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Anthelmintics: Mode of Action on Helminth

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The mode of action of anthelmintic basically depends on interference with essential biochemical processes of the parasite, but not of the host.

(1) Benzimidazoles / Probenzimidazoles

This pharmacological class of drugs exhibits broad-spectrum efficacy against various helminths, encompassing nematodes, cestodes, and trematodes. Specifically, benzimidazoles demonstrate significant activity against nematodes, including their larvae and eggs. Mebendazole, within this class, also displays modest efficacy against tapeworms and proves highly effective against larval tapeworms. Notably, albendazole exhibits efficacy against adult liver fluke, while the most recent addition to the group, triclabendazole, manifests exceptional potency against all stages of liver fluke.

The considerable safety margin of these drugs, characterized by a high therapeutic index, is particularly noteworthy. In certain instances, they maintain efficacy even when administered at dosages surpassing the recommended levels by tenfold. However, prudent caution must be exercised concerning the development of parasite resistance, which has been primarily associated with repetitive use of these drugs against nematodes in ovine and equine populations. Moreover, special consideration is warranted when administering these drugs to pregnant animals, as benzimidazoles have demonstrated embryotoxic effects.

Mechanistically, this drug class exerts its action predominantly on the intestinal cells of helminths, effectively impeding glucose uptake and resulting in a state of "starvation" within the parasites. This mode of action underlies their potency against a wide range of helminthic infections.

(2) Piperazines

These drugs exert their pharmacological effects by inducing reversible paralysis in helminths through their anticholinergic action at the neuromuscular junction. This mechanism hinders the worms from maintaining their position within the host's gastrointestinal tract, ultimately leading to their expulsion through the feces.

Piperazine salts find extensive use in combating ascarid worms. On the other hand, diethylcarbamazine has been employed in the treatment and control of lungworm infestations and canine heartworm disease.

(3) Imidothaiazoles / Tetrahydropyrimidines

These compounds function as depolarizing neuromuscular blocking agents, affecting both nematodes and their hosts. This mode of action results in paralysis and eventual death of the

Ivermectins and Milbemycin, which belong to the microcyclic lactone group or Macrolides, are antibiotics derived from the fermentation of actinomycete microorganisms. Streptomyces avermectilis is the source of eight major ivermectins, while various Streptomyces spp. produce over 30 Milbemycin compounds.

These drugs exhibit remarkable potency and efficacy against a broad spectrum of parasites, including nematodes and ectoparasitic arthropods. Their high effectiveness is notable even at very low doses, making them highly efficient in treating parasitic infestations.When administered orally or parenterally, the activity of these drugs persists for an extended period, up to two weeks, after dosing. However, it is important to note that Ivermectins do not exhibit any activity against platyhelminths.

The mechanism of action involves causing paralysis in nematodes and ectoparasites by disrupting γ-amino butyric acid (GABA)-mediated signals between nerves and muscles. Specifically, Ivermectins enhance the release and binding of GABA in certain nerve synapses. As GABA serves as a neurotransmitter in nematodes and ectoparasites, the interference of these signals by Ivermectins leads to the eventual paralysis of these parasites.

Flukes and tapeworms, in contrast, do not employ GABA as a neurotransmitter. Mammalian GABA-ergic neurons are present in the central nervous system (CNS), but Ivermectins have limited ability to cross the mammalian blood-brain barrier. As a result, these drugs exhibit low toxicity in mammals, which is a favorable safety characteristic.

(4) Organophosphates

Certain organophosphorus compounds have demonstrated activity against nematodes. However, it is important to note that this group of drugs is relatively toxic and is predominantly used in horses, likely due to their additional effectiveness as insecticides against larvae of horse bots.

The mode of action of these compounds involves the inhibition of the enzyme acetylcholinesterase in worms. This disruption leads to neuromuscular paralysis of the nematodes, ultimately resulting in their expulsion from the host's body.

(5) Salicylanilides / Substituted Phenols

The primary mechanism of action of these drugs involves disrupting ATP production in parasites by uncoupling oxidative phosphorylation. Among their various applications, they are particularly effective against liver flukes. Notably, Nitroscanate is marketed for treating nematode and cestode infections in dogs, while Niclosamide finds extensive use in combating tapeworms across various domestic species.

(6) Sulphonamide

This drug exerts its effect on the worm's energy production by binding to two crucial enzymes, namely Phosphoglycerate kinase and Phosphoglycerate mutase, which are essential for glucose metabolism (glycolysis). While its primary activity targets adult flukes, it has shown efficacy against worms as young as 6 weeks in sheep and 8 weeks in cattle from a single dose.

The drug can be administered through either the oral or parenteral route and is rapidly absorbed, becoming bound to red blood cells (RBCs). This binding ensures its availability to blood-feeding flukes, contributing to its effectiveness in controlling these parasites.

(7) Pyrazinoisoquinolines And Benzazepines

These drugs surpass all other tapeworm remedies in terms of effectiveness. When administered at higher doses, they can eliminate the larval forms of tapeworms in their intermediate hosts, although their efficacy against hydatid cysts is comparatively lower. Their impact on helminths involves triggering rapid muscular contractions by altering the ionic balance within the muscle cells. Additionally, they induce vacuolation and disruption of the worm's tegument, contributing to their parasiticidal activity.