy in the form of adenosine triphospate. Anaerobic metabolism may also be inhibited. The drug is lethal for the cestode's scolex and segments of cestodes but not for the ova. A laxative is administered prior to oral administration of *niclosamide*. This is done to purge the bowel of all dead segments and so preclude digestion and liberation of the ova, which may lead to cysticercosis. Alcohol should be avoided within 1 day of *niclosamide*.

B. Albendazole

Albendazole is a benzimidazole that, like the others*, inhibits microtubule synthesis and glucose uptake in nematodes*. Its primary therapeutic application, however, is in the treatment of cestodal infestations, such as cysticercosis (caused by Taenia solium larvae) and hydatid disease (caused byEchinococcus granulosis).

Albendazole is erratically absorbed after oral administration, but absorption is enhanced by a high- fat meal. It undergoes extensive first-pass metabolism, including formation of the sulfoxide, whichis also active. *Albendazole* and its metabolites are primarily excreted in the urine.