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Helminthiasis and medicinal plants: a review

Mahesh Bandappa Manke*, Shashikant Chaburao Dhawale, Prasad Govindrao Jamkhande

Department of Pharmacology, School of Pharmacy, SRTM University, Nanded-431 606 (MS), Maharashtra, India

PEER REVIEW

Peer reviewer

Prof. Ravi U. Mane, Assistant Professor, K.S.S. College of Pharmacy, Shikrapur, Dist. Pune, Maharashtra, India.
Tel: +918483925816
E-mail: maneravi13@gmail.com

Comments

This is a good study in which the authors have compiled the information about helminthiasis and medicinal plants with anthelmintic effect. All the information will help researchers to explore its scientific evidence in the prospect studies.
Details on Page 178

ABSTRACT

Helminthiasis is the most common infection caused by worms that is contaminant to human body parts. Normally, the worms live in the gastrointestinal tract, liver and other organs. The currently available anthelmintic drugs, including albendazole, mebendazole, thiabendazole, niridazole, dietylcarbamazine, ivermectin, praziquantel, are widely used to control helminthiasis. But these drugs have serious drawbacks such as hepatotoxicity, loss of appetite, dizziness, nausea, vomiting, abdominal pain, headache and diarrhea. Thus, it is necessary to look for more effective anthelmintic drugs with the minimum side effects. Eighty percent of the world's population relies on traditional medicines and plant extracts and the active constituents are used to meet people's primary health care needs. This review focuses on helminthiasis and the role of traditional plants in the treatment of helminthiasis.

KEYWORDS

Anthelmintics, Cysts, Helminthiasis, Medicinal plants, Nematodes

1. Introduction

Helminth infections are the most common infections in man, and exaggerated worldwide population. It may cause anemia, eosinophilia, pneumonia and prevalence of malnutrition[1]. Helminthiasis is the most common infection caused by worms that is contaminant to human body parts. Normally, the worms not only live in the gastrointestinal tract but may also reside into liver and other organs. When infected people excrete faeces with helminth eggs, the soil in the areas with poor sanitation will be contaminated[2]. There are two clinically important types of worm infections, one is the worms live in the host's alimentary canal and the other is worms live in other tissues of the host's body. Tapeworms or cestodes (*Taenia saginata, Taenia solium, Hymenolepis nana, Diphyllobothrium latum*) and intestinal roundworms or nematodes (*Ascaris lumbricoides, Enterobius vermicularis, Trichuris trichiura, Strongyloides stercoralis, Necator americanus, Ankylostoma duodenale*) are live in the host's alimentary canal while trematodes or flukes (*Schistosoma haematobium, Schistosoma mansoni, Schistosoma japonicum*), tissue roundworms (*Trichinella spiralis, Dracunculus medinensis*) and hydatid tapeworm (*Echinococcus* species) are live in the host's tissues[3]. Several nematodes that usually live in the gastrointestinal tract of animals may communicate a disease to humans and penetrate tissues. A skin infestation, termed creeping eruption, is caused by the larvae of dog and cat hookworms. Toxocariasis is caused by larvae of cat and dog roundworms of the *Toxocara* genus[3].

2. Epidemiology

Helminthiasis is the most common infection mainly

*Corresponding author: Mahesh Bandappa Manke, Department of Pharmacology, School of Pharmacy, SRTM University, Nanded-431 606, Maharashtra, India.
Tel: +91 9923 092833
Fax: +91 2462 229242
E-mail: mahesh.bmanke@rediffmail.com

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caused by the helminths. It is observed in various tropical and subtropical areas, and it is also classified as neglected tropical diseases. They spread the majority of common parasitic infection of human in developing countries. *Ascaris limbricoides*, *Trichuris tritura*, *Necator americanus*, *Ancylostoma duodenale*, schistosomes and filarial worms cooperatively infect more than one billion people, rivaling AIDS and malaria[4]. As the recent evaluations, over a billion people have been infected due to at least one helminth species in Asia, Africa, America and Su-saharan, which leads to severe morbidity, accompanied by persistent shortage, decreased efficiency, and poor socioeconomic development. Helminthiasis has immunomodulatory effects on the host cells, with implications for many affecting pathogens. In fact, in endemic areas, AIDS, malaria and tuberculosis are recognized to be caused by helminthiasis. In most cases, they can induce severe hypersensitivity reaction that leads to chronic allergic reactions called anaphylaxis[4].

3. Etiology of helminthiasis

Helminths have a complex life cycle that often links several species. Helminth infections are mainly caused due to improper sanitation. They enter by mouth in unpurified drinking water or in poorly cooked meat from infected animals. It is also enter through the skin by a skin cut, an insect bite or even after swimming or walking on polluted soil. Humans are the primary hosts for the helminth infections and most of the worms reproduce sexually in the human host, producing eggs or larvae that pass out of the body and infect the secondary host. In some cases, the eggs or larvae may persevere in the human host and become encysted, enclosed with granulation tissue, giving rise to cysticercosis. This is characterized by encysted larvae in the muscles, viscera and more critically in the eye or the brain[3,4].

4. Pathogenesis of helminthiasis

4.1. Direct damage caused by worms

The most evident forms of direct damage are those resulting from the blockage of internal organs or from the effects of pressure exerted by growing parasites (Figure 1). Physically blockage of intestine due to large nematodes (*Ascaris*) or tapeworms (*Taenia*, *Diphyllobothrium*) that produced the formation of granulomas around schistosome eggs and the blockage of blood flow through the liver occured, which leads to pathological changes. Cysts of the tapeworm (*Echinococcus multilocularis*) develop in the liver, brain, lungs or other parts of body cavities can lead to unusal enlargement, organ metastasis and cause necrosis due to pressure exerted by cysts[5].

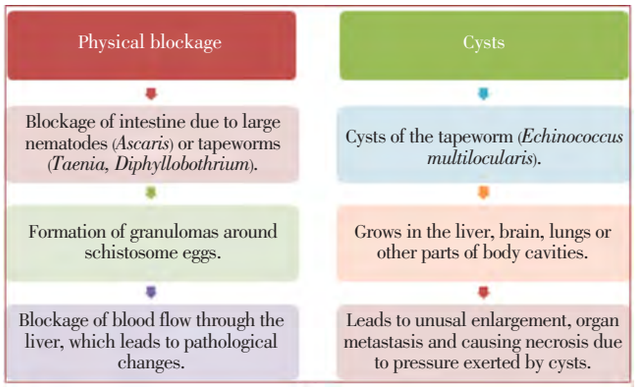

Figure 1. Direct damage caused by large helminths.

4.2. Indirect damage caused by host responses

Indirect damage is seen in the pathology related with schistosome infections, especially with *Schistosoma mansoni* (Figure 2). Hypersensitivity-based, formation of granuloma produced blockage of liver sinusoids and impeding blood flow, which leads to changes in liver pathology. Hypersensitivity-based inflammatory changes probably also contribute to the lymphatic blockage related with filarial infections[5].

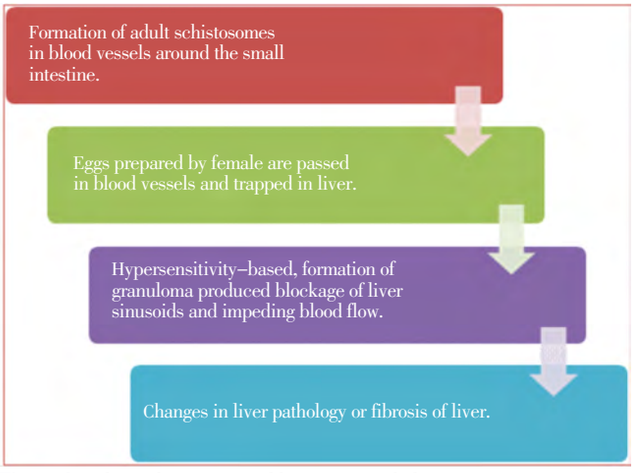

Figure 2. Indirect damage caused by immunopathologic responses.

5. Diagnosis of helminthiasis

Technical limitations of currently available diagnostic methods are the most important problems in the control of helminthiasis. Lacking of standard clinical tests encourages extensive invasion and poses a hindrance to health managements. For basic diagnosis of helminths infection, the specific helminths can be identified from the faeces and their eggs microscopically examined and established using fecal egg count method. This is commonly useful for most species, particularly in veterinary investigations[6]. A range of diagnostic tools currently available is (Figure 3): 1) Parasitological tests, the parasites are identified microscopically; 2) Serological assays, the parasite-specific antibodies are detected in serum samples; 3) Antigen tests, a parasite biomarker is

detected; 4) Molecular diagnosis, the parasite nucleic acid is detected; and 5) Other specific tools for detection in the intermediate hosts[6,7]. However, there are certain limitations such as the failure to identification of mixed infections and the technique is extremely incorrect and unpredictable for schistosomes and soil-transmitted helminths[8].

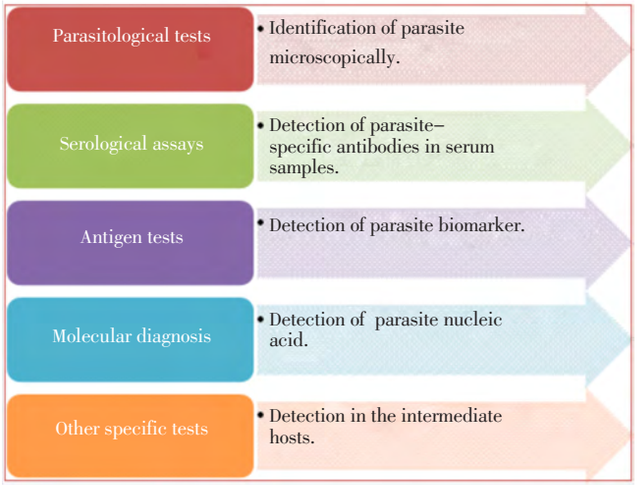

Figure 3. Currently available diagnostic tools for helminthiasis.

6. Clinical features of helminthiasis

These features are depending on the helminth species, intensity of infection, and host age. *Taenia solium* can cause not only neurocysticercosis but also mass lesions in brain. Chronic infection with *Schistosoma* causes granulomas, fibrosis, and inflammation of the spleen and liver. *Echinococcus granulosis* ingested eggs can cause life-threatening anaphylaxis if antigens are released from the cysts. Hookworm and schistosomiasis can infect pregnant women, cause neonatal prematurity and increase maternal morbidity and mortality[9]. Intestinal worms and schistosomes infection are observed in children at school age or younger as compared with any other age group patients. As a result, the young patients suffer from growth retardation, diminished physical fitness, and impairment in memory and cognition[10].

7. Therapy for helminthiasis

Anthelmintic are drugs that act either locally to expel worms from the gastrointestinal tract or systemically to eradicate adult helminthes or developmental forms that invade organs and tissues[11]. An anthelminthic drug can act by causing paralysis of the worm, or by damaging its cuticle, which lead to partial digestion or rejection by immune mechanisms. Anthelminthic drugs can also interfere with the metabolism of the worm, and since the metabolic requirements of these parasites vary greatly from one species to another, drugs that highly effective against one type of worm but be ineffective against others[3]. Anthelmintic drugs with their proper mechanism of actions are given in Table 1[12].

8. Plant remedies in the management of helminthiasis

Most of the existing anthelminthic drugs produce side effects such as abdominal pain, loss of appetite, nausea, vomiting, headache and diarrhea. Mebendazole is a well tolerated drug. However, gastrointestinal side-effects, dizziness have been noted in few patients. Also prolonged use in hydrated or in cysticercosis, causes headache, fever, alopecia, jaundice and neutropenia[13]. In order to eliminate the harmful side-effects of these synthetic anthelmintic drugs, it is important for us to promote the studies of traditionally used anthelmintic plants which will lead to the development of new anthelmintic substances with ease of availability and lesser side-effects[14]. As per World Health Organization, 80% world's population relies on traditional medicines to meet their primary health care needs, most types of which use remedies from plants.

Table 1

Anthelmintic drugs with their mechanism of actions.

Drug	Mechanism of action
Albendazole	Albendazole is thought to act against nematodes by inhibiting microtubule synthesis. It also has larvicidal effects in hydatid disease, cysticercosis, ascariasis, and hookworm infection and ovicidal effects in ascariasis, ancylostomiasis, and trichuriasis.
Mebendazole	Mebendazole probably acts by inhibiting microtubule synthesis; the parent drug appears to be the active form. Efficacy of the drug varies with gastrointestinal transit time, with intensity of infection, and perhaps with the strain of parasite. The drug kills hookworm, *Ascaris*, and *Trichuris* eggs.
Thiabendazole	Thiabendazole is thought to act against nematodes by inhibiting microtubule synthesis.
Diethylcarbamazine citrate	Diethylcarbamazine citrate immobilizes microfilariae and alters their surface structure, displacing them from tissues and making them more susceptible to destruction by host defense mechanisms. The mode of action against adult worms is unknown.
Ivermectin	Ivermectin appears to paralyze nematodes and arthropods by intensifying GABA-mediated transmission of signals in peripheral nerves. It is microfilaricidal. It does not effectively kill adult worms but blocks the release of microfilariae for some months after therapy.
Metrifonate	The mode of action is thought to be related to cholinesterase inhibition. This inhibition temporarily paralyzes the adult worms, resulting in their shift from the bladder venous plexus to small arterioles of the lungs, where they are trapped, encased by the immune system, and die.
Niclosamide	Adult worms are rapidly killed, presumably due to the inhibition of oxidative phosphorylation or stimulation of ATPase activity.
Oxamniquine	The mechanism of action is unknown. Contraction and paralysis of the worms results in detachment from terminal venules in the mesentery and transit to the liver, where many die; surviving females return to the mesenteric vessels but cease to lay eggs.
Piperazine	It reversibly inhibits neuromuscular transmission in the worm, probably by acting like GABA, the inhibitory neurotransmitter on GABA-gated Cl^- channels in nematode muscle.
Praziquantel	Praziquantel appears to increase the permeability of trematode and cestode cell membranes to calcium, resulting in paralysis, dislodgement, and death.
Pyrantel pamoate	The drug is a neuromuscular blocking agent that causes release of acetylcholine and inhibition of cholinesterase and results in paralysis, which is followed by expulsion of worms.

Even the modern pharmacopoeia still contains at least 25% of drug derived from plants and many others which are semi-synthetic, built on prototype compounds isolated from plants[15]. The phytoconstituents showing anthelmintic effect includes alkaloids, saponins, polyphenols, tannins, *etc*. Alkaloids suppress the transfer of sucrose from stomach to small intestine, diminish the support of glucose to the helminths, and act on CNS causing paralysis. Saponins possess vacuolization and disintegration of teguments. Polyphenols and tannins increase the supply of digestible proteins by animals via forming protein complexes in rumen, interfere with energy generation by uncoupling oxidative phosphorylation, cause a decrease in gastrointestinal metabolism which leads to paralysis and death of helminths[16]. Medicinal plants list with proven anthelmintic effects are compiled in Table 2.

Table 2
Medicinal plants with anthelmintic potential.

Plant name	Family	Part of the plant used	Reference
Achyranthes aspera	Amaranthaceae	Stem	[17]
Aerva lanata	Amaranthaceae	Aerial parts	[18]
Alstonia boonei	Apocynaceae	Bark	[19]
Annona sqamosa	Annonaceae	Leaves	[20]
Baliospermum montanum	Euphorbiaceae	Root	[21]
Bambusa vulgaris	Bambusoideae	Leaves	[22]
Barleria buxifolia	Acanthaceae	Leaves	[23]
Benincasa hispida	Cucurbitaceae	Leaves	[24]
Borassus flabellifer	Palmae	Leaves	[25]
Capparis zeylanica	Cappardiaceae	Root	[26]
Cassia auriculata	Ceasalpinaceae	Leaves	[27]
Croton bonplandianium	Euphorbiaceae	Leaves	[28]
Citrus medica	Rutaceae	Leaves	[29]
Clerodendrum viscosum	Verbenaceae	Leaves	[30]
Cocos nucifera	Palmae	Fruit	[31]
Coldenia Procumbens	Boraginaceae	Aerial parts	[32]
Coleus aromaticus	Lamiaceae	Root	[33]
Cotyledon orbiculata	Crassulaceae	Shoots	[34]
Curcuma amada	Zingiberaceae	Rhizome	[35]
Diplazium esculentum	Athyriaceae	Rhizome	[36]
Drypetes sepiaria	Euphorbiaceae	Leaves	[37]
Ficus bengalensis	Moraceae	Fruit	[38]
Flacourtia sepiaria	Flacourtiaceae	Leaves	[39]
Gymnema sylvestre	Asclepiadaceae	Leaves	[40]
Hedychium spichatum	Zingiberaceae	Rhizome	[41]
Helicteres isora	Sterculiaceae	Fruit	[42]
Heliotropium indicum	Boraginaceae	Leaves	[43]
Hermannia depressa	Malvaceae	Shoots	[34]
Jasminum mesnyi	Oleaceae	Leaves	[44]
Juglans regia	Juglandaceae	Stem bark	[45]
Leea asiatica	Vitaceae	Leaves	[46]
Leonotis nepetiifolia	Lamiaceae	Leaves	[47]
Luffa cylindrica	Cucurbitaceae	Leaves	[48]
Millingtonia hortensis	Bignoniceae	Bark	[49]
Mimuosops elengi	Sapotaceae	Root and bark	[37,50]
Murraya koenigii	Rutacae	Root	[51]
Nicotiana glauca	Solanaceae	Shoots	[34]
Oenothera rosea	Onagraceae	Stem and root	[52]
Paederia foetida	Rubiaceae	Leaves	[53]
Pajanelia longifolia	Bignoniaceae	Bark	[54]
Portulaca oleracea	Portulacaceae	Leaves	[55]
Saraca indica	Leguminosae	Leaves	[56]
Spermacoce ocymoides	rubiaceae	Leaves	[57]
Tamarindus indica	Caesalpiniaceae	Bark	[58]
Tephrosia purpurea	Fabaceae	Leaves	[59]
Terminalia arjuna	Combretaceae	Bark	[60]
Uncaria gambier	Rubiaceae	Leaves	[61]
Vernonia amygdalina	Asteraceae	Leaves	[19]
Zingiber zerumbet	Zingiberaceae	Rhizome	[41]
Ziziphus mauritiana	Rhamnaceae	Leaves	[62]

Conflict of interest statement

We declare that we have no conflict of interest.

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Comments

Background

Helminth infections have severe consequences for the health of millions of people worldwide. The synthetic drugs used in the treatment of helminthiasis can cause various side effects, therefore, to overcome these traditional drug therapies have mainly preferred. The authors have compiled information about helminthiasis and medicinal plants for its treatment.

Research frontiers

The aim of this review article is to compile the entire information of helminthiasis and the role of traditional plants in the treatment of helminthiasis.

Related reports

The authors have summarized the whole pathophysiological information about helminthiasis and medicinal plants used in the treatment of helminthiasis.

Innovations & breakthroughs

This review article is very important to promote the studies of traditionally used anthelmintic plants which will lead to the development of new anthelmintic substances with ease of availability and lesser side-effects.

Applications

This review article has been found out to ba a new prospect in the treatment of helminthiasis with the help of herbal drugs.

Peer review

This is a good study in which the authors have compiled the information about helminthiasis and medicinal plants with anthelmintic effect. All the information will help researchers to explore its scientific evidence in the prospect studies.

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