Chapter-13

Anthelmintics

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ABSTRACT

Anthelmintics are a class of drugs used to treat infections caused by helminths, or parasitic worms, which include nematodes (roundworms), trematodes (flukes), and cestodes (tapeworms). These medications work by targeting various biological processes essential for the survival and reproduction of these parasites. Common anthelmintics include albendazole, mebendazole, ivermectin, praziquantel, and pyrantel pamoate. Albendazole and mebendazole inhibit the polymerization of tubulin, impairing glucose uptake and depleting energy stores in helminths. Ivermectin increases the permeability of the parasite's cell membrane to chloride ions, leading to paralysis and death. Praziquantel induces severe spasms and paralysis of the worms' muscles by increasing calcium ion permeability. Pyrantel pamoate acts as a neuromuscular blocker, causing paralysis of the parasites. The choice of anthelmintic depends on the type of helminth infection and its location in the body. Effective treatment not only alleviates symptoms but also prevents the spread of infection and reduces the risk of complications. Continued research and development of anthelmintics are crucial to address emerging resistance and improve global health outcomes.

Introduction to Anthelmintics

Anthelmintics are a group of antiparasitic drugs designed to expel or destroy helminths (parasitic worms) from the host body. These parasites can cause a variety of diseases in humans and animals, impacting the gastrointestinal tract, blood, lymphatic system, and other tissues. Helminth infections are prevalent in many parts of the world, particularly in areas with poor sanitation and hygiene. Effective anthelmintic treatment is essential for controlling these infections, improving health, and preventing the spread of these parasites.

Classification of Anthelmintics

Anthelmintics can be classified based on their chemical structure, mechanism of action, and the type of helminth they target. The main classes include:

1. Benzimidazoles
2. Avermectins and Milbemycins
3. Tetrahydropyrimidines
4. Praziquantel and Pyrantel
5. Salicylanilides and Substituted Phenols
6. Other Anthelmintics

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1. **Benzimidazoles**

   Examples: Albendazole, Mebendazole, Thiabendazole

   Mechanism of Action: Benzimidazoles bind to β-tubulin, inhibiting the polymerization of microtubules. This disruption affects cellular processes such as glucose uptake and energy production, leading to the depletion of energy stores and the death of the parasite.

   Targeted Helminths: Effective against a broad spectrum of nematodes (roundworms) and some cestodes (tapeworms).

2. **Avermectins and Milbemycins**

   Examples: Ivermectin, Abamectin, Milbemycin Oxime

   Mechanism of Action: These drugs bind to glutamate-gated chloride channels, increasing the permeability of the cell membrane to chloride ions. This results in hyperpolarization of the nerve and muscle cells, causing paralysis and death of the parasite.

   Targeted Helminths: Primarily effective against nematodes and ectoparasites (e.g., mites, lice).

3. **Tetrahydropyrimidines**

   Examples: Pyrantel Pamoate, Oxantel

   Mechanism of Action: Tetrahydropyrimidines act as depolarizing neuromuscular blocking agents, causing spastic paralysis of the helminths. The paralyzed worms are then expelled from the host's body.

   Targeted Helminths: Effective against a variety of gastrointestinal nematodes.

4. **Praziquantel and Pyrantel**

   Examples: Praziquantel, Pyrantel Pamoate

   Mechanism of Action: Praziquantel increases the permeability of the cell membrane to calcium ions, causing muscle contraction, paralysis, and death of the parasite. Pyrantel pamoate acts as a neuromuscular blocker, leading to paralysis and expulsion of the worms.

   Targeted Helminths: Praziquantel is effective against trematodes (flukes) and cestodes (tapeworms), while pyrantel pamoate is used for nematode infections.

5. **Salicylanilides and Substituted Phenols**

   Examples: Niclosamide, Oxyclozanide

   Mechanism of Action: These drugs disrupt oxidative phosphorylation in the parasite, inhibiting ATP production and leading to energy depletion and death of the parasite.

   Targeted Helminths: Primarily effective against cestodes and trematodes.

6. **Other Anthelmintics**

   Examples: Levamisole, Piperazine

Mechanism of Action: Levamisole acts as a nicotinic acetylcholine receptor agonist, causing spastic paralysis of the helminths. Piperazine induces flaccid paralysis by acting as a GABA agonist.

Targeted Helminths: Levamisole is used for nematode infections, while piperazine is effective against pinworms and roundworms.

Albendazole

Mechanism of Action

- Albendazole inhibits microtubule polymerization in the parasite, disrupting its microtubule structure. This interferes with the energy metabolism of the parasite and leads to immobilization and death.

Pharmacokinetics

- **Absorption:** Albendazole is poorly absorbed in the gastrointestinal tract.
- **Metabolism:** It undergoes extensive hepatic metabolism to its active form, albendazole sulfoxide, which is responsible for its anthelmintic activity.
- **Elimination:** The metabolites are primarily excreted in the bile.

Clinical Uses

- Albendazole is used to treat a variety of parasitic infections, including intestinal helminthiasis (such as hookworm, roundworm, and whipworm infections) and tissue helminthiasis (such as cysticercosis and hydatid disease).

Mebendazole

Mechanism of Action

- Mebendazole acts by disrupting the microtubule structure in the parasites, inhibiting glucose uptake and disrupting the parasite's energy metabolism.

Pharmacokinetics

- **Absorption:** Mebendazole is poorly absorbed in the gastrointestinal tract.
- **Metabolism:** It undergoes extensive hepatic metabolism to its active form.
- **Elimination:** The drug and its metabolites are excreted in the feces.

Clinical Uses

- Mebendazole is commonly used to treat intestinal helminth infections, including infections caused by roundworms, hookworms, and whipworms.

Levamisole

Mechanism of Action

- Levamisole is an immunomodulator and acts as a nicotinic acetylcholine receptor agonist. It stimulates the release of acetylcholine at the neuromuscular junction, leading to paralysis and expulsion of the worms.

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Pharmacokinetics

- **Absorption:** Levamisole is well-absorbed after oral administration.
- **Metabolism:** It undergoes hepatic metabolism.
- **Elimination:** The drug and its metabolites are excreted in the urine.

Clinical Uses

- Levamisole is used to treat various worm infections, including roundworm and hookworm infections.

Adverse Effects

- Adverse effects may include nausea, vomiting, diarrhea, and rash.
- Levamisole can cause agranulocytosis (a severe reduction in white blood cells), and regular monitoring of blood counts is recommended during treatment.

Piperazine

Mechanism of Action

- Piperazine paralyzes the helminths by blocking the response of the worm's musculature to acetylcholine.

Pharmacokinetics

- **Absorption:** Piperazine is well-absorbed after oral administration.
- **Metabolism:** It has minimal metabolism in the body.
- **Elimination:** Piperazine and its metabolites are primarily excreted in the urine.

Clinical Uses

- Piperazine is mainly used to treat infections caused by roundworms, particularly Ascaris lumbricoides.

Adverse Effects

- Piperazine is generally well-tolerated, but side effects may include nausea, vomiting, and dizziness.

Ivermectin

Mechanism of Action

- Ivermectin acts as an agonist at the glutamate-gated chloride ion channels in invertebrates, leading to an increase in chloride ion permeability and hyperpolarization of the cell membrane. This results in paralysis and death of the targeted parasites.

Pharmacokinetics

- **Absorption:** Ivermectin is well-absorbed after oral administration.
- **Distribution:** It has a large volume of distribution, and it mainly stays within the tissues.

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- **Metabolism:** Ivermectin undergoes hepatic metabolism.
- **Elimination:** The drug and its metabolites are primarily excreted in the feces.

Clinical Uses

- Ivermectin is used to treat a variety of parasitic infections, including onchocerciasis (river blindness), strongyloidiasis, and certain types of skin conditions caused by parasitic mites.

Adverse Effects

- Adverse effects are generally mild and include headache, dizziness, and gastrointestinal symptoms.
- In some cases, particularly when used in high doses, there have been reports of neurological effects.

Abamectin

Mechanism of Action

- Abamectin is a mixture of avermectins, and its mechanism of action is similar to that of Ivermectin. It acts on glutamate-gated chloride ion channels in invertebrates.

Pharmacokinetics:

- **Absorption:** Abamectin is not well-absorbed after oral administration.
- **Distribution:** It also has a large volume of distribution.
- **Metabolism:** The metabolism of abamectin is not well-documented.
- **Elimination:** The drug and its metabolites are primarily excreted in the feces.

Clinical Uses

- Abamectin is often used in veterinary medicine, particularly as an anthelmintic for livestock.

Adverse Effects

- Adverse effects are generally similar to those of Ivermectin, including mild gastrointestinal symptoms.

Pyrantel Pamoate

Mechanism of Action

- Pyrantel pamoate acts as a depolarizing neuromuscular blocking agent in nematode parasites. It stimulates the release of acetylcholine at the neuromuscular junction, leading to spastic paralysis of the worms.

Pharmacokinetics

- **Absorption:** Pyrantel pamoate is poorly absorbed from the gastrointestinal tract.
- **Distribution:** It remains largely within the gastrointestinal tract.
- **Metabolism:** Pyrantel undergoes minimal metabolism.

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- **Elimination:** The drug and its metabolites are excreted in the feces.

Clinical Uses

- Pyrantel pamoate is commonly used to treat infections caused by intestinal nematodes, including roundworms (Ascaris lumbricoides), hookworms (Necator americanus, Ancylostoma duodenale), and pinworms (Enterobius vermicularis).

Adverse Effects

- Adverse effects are generally mild and may include nausea, vomiting, and abdominal cramps.

Morantel

Mechanism of Action

- Morantel, like Pyrantel, acts as a depolarizing neuromuscular blocking agent in nematode parasites. It causes spastic paralysis by stimulating the release of acetylcholine.

Pharmacokinetics

- **Absorption:** Morantel is absorbed from the gastrointestinal tract.
- **Distribution:** It remains largely within the gastrointestinal tract.
- **Metabolism:** Morantel undergoes minimal metabolism.
- **Elimination:** The drug and its metabolites are excreted in the feces.

Clinical Uses

- Morantel is used primarily in veterinary medicine, particularly in the treatment of intestinal nematode infections in livestock.

Adverse Effects

- Adverse effects are generally mild and may include gastrointestinal symptoms.

Niclosamide

Mechanism of Action

- Niclosamide disrupts the energy metabolism of the parasite by inhibiting oxidative phosphorylation. It uncouples mitochondrial oxidative phosphorylation, leading to a decrease in ATP production, which is essential for the survival of the parasite.

Pharmacokinetics

- **Absorption:** Niclosamide is poorly absorbed from the gastrointestinal tract.
- **Distribution:** It remains largely within the gastrointestinal tract.
- **Metabolism:** Niclosamide undergoes minimal metabolism.
- **Elimination:** The drug and its metabolites are primarily excreted in the feces.

Clinical Uses

- Niclosamide is used to treat intestinal tapeworm infections, such as those caused by Taenia solium (pork tapeworm) and Hymenolepis nana (dwarf tapeworm).

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Adverse Effects

- Adverse effects are generally mild and may include gastrointestinal symptoms such as nausea and abdominal pain.

Praziquantel

Mechanism of Action

- Praziquantel increases the permeability of the schistosome cell membrane to calcium ions, leading to muscle paralysis, tegumental disruption, and subsequent death of the parasite. It is particularly effective against flatworms, including schistosomes and various types of tapeworms.

Pharmacokinetics

- **Absorption:** Praziquantel is well-absorbed from the gastrointestinal tract.
- **Distribution:** It has a large volume of distribution.
- **Metabolism:** Praziquantel undergoes hepatic metabolism.
- **Elimination:** The drug and its metabolites are excreted in the urine.

Clinical Uses

- Praziquantel is used to treat a broad spectrum of parasitic infections, including schistosomiasis, cysticercosis, and infections caused by liver, lung, and intestinal flukes, as well as various types of tapeworms.

Adverse Effects

- Adverse effects are generally mild and may include dizziness, headache, and gastrointestinal symptoms. Allergic reactions are rare.

TRICLABENDAZOLE

Mechanism of Action

- Triclabendazole is effective against liver flukes, particularly Fasciola hepatica. It disrupts the microtubule system in the parasites, causing a disturbance in their energy metabolism, which leads to paralysis and death.

Pharmacokinetics

- **Absorption:** Triclabendazole is well-absorbed after oral administration.
- **Distribution:** It has a high affinity for liver tissues.
- **Metabolism:** Triclabendazole undergoes extensive hepatic metabolism.
- **Elimination:** The drug and its metabolites are excreted in the bile.

Clinical Uses

- Triclabendazole is specifically used to treat infections caused by liver flukes, such as Fasciola hepatica.

Adverse Effects

- Adverse effects are generally mild and may include gastrointestinal symptoms like nausea and abdominal pain.

Oxyclozanide

Mechanism of Action

- Oxyclozanide is effective against a variety of trematodes, including liver flukes. It interferes with the energy metabolism of the parasites, inhibiting oxidative phosphorylation and leading to their death.

Pharmacokinetics

- **Absorption:** Oxyclozanide is well-absorbed from the gastrointestinal tract.
- **Distribution:** It distributes throughout the body.
- **Metabolism:** The metabolism of oxyclozanide is not well-documented.
- **Elimination:** The drug and its metabolites are excreted in the feces.

Clinical Uses

- Oxyclozanide is used to treat infections caused by liver flukes and other trematodes.

Adverse Effects

- Adverse effects are generally mild and may include gastrointestinal symptoms such as nausea and abdominal pain.

Rafoxanide

Mechanism of Action

- Rafoxanide acts on the respiratory chain of the parasite, disrupting mitochondrial function. It interferes with the production of ATP in the parasite, leading to its death.

Pharmacokinetics

- **Absorption:** Rafoxanide is well-absorbed from the gastrointestinal tract.
- **Distribution:** It distributes throughout the body.
- **Metabolism:** Rafoxanide undergoes hepatic metabolism.
- **Elimination:** The drug and its metabolites are primarily excreted in the feces.

Clinical Uses

- Rafoxanide is used in veterinary medicine to treat infections caused by liver flukes and certain gastrointestinal nematodes in ruminants.

Adverse Effects

- Adverse effects are generally mild and may include gastrointestinal symptoms.

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Closantel

Mechanism of Action

- Closantel interferes with the energy metabolism of the parasites, disrupting oxidative phosphorylation. It inhibits mitochondrial electron transport, leading to the depletion of ATP and subsequent paralysis and death of the parasites.

Pharmacokinetics

- **Absorption:** Closantel is well-absorbed after oral administration.
- **Distribution:** It has a large volume of distribution.
- **Metabolism:** Closantel undergoes hepatic metabolism.
- **Elimination:** The drug and its metabolites are excreted in the feces.

Clinical Uses

- Closantel is used in veterinary medicine to treat infections caused by liver flukes, gastrointestinal nematodes, and certain external parasites in ruminants.

Adverse Effects

- Adverse effects are generally mild and may include gastrointestinal symptoms.