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Helminthiasis- Causes and Treatments

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Abstract:

Helminthiasis is a common infestation, which affects the human body parts like liver, gastrointestinal tract and other organs. It may cause malnutrition, loss of appetite, anemia, pneumonia and eosinophilia. There are two clinically important types of worm infestation, one in which the worms live in the host alimentary canal and the other in which worms live in other tissue of the host's body. Almost one-third of the world population is suffering from these intestinal parasites. Though a large number of conventional drugs like albendazole, mebendazole, ivermectin and praziquental are available, they have been reported to produce side effects and dose-relatedtoxicity. This has led to increased demand of screening medicinal plant for their anthelmintic activity. Anthelmintic drug compounds including arecoline, pelletierine, filixic acid, aspidin, ascaridole and Curcumin are also reported to be obtained from plants. The article focuses on the limitations of the conventional treatment of helminthiasis and throws light on various herbal drugs that have been successfully used as anthelmintic compounds.

Key words:*Helminthiasis, anthelmintic, Nematodes, Cestodes, herbal drugs*

1. Introduction

The word Helminth is derived from the Greek word"helmins" which means worms. Unlike other parasites, the body of worms is multicellular and they havea complex life cycle. Humans and animals are more prone to helminth infestation than to any other parasites. Helminths fulfil their nutritional requirement by feeding on the host's nutrient supply, which results in the malnutrition like condition in the host [1]. Helminths infestations such as ascariasis, ancylostomiasisand schistosomiasis constitute the bulk of the thirteen diseases classified as neglected tropical diseases by the WHO [1]. Helminthiasis is the most common infestation, which affects the human body parts like liver, gastrointestinal tract and other

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organs. It may cause malnutrition, loss of appetite, anemia, pneumonia and eosinophilia. There are two clinically important types of worm infestation, one in which the worms live in the host alimentary canal and the other in which worms live in other tissue of the host's body [2]. Helminths infestation in gut and tissue constitute a major cause of death in the developing countries [3]. Mainly, the helminths are divided into two phyla; nematodes and platyhelminths. Nematodes (commonly known as roundworms) consist of the major intestinal worms (also known as soil-transmitted helminths) and the filarial worms that cause lymphatic filariasis (LF) and onchocerciasis. Platyhelminths (commonly known as flatworms) consist of the flukes (also known as trematodes) and the tapeworms (also known as cestodes) [4]. Among the helminths, soil-transmitted helminths (STHs) are the most common intestinal parasites. Common soil transmitted helminths comprise are *Ascaris lumbricoides*, *Trichuris trichiura*and*Ancylostoma duodenale*[5].

2. Epidemiology

Helminthiasis is the most common type of the intestinal infestation. Almost one-third of the world population is suffering from these intestinal parasites. The disease gains much attention as it affects both the nutrition and immune status of the infected individual, particularly those living in the tropical and sub-tropical regions [4]. This infestation is highly spread in the regions of South Asia, China, Central Africa and in the coastal regions of west Africa. There is the widespread presence of Trichuris infestations in Central Africa, Southeast Asia and, southern India.

Hookworm infestation influences approximately 500 million populations, accompanied by 5.1 billion people at risk for receiving this infestation all over the world [6]. In India, the pervasiveness of hookworm infestationswas found to be unpredictable[7].

3. Economic burden of helminthiasis

3.1 Indian scenario

The economic liability of helminthiasis can be evaluated by adding the direct costs and indirect costs including the expenditure on prevention and treatment, as well as productive labour cost for the reason of morbidity and mortality [8]. In total, it has been projected as an average of $1 billion per year fromIndia only [9]. The struggles on treatment and control have resulted in protection of nearly 22 million populations from above-mentioned disease with an estimation of $24.2 billion savings [10]. As per certain estimations, the patients suffering

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from chronic lymphatic filariasis in India drop as much as 11 years of productivity, which is about $50 lost per year or equal to 15% of an individual income [11]. The treatment cost of Cysticercosis affected by *Taenia solium* was assessed at $15.27 million [8]. On the other hand, 11.78 million people suffered from Hookworm infestation caused by *Ancylostoma duodenale and Necator americanus*and treatmentcost sum up as $471 million [6].

3.2 Worldwide scenario

In humans, infestations caused by Helminths are highest incomparison to other infestations [12]. The World Health Organization carried out eight-yearprogram to eliminate Lymphatic Filariasis by which direct economic benefit of $21.8 billion would be gained by treating and considering 31.4 million patients [9]. In China, each person invests $1 in the treatment of lymphatic filariasis [13].The cost for treatment of Cysticercosis caused by *Taenia solium* was estimated at $28.3 million in Central America and $16.6 million in the Eastern Cape [8]. In sub-Saharan Africa, soil-transmitted helminths infect about 90 million from child population, but these children can be treated with single dose of anthelmintic which is the practiced school-based approach of treating children at an estimation cost of $5-$7.6 million [14]. A broad range of deworming program was conducted at Vietnam that involved around 2.7 million children which costed $0.03 per student [15]. Based on the future scenario, controlling soil-transmittedhelminths in the Caribbean and Latin America would cost approximately $41 million [16]). The treatment of hookworm infestation cost $20.9 billion worldwide. In china, the presence of 35.91 million hookworm patients associated with health outcomes leads to $6.7 billion in productivity losses.After the STHs, the second biggest cause of parasite infestation is schistosomiasis [17]. In order to control the Schistosomiasis, some programs were started. In Burkina Faso, the mass drug administration (MDA) of praziquantel and albendazole to children by the community and school attain more than 90% coverage at a rate of $0.32 per child [18]. The total cost of the program was reported to be $1.07 million, from which about two third was spent on medications [19].

4. Etiology

In the transmission of the infestation, sanitation plays a major role. Unpurified drinking water and improperly cooked meat from infected animals are the most common source of the infestation. Also, the infestation may be spread by insect bites, swimming in polluted water and contact between the wound and polluted soil. These worms mainly infect the humans. They reproduce inside the host, producing eggs and larvae, which pass from the primary host

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to the secondary host spreading the infestation. The presence of eggs or larvae in the host may lead to cysticercosis. This condition is characterized by encysted larvae in the muscles, viscera and more critically in the eye or the brain [2].

5. Pathology

5.1 Direct damage caused by the helminths

Blockage of internal organs physically or by pressure exerted by worms is considered as direct damage. Large nematodes (*Ascaris*) or tapeworms (*Taenia*) physically block the intestines and blood flow to the liver leading to a pathological condition. Cysts of the tapeworm (*Echinococcus multilocularis*) develop in the liver, brain, lungs or other parts of bodycavities and can lead to unusual enlargement, organ metastasisand may cause necrosis due to pressure exerted by cysts[2].

5.2 Indirect damage by the helminths

Schistosome infestations, especially with *Schistosoma mansoni*, are one of the examples of indirect damage. Hypersensitivity-based, formation of granuloma produces blockage of liver sinusoids impeding blood flow that further leads to liver diseases. Inflammatory changes based on hypersensitive reaction may also lead to the lymphatic blockage related with filarial infestations [2].

6. Treatment of helminthiasis

6.1 Conventional treatment

Parasitic helminth infestations are reported to increase the mortality and morbidity rate worldwide [20]. Anthelmintic drugsact locally to throw out worms from the gastrointestinal track (GIT) or systemically eliminate adult helminths or/and development forms that invade tissues& organs [21]**.** Almost all types of helminth infestations can be treated with the use of five anthelmintic drugs i.e. praziquantel, albendazole, ivermectin,mebendazole, and diethylcarbamazine (DEC) [22].

Albendazole and mebendazole are broad spectrum oral anthelmintics. Albendazole acts by inhibiting the microtubule synthesis in roundworms. Mebendazole irreversibly blocks glucose uptake, which in turn, leads to paralysis and death of roundworm and tapeworm [1]. Standard

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doses of albendazole 400 mg and mebendazole 500 mg are used for the treatment of patients above the age of one year. These treatments may not eliminate heavy infestation, but efficiently reduce the morbidity and worm burden [22]. Albendazole is reported to be better tolerated and slightly more efficacious than mebendazole [3].

Ivermectin is most effective semisynthetic macrocyclic lactone with a broad spectrum. The drug shows activity against a wide range of the helminthic parasites. Ivermectin is effective against a number of human infestations including lymphatic filariasis and Ascaris onchocerciasis [22].

Ivermectin causes ion channel mediated helminth muscle paralysis while praziquantelcauses muscle paralysis of helminths only. The other drugs include piperazine, niclosamide, and levamisole which expel the worms from GIT [3].

Concomitant administration of two or three drugs is effective treatment option and serves two purposes i.e. to increase the efficacy of the drug against parasites such as *Trichuris trichiura* which are very difficult to treat with a single drug and to reduce the drug administration frequency, especially in mass treatment programs. Pyrantel and mebendazole are effectively used for the treatment of trichuris infestation which is more effective than treatment with the single drug [22].

Recently, newer anthelmintic drugs have been reported. Tribendimidine is licensed in China since 2004 as an effective treatment of intestinal helminths and acts by binding tonicotinic acetylcholine receptor as an agonist. A single dose of tribendimidine is specifically effective against *Ascaris lumbricoides* and *Ancylostoma duodenale* but not against *Trichuris trichiura*. Another new drug is monepantel, an amino acetonitrile derivative that acts on nicotine acetylcholine receptor and leads to paralysis and death of worms [23].

Table 1. Conventional drugs for the treatment of helminths

S.No	Disease	Treatment	Dose	Reference
1		**Nematodes**		
1.1	Enterobiasis	Albendazole or mebendazole	400 mg daily oncea day 100 mg daily once a day	[24]
1.2	Trichuriasis	Albendazole or mebendazole	400 mg daily oncea day 100 mg daily twice a day	[24, 25]
1.3	Ancylostomiasis	Albendazole or mebendazole	400 mg orally oncea day 100 mg orally twice a day	[25, 26]
1.4	Trichinosis	Albendazole or mebendazole	400 mg orally twice a day 200-400 mg orally twice a day	[27]
2		**Cestodes**		

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2.1	Cysticercosis	Praziquantel	5-10 mg/kg orally once a day	[28]
2.2	Echinococcosis	Albendazole	400 mg orally twice a day	[29]
3		**Trematodes**		
3.1	Fascioliasis	Triclabendazole	10mg/kg orally once or twice	[30]
3.2	Schistosomiasis	Praziquantel	20mg/kg orally twice a day	[31]

6.2 Limitations of Conventional treatment

Conventional drugs have been reported to produce side effects and dose-relatedtoxicity[20]. Albendazole, when used for short-term therapy of gastrointestinal helminths produces side effects like headache, nausea, dizziness, vomiting, rashes and edema.

Dose-dependent side effects of Mebendazole include allergic reaction, alopecia, and hypothermia.All the anthelmintic drugs are unsafe to prescribe for pregnant women and young children.Praziquantelcause headache, diarrhoea, abdominal pain, seizures and mental changes.The side effects of Ivermectin include nausea, diarrhoea, hepatitis or dizziness [1]. Drug resistance is the major limitation to the helminths which is threatening human health [32].

6.3 Herbal treatment

About 80% of world population, specially in developing countries rely on natural sources for primary health care [20]. Conventional anthelmintic drugs are less effective due to development of resistance in helminths.This has led to increased demand of screening medicinal plant for their anthelmintic activity [33].Plant-based medicines have shown great efficacy against a variety of parasites of medical and veterinary importance. Moreover, the chances of drug resistance against phytoanthelmintics are less than that for chemical anthelmintics [32]. Herbal compounds like artemisinin and quinine alkaloids are effective against schistosomiasis. Anthelmintic drug compounds are also reported to be obtained from plants including arecoline, pelletierine, filixic acid, aspidin, ascaridole and Curcumin [34]. Curcumin extracted from turmeric is well known to exhibit anti-parasitic effect against Schistosoma [35]. Ascaridole is an anthelmintic compound isolated from chenopodium plant. It is reported to be effective against hookworm infestation [36]. Aspidin and filixic acid isolated from *Dryopteris filixmas* show activity against intestinal cestodes. Pelletierine isolated from *Punica granatum* and arecoline from *Areca catechu*, which targets acetylcholine receptors show anthelmintic activity [34]. Rottlerin and isorottlerin isolated from *Mallotus philippensis* or kamala tree also have shown strong anthelmintic activity.

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Table 2. Herbal drugs used for the treatment of helminthiasis

S.no	Name of plant	Part used	Active ingredient	Parasite	Reference
1	*Allium sativum*	Bulb	Allicin	Roundworm	[33]
2	*Artemisia annua*	Not reported	Artemisinin	Schistosoma mansoni	[37]
3	*Butea monosperma*	Seeds	Palasonin	Nematode	[38]
4	*Carica papaya*	Seeds	Benzylisthiocynate	Ascaris lumbricoides	[39]
6	*Curcubita maxima*	Seeds	Cucurbitin	Ascaris lumbricoides	[40]
7	*Curcurbita moschata*	Seeds	Cucurbitin	Cestodes	[41]
8	*Cymbogon martini*	Whole Plant	Geraniol	Nematode	[42]
9	*Cyperus rotentus*	Roots	Not Reported	Tapeworm	[43]
10	*Embelia ribes*	Seeds	Embelin	Tapeworm	[44]
11	*Evodia ruteacarpa*	Fruit	Atanine	Nematode	[45]
12	*Famariaparviflora*	Plant Powder	Alkaloids	Trichuris infestation	[46]
13	*Hyoscyamus niger*	Seeds	Not Reported	Nematode	[47]
14	*Mallotus philippinesis*	Fruit	Rottlerin	Tapeworm	[48]
15	*Mangifera indica*	Stem	Mangiferin	Trichinella spiralis	[49]
16	*Melia azedarach*	Fruit, Leaves	Not Reported	Taenia species	[50]
17	*Moringa oleifera*	Seeds	Tannins, Saponins	Ascaris summ	[51]
18	*Nigella sativa*	Seeds	Thimoquinone	Antifasciolic	[52]
19	*Ocimum sanctum*	Leaves	Eugenol	Caenorhabditis elegans	[53]
20	*Piper longum*	Fruit, Leaves	Piperine	Ascaris lumbricoides	[54]
21	*Punica granatum*	Fruit	Not reported	Nematode	[46]
22	*Zingiber officinale*	Rhizomes	Zingiberene	Ascaris lumbricoides	[55]

7. Conclusion

Last few decades conventional drugs were used for the treatment of helminthiasis. These drugs are associated with a number of side effects e.g. nausea, headache, alopecia, hypothermia and dizziness etc. Also conventional drugs produce drug resistance against helminths that led to increased demand of screening medicinal plants for their anthelmintic activity. Herbal drugs, on the other hand, have proved to be cost-effective, easily available, effective and safe.

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