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ANTHELMINTICS DRUGS USED IN TRATEMENT OF PARASITE INFECTION CAUSED BY HELMINTHS

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ABSTRACT

Recent advancements in parasitology have led to the discovery of new drug targets for anthelmintic therapy, including ion channels, neuromuscular junctions, and metabolic enzymes unique to helminths. Commonly used drugs such as albendazole and mebendazole function by inhibiting microtubule formation, effectively starving the parasites by blocking glucose uptake. However, the growing incidence of anthelmintic resistance, especially in livestock and endemic regions, has raised concerns over treatment efficacy. This has prompted research into combination therapies and novel drug candidates derived from natural products, such as plant alkaloids and marine peptides. Additionally, RNA interference (RNAI) and CRISPR gene editing are being explored in experimental models to better understand parasite biology and identify resistance mechanisms. These strategies represent promising directions for the development of next-generation anthelmintic agents.

KEYWORDS: Parasitology, Helminths, Glucose uptake, RNA interference, Malnutrition, Non-anthelmintics.

INTRODUCTION

One of the key challenges in managing helminthiasis lies in the limited availability of rapid, affordable, and accurate diagnostic tools, particularly in remote or under-resourced areas. Traditional stool-based microscopy methods, although still widely used, often lack sensitivity and require skilled technicians. As a result, many light or asymptomatic infections remain undetected, contributing to sustained community transmission. Furthermore, even after successful treatment, reinfection rates remain alarmingly high, especially in endemic regions with poor sanitation and limited access to clean water. This has prompted global health programs to shift from isolated treatment efforts to integrated approaches that combine mass drug administration (MDA), health education, improved hygiene practices, and sanitation infrastructure. Notably, the WHO's 2021–2030 roadmap for NTDs emphasizes eliminating soil-transmitted helminthiases as a public health problem in at least 96 countries by 2030. Achieving this goal will require not only consistent drug supply and delivery but also international cooperation, sustained political will, and community-level engagement to break the cycle of infections.

The market offers a wide range of anthelmintic drugs, and parasite control is often achieved through combined therapies. However, there remains a pressing need for the development of newer and stronger anthelmintics, since the currently available synthetic drugs are expensive and tend to lose their effectiveness within two decades due to resistance issues. In recent years, interest in herbal medicines has grown substantially, leading to a rapid increase in the demand for plant-based formulations. At present, only a limited number of plants, such as *Aloe barberi*, *TrachipterusAmmi*, and *Annona senegalensis*, are commonly used as natural anthelmintics, functioning either as vermifuges or vermicides. Additionally, plants like tobacco, walnut, clove, garlic, pineapple, soybean, and other legumes have shown deworming potential, especially when consumed with warm water.

ANTHELMINTICS DRUGS

Helminthic infections are among the most common infections in humans, affecting a large proportion of the world's population. In the treatment of parasitic diseases, anthelmintic drugs are often used indiscriminately. However, the overuse of synthetic anthelmintics has led to increasing concerns about toxicity in humans and the development of drug resistance.

As a result, there is growing interest in discovering and developing new anthelmintic agents from natural sources. Plants, in particular, are considered one of the best sources of bioactive compounds due to their long history of use in traditional medicine. Various medicinal plants have been traditionally employed in the treatment of venereal diseases, wound healing, swellings, abscesses, rheumatism, pain in the lower extremities, skin diseases, leucorrhoea, dysentery, dysuria, and fever.

Anthelmintics are drugs that act by either stunning or killing parasitic worms, thereby expelling them from the host body. They are commonly referred to as **vermifuges** (which paralyze worms) or **vermicides** (which kill worms).

Examples of Natural Anthelmintics

- Adulsa
- Walnut
- Wormwood
- Clove
- Kalonji seeds (Nigella sativa)
- Garlic
- Male fern
- Pineapple
- Diatomaceous earth
- Soya and other legumes
- Honey, water, and vinegar mixture (taken with warm water)

In other words, anthelmintics are drugs used for the treatment of infections caused by parasitic worms, including flukes, nematodes, roundworms, and tapeworms. These drugs are of great importance not only in human medicine but also in tropical and veterinary medicine. Parasitic worms infect not only humans but also livestock and crops, thereby reducing food production and causing significant economic losses. It is therefore not surprising that many drugs currently used in human treatment were initially developed as veterinary medicines. The success of **ivermectin** over the past two decades has revolutionized the treatment of several parasitic diseases. However, this success has also inadvertently reduced the motivation for new anthelmintic drug discovery programs. Broad-spectrum anthelmintics are effective against both parasitic flatworms and nematodes. Nevertheless, the majority of currently available drugs are more limited in their action. For example, **praziquantel**, a widely used drug for the treatment of schistosomiasis, acts primarily by disrupting calcium homeostasis in the parasite. While highly effective against trematodes and cestodes, it shows no significant activity against nematodes.

PHARMACOLOGY OF ANTHELMINTICS

Worldwide, parasitic helminth infections continue to contribute significantly to morbidity and mortality. These infections are primarily caused by intestinal nematodes (roundworms), trematodes (flukes), and cestodes (tapeworms). The burden of disease is unevenly distributed, with low-income countries being the most severely affected. In these regions, helminth infections are associated with poor sanitation, environmental contamination, and conditions that Favor rapid transmission. Consequently, populations in such areas face the highest risk of morbidity.

Roundworms

The migration of larval forms and the transmission of eggs through skin contact with contaminated moist soil, particularly in tropical regions, can result in migraine, eosinophilia, and pulmonary complications. The most common intestinal helminth infections include Ascaris lumbricoides, Trichuris trichiurid, Nicator americanus, and Ancylostoma duodenale, which often show patterns of household aggregation. Autoinfection is frequent, as eggs may be deposited in the perianal region and subsequently re-ingested. Additional transmission routes include contact with contaminated surfaces such as carpets and curtains, as well as airborne inhalation of eggs or ingestion of contaminated food and water. In these cases, humans serve as accidental hosts. Once ingested, the larvae may migrate through various tissues, leading to immunological and pathological damage in the lungs, liver, and central nervous system.

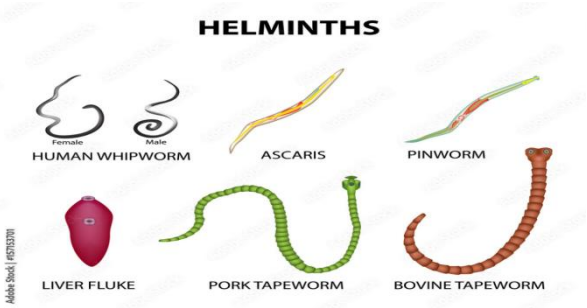
Flukes (Trematodes)

Flukes are parasitic trematodes, primarily of the Schistosoma species, which are transmitted through direct contact with contaminated freshwater. The cercariae penetrate intact human skin, enter the capillaries, and subsequently migrate to the central and portal venous systems, where they mature. Acute schistosomiasis, also known as Katayama fever, is an early manifestation characterized by systemic hypersensitivity reactions and visceral larval migration. Mature adult male and female worms' pair and migrate to the superior mesenteric veins or the vesical venous plexus, depending on the species. The eggs produced are ultimately shed in faeces or urine, perpetuating the transmission cycle.

Tapeworms (Cestodes)

Humans may act as intermediate or definitive hosts for tapeworms. Taenia solium (pork tapeworm) and Taenia saginata (beef tapeworm) are transmitted through ingestion of undercooked pork or beef, respectively. After ingestion, cysticerci develop in the intestines and may cause mild abdominal symptoms. In the case of T. solium, humans may also serve as intermediate hosts, leading to the development of tissue cysts in

extraintestinal sites. Infestation of the central nervous system by T. solium cysts results in neurocysticercosis, a serious condition associated with seizures and neurological deficits. Treatment typically involves albendazole or praziquantel, often in combination with corticosteroids to reduce inflammation.



CLASSIFICATION OF ANTHELMINTICS

Studies on large parasitic nematodes such as *Ascaris sum* and the model organism *Caenorhabditis elegans* have been instrumental in identifying molecular targets for anthelmintic drugs.

1. Benzimidazoles

The first benzimidazole, thiabendazole, was discovered in 1961, followed by the introduction of several other benzimidazoles as broad-spectrum anthelmintics. Their primary mechanism of action lies in disrupting the parasite's cytoskeleton through a specific interaction with β-tubulin, which underpins their efficacy. Benzimidazole (BZD)-containing anthelmintics are extensively metabolized in all mammalian species studied. This class of drugs includes thiabendazole, mebendazole, and albendazole. Their action hampers microtubule formation, leading to the loss of cytoskeletal integrity and motility in the parasite. Consequently, the parasite dies. In addition, these drugs inhibit glucose uptake and ATP synthesis, further compromising parasite survival.

2. Albendazoles

Inhibitors of microtubule polymerization have been shown, both experimentally and clinically, to possess significant antitumor activity. Among these, the benzimidazole (BZD) methylcarbamate derivative albendazole (ABZ) demonstrates high efficacy against a wide range of helminth parasites. These include lungworms, as well as the adult and larval stages of most gastrointestinal (GI) nematodes, cestodes, and trematodes. Clinical trial findings indicate that albendazole is an effective single-dose treatment for several human helminth infections, including *Ascaris lumbricoides*, *Ancylostoma duodenale*, *Necator americanus*, *Trichuris trichiura*, and *Enterobius vermicularis*. Activity against *Strongyloides stercoralis* was also observed, though reduced compared to the other species.

3. Thiabendazoles

Benzimidazole drugs act by binding selectively to β-tubulin in nematodes, cestodes, and flukes, thereby suppressing microtubule formation. This disruption affects essential cellular processes, ultimately leading to parasite death. Thiabendazole, a benzimidazole compound, has been widely used in the treatment of strongyloidiasis, cutaneous larva migrants, and trichinosis. It interferes with microtubular aggregation and has demonstrated an efficacy rate of 75–96% in treating human strongyloidiasis. However, its use is often limited by the occurrence of significant side effects. Albendazole, an alternative therapeutic option, has shown cure rates ranging from 42–100%, depending on dosage regimen and duration of follow-up. While early studies provided little understanding of the mechanisms of action of benzimidazoles in echinococcosis, experimental progress has since expanded knowledge in this area. At present, thiabendazole and albendazole remain the only available therapeutic options for the management of human strongyloidiasis. Nonetheless, the frequent and sometimes severe side effects associated with thiabendazole highlight the urgent need for safer and more effective therapeutic alternatives.[1]

4. Levamisole, Butamisole, Pyrantel, Morantel, Oxantel, Bephenium, and Thenium

Although these drugs have been available for as long as the benzimidazole class, resistance patterns differ significantly. Notably, *Haemonchus contortus* has not developed resistance to levamisoleto the same extent as it has to benzimidazoles.

This group of anthelmintics includes:

1. **Imidazothiazoles**: levamisole, butamisole
2. **Tetrahydropyrimidines**: pyrantel, morantel, oxantel
3. **Quaternary ammonium salts**: bephenium, thenium
4. **Pyrimidines**: Methyridine

These compounds act as agonists at synaptic and extra synaptic nicotinic acetylcholinereceptors (nAChRs) located on nematode body-wall muscle cells. By persistently activating these excitatory receptors, they cause sustained contraction and spastic paralysis, ultimately leading to expulsion of the parasite.

5. Pyrantel and Its Analogues

Pyrantel and related tetrahydropyrimidines function as nicotinic receptor agonists, producing spastic paralysis of nematode musculature. Their mode of action has been studied in detail using *Ascaris suum* body-wall muscle preparations, including analyses at the single-channel electrophysiological level.

Natural Anthelmintics

Most synthetic anthelmintics are not recommended for children under the age of six or for pregnant women due to concerns about toxicity and side effects. In addition, these drugs are often used indiscriminately in the

treatment of parasitic diseases, which raises concerns about resistance and safety. As a result, there is growing interest in developing and discovering new anthelmintic compounds from natural sources, particularly plants. Many plants have long been used in traditional medicine to treat conditions such as rheumatism, leucorrhoea, dysentery, fever, swellings.

Adulsa

Adulsa is a medicinal plant widely used in traditional systems like Ayurveda and Unani. While it is best known for its expectorant, bronchodilator, and anti-inflammatory effects, studies have also demonstrated its anthelmintic (anti-worm) potential.

Active constituents: Vasicine and vasicinone (alkaloids), Flavonoids, tannins, saponins, and phenolic compounds. These phytochemicals are responsible for its paralyzing and killing action on worms.

Mechanism of Anthelmintic Action

1. Paralysis of worms: Alkaloids like *vasicine* interfere with neuromuscular activity of helminths.
2. Cuticle damage: Phenolic compounds disrupt the worm's surface integrity, leading to death.
3. Energy metabolism interference: Extracts may block glucose uptake or mitochondrial function in worms.

Combined Effect with pyrantel pamoate

Adulsa extract improves absorption and distribution of Pyrantel. Its phytochemicals help repair intestinal mucosa and detoxify oxidative stress caused by parasite death. Together, they may reduce reinfection rates and improve overall therapeutic outcome.

CONCLUSION

Currently, only a limited number of anthelmintic drugs are available on the market. Many of these agents are hindered by limitations such as a narrow spectrum of activity, safety concerns, high cost, or impractical delivery systems. In addition, unforeseen issues—most notably the emergence of drug resistance—are likely to further reduce their effectiveness and shorten their lifespan. Before entering clinical trials, any new drug must undergo rigorous evaluation of its toxicity, safety, mechanism of action, and pharmacokinetics through the most precise quantitative assays available. However, the process of drug development remains expensive, time-consuming, and highly interdisciplinary, requiring collaboration across multiple fields of expertise. To ensure efficiency and reliability, there is a growing need for standardized testing requirements agreed upon by all stakeholders. One promising approach in this area is the rational design of new compounds. By applying rational design principles, researchers aim to develop safer, more effective, and broad-spectrum anthelmintics suitable for both clinical use and large-scale treatment programs. With continued efforts in this direction, the future of anthelmintic therapy looks increasingly promising for the millions of people affected by helminth diseases.

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