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Review Article

ANTHELMINTIC POTENTIAL OF HERBAL DRUGS

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ABSTRACT

The present paper deals with the field observations recorded on the traditional indigenous therapeutic applications of the plants *Butea monosperma* (Lam.) seeds used by the inhabitants of the Sagar district, M.P. (India). Even today a number of plants of the local flora are used for curing various ailments and diseases. The information is given in a tabular form as scientific names of plants in alphabetic order followed by family, part used, effective against, and target animals. Information on local/vernacular names of plants, uses, parts used names of ailments and modes of usage are given in detail. Information on traditional uses and commercial uses as well as biological activities of the related species is included on the basis of the existing relevant literature so as to present a comprehensive account. In this review we compiled available literatures from libraries, scientific journals and online database query's on plants and remedies used in traditional medicinal systems for such diseases.

Keywords: Butea monosperma, helminthes, Albendazole.

INTRODUCTION

Helminthes effecting man and cattle: Helminthes are recognized as a major problem to livestock's throughout tropics (Adewunmi et al, 2001). Helminth infections are one of the most prevalent diseases in developing and developed countries (Krogstad et al, 1998). Globally, an estimated 2 billion people are infected by intestinal nematodes (Wen et al, 2008). Most diseases caused by helminthes are of a chronic and debilitating in nature, they probably cause more morbidity and greater economic and social deprivation among humans and animals than any other single group of parasites. The parasitic gastroenteritis is caused by mixed infection with several species of stomach and intestinal worms, which results in weakness, loss of appetite, decreased feed efficiency, reduced weight gain and decreased productivity (Gibbs, 1986). Helminths consume nutrients from their host, thereby causing or aggravating malnutrition which results in retarded growth and physical development. Consequently, symptoms like retarded cognitive development, iron-deficiency anaemia, abdominal pains and related health problems are characteristic features of most heavy helminth infections (Crompton et al, 2002, Kirwan et al, 2009). In addition, research on development of new treatment regimes against helminth infections has been relegated to the background by the western governments,

researchers and the pharmaceutical industries due to poor economic prospects and the presumed low priority of the diseases that go with it (Geary et al, 1999, Gilles et al, 2002).

Helminth infections resulting to diseases such as ascariasis, hookworm infection and schistosomiasis constitute the bulk of the 13 diseases classified as neglected tropical diseases (NTDs) by the WHO (Hotez et al, 2007a). These incapacitating diseases have continued to inflict severe disability and often deaths. It is more pronounced among the impoverished population living in marginalized areas of the world (Hotez et al, 2007b). In most developing countries, intestinal helminth infections are a major health concern because factors that pre-dispose humans to these infections abound in these areas (Ijagbone et al, 2006). Estimated that the global burden of helminth infections, in terms of disability-adjusted life years (DALYs), is 39 million life years which was comparable to that of tuberculosis (34.7 million DALYs) or malaria (46.5 million DALYs), the two major human infectious diseases associated with a high mortality rate. Factors that sustain the parasite life cycles and favour the proliferation of the disease vectors include poor sanitation, poverty, unsafe water, malnutrition and ignorance (Brooker et al, 2006b). Children, especially those at a preschool age (less than five years), have been identified as the most vulnerable group with very high rates of infection (De silva et al, 2003, Sinniah et al, 1984). Due to the asymptomatic nature of these diseases, the helminths remain undetected and children born in an endemic region may harbour the worms for the most part of their lives (WHO, 1987). The manifestation of most parasitic diseases is due to the host responses to the presence of the parasite (Murray et al, 1998). Also worth considering is the fact that the immune response triggered by helminth infection may drain the body's ability to fight other diseases, making affected individuals more prone to co-infection (Watkins et al., 1997).

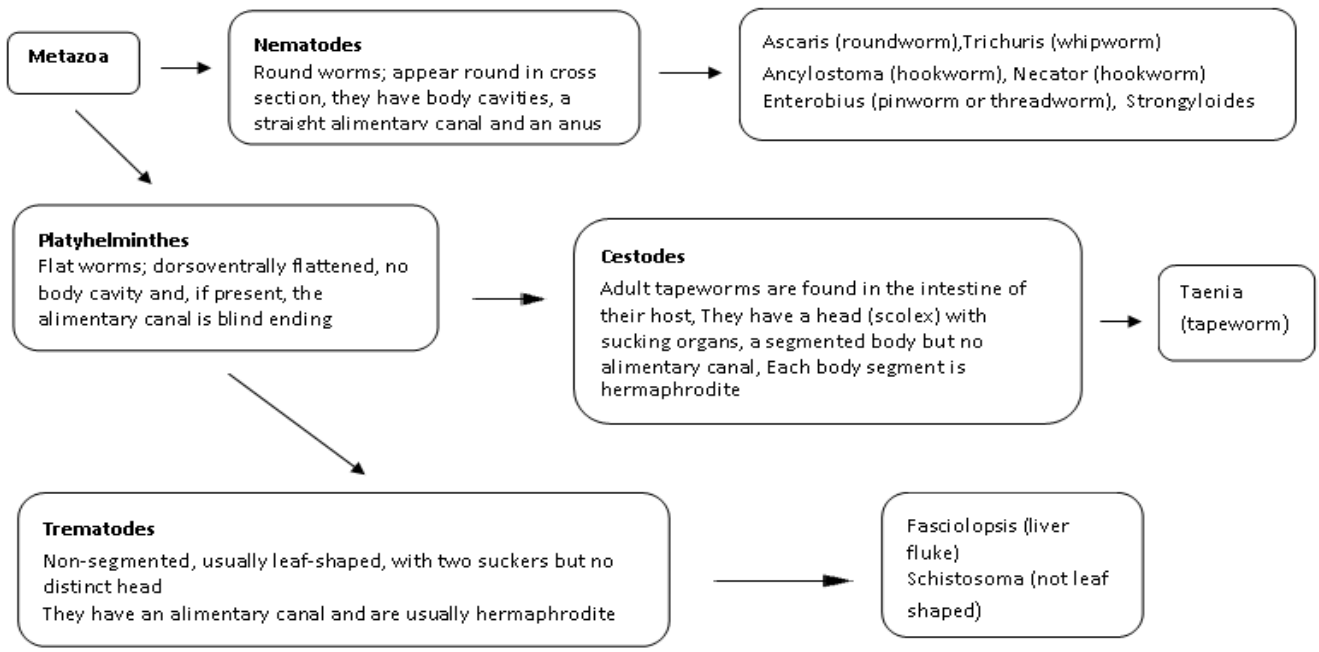
Classification of helminths : Helminths are divided into three groups based on their body segmentations, namely: Trematodes (flukes), Nematodes (roundworms) and Cestodes (tapeworms). Helminths have multi-cellular bodies and complex life cycles involving maturation in a host organism. The word helminth comes from Greek hélmins, a kind of worm.

Common cattle parasite (Floron et al, 1914)

Internal parasites:

1. (Hairworms (*Nematomorpha*): The gastrointestinal tract of cattle is often infected with hairworms, also called stomach worms and intestinal worms.

Classification of helminths



2. Coccidia (*Hepatozoon, Toxoplasma)*: Coccidia cause an intestinal disease of young cattle, usually 3 weeks to 6 months old, but can affect cattle up to 2 years old.
3. Liver flukes (*Clonorchis sinensis, Fasciola hepatica)*: Cattle living in wet areas with alkaline soils may develop liver fluke infections.
4. Strategic worming: Wormers are administered to cattle not only as a treatment to kill internal parasites and to stop damage caused by parasites

External parasites:

1. Horn flies (*Haematobia irritans)*: Horn flies reproduce in fresh cattle manure from early spring to late fall. Horn fly populations usually peak in late spring and again in late summer or early fall.
2. Lice (*Pediculus humanus capitis*): Biting lice and blood-sucking lice are transmitted between cattle by contact, especially in the fall, winter and spring when egg production increases in cool weather.
3. Grubs (*Trichlorfon, Halofenozide)*: Cattle grubs (warbles, wolves) are larvae of heel flies, which lay eggs on hairs of the lower legs of cattle in late winter and spring.

Mechanism of action of helminths:

Parasitic worms or helminths required nutrients are derived from the host, causing the parasitic activity of most helminths. Helminths consume nutrients from their host, thereby causing or aggravating malnutrition which results in retarded growth and physical development. Consequently, symptoms like retarded cognitive development, iron-deficiency anaemia, abdominal pains and related health problems are characteristic features of most heavy helminth infections (Crompton et al, 2002, Kirwan et al, 2009). The increase in helminth infection and their growing resistance to most broad spectrum chemotherapeutics is a major problem facing human health (James et al, 2007, 2009). A decline in host immune status as a result of helminth infection thereby increasing the host susceptibility to other pathogens (Brooker et al, 2006, Borkow et al, 2006). Also worth considering is the fact that the immune response triggered by helminth infection may drain the body's ability to fight other diseases, making affected individuals more prone to co-infection (Watkins et al., 1997).

A division of eukaryotic parasites,live inside their host (Maizels et al., 2003). They are worm-like organisms that live and feed off living hosts, receiving nourishment and protection while disrupting their hosts' nutrient absorption,

Burden states of some major parasitic infections (Bell, 1996, Crewe, 1985)

Parasite	**Disease**	**Population infected**	**Deaths/yr**
Soil transmitted helminths: Roundworm (*Ascaris*) Whipworm (*Trichuris*) Hookworm (*Ancylostoma* and *Necator*)	Pnemonitis, intestinal obstruction, Bloody diarrhoea, rectal prolapse , Coughing, wheezing, abdominal pain and anaemia	2 billion	200,000
Schistosoma	Renal tract and intestinal diseases	200 million	15,000
Filariae	Lymphatic filariasis and elephantiasis	120 million	Not fatal but 40 million disfigured or incapacitated
Trypanasoma cruzi	Chagas disease (cardiovascular)	13 million	14,000
African Trypanosomes	African sleeping sickness	0.3 – 0.5 million	48,000
Leishamania	Cutaneous, mucocutaneous and visceral leishmaniasis	12 million (2 million new cases/yr)	50, 000

causing weakness and diseases. Those that live inside the digestive tract are called intestinal parasites. They can live inside humans as well as animals.

Helminths infection is frequently symptomatic. Conditions associated with intestinal helminth infection include intestinal obstruction, insomnia, vomiting, weakness, and stomach pains. (John et al., 2006).A part the natural movement of worms and their attachment to the intestine may be generally uncomfortable for their hosts (Watkins et al., 1997). The migration of Ascaris larvae through the respiratory can also lead to temporary asthma and other respiratory symptoms (John et al., 2006).

Helminths act by a different ways to produce various symptoms.

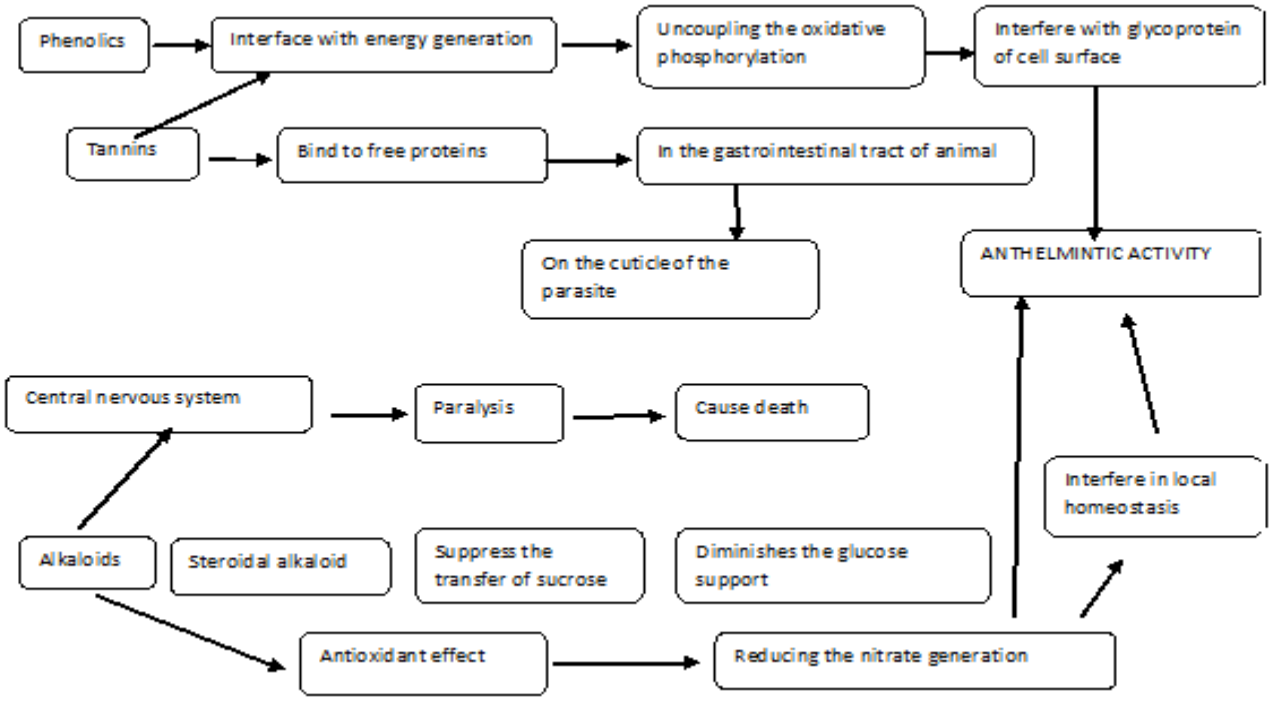
Nutrition: Intestinal helminths may impair the development of their human hosts through their impact on nutrition. Intestinal helminth infection has been associated with problems such as vitamin deficiencies, stunting, anemia, and protein-energy malnutrition, which in turn affect cognitive ability and intellectual development. (WHO Expert Committee., 1987) Parasite infection may affect nutrition in several ways. Whipworm (Levinger B., 1992) and Roundworm may compete directly with their hosts for access to nutrients.

In humans and pigs, Ascaris has been tied to temporarily induced lactose intolerance and Vitamin A, nitrogen, and fat mal absorption. (WHO Expert Committee., 1987) Impaired nutrient uptake may result from direct damage to the intestine's mucosal walls as a result of the worms' presence, but it may also be a consequence of more nuanced changes such as chemical imbalances caused by the body's reaction to the helminths (Crompton et al., 1993). Alternatively, (Watkins and Pollitt 1997) reported that the worms' release protease inhibitors to defend against the body's digestive process which may impair the breakdown of other nutritious substances as well (Watkins et al., 1997). . Finally, worm infections may also cause diarrhoea and speed "transit time" through the intestinal system, further reducing the body's opportunity to capture and retain the nutrients present in food (WHO Expert Committee., 1987).

Immunology of Parasitic Helminth Infections: Many helminth parasites are long-lived and cause chronic infections. The immune response develops during the infection often proceeds to cause pathologic changes that may act as the primary cause of disease. A well studied example of this is the granulomatous reaction that sequesters schistosome eggs. Some of the eggs of adult *Schistosoma mansoni* parasites living within the portal vasculature, are carried to the liver where they become lodged in the sinusoids. Antigens (Ag) released from eggs induce a marked Th2 response that orchestrates the development of granulomatous lesions in the liver (Cheever et al., 2000). The host-protective nature of these lesions has been demonstrated by work in a mouse model of infection with the human parasite. Infected mice that lack CD4 cells are incapable of making granulomas and die due to the toxic effects on hepatocytes of certain egg proteins (Amiri et et al., 1992, Dunne et al., 1983). By surrounding the eggs, the CD4 cells help in the formation of granulomes which essentially segregates the eggs from the hepatic tissues and allows continuing liver function. However In long term, as the eggs die and the granulomas resolve, fibrosis can develop (Cheever et al., 2000). This can lead to increased portal blood pressure and the development of portal varices. Bleeding from varices is the most common cause of death due to schistosomiasis. The IL-13 plays a central role in the development of fibrosis (Cheever et al., 2000, Chairamonte et al., 1999, Fallon et al., 2000). Extensive research showed that parasitic worm have the ability to deactivate certain immune system cells, leading to a moderate immune response (Cooke, 2008, Melendez et al., 2007, Bashir et al., 2002, Moreels et al., 2004, Weinstock et al., 2004). Often, such a response is beneficial to both parasite and host. This immune "relaxation" is incorporated throughout the immune system, decreasing immune responses against harmless allergens, gut flora, and the body itself. In the past, helminths were thought to simply suppress T-helper Type 1 (Th1) cells while inducing T-helper Type 2 (Th2) cells and (Rook 2008) only explained the regulatory effects of parasitic worms on autoimmune diseases caused by Th1 cells. However, a part from this helminths also regulate Th2-caused diseases, such as allergy and asthma. According to (Rook 2008), although different parasitic worms suppress different Th types, but always in favour of regulatory T (Treg) cells. He explained that these regulatory T cells release interleukins that fight inflammation (Rook et al., 2008).

The reduction in the intensity of some human helminth infections with age might be indicative of host immunity. It seems that immune responses to helminths are intriguing not only from the perspectives of understanding protective immunity and immunopathology, but it is also important but it appears as if, type 2 immunity, seems to have evolved specifically to deal with this class of pathogens. Type 2 immunity involves the rapid activation and engagement of cells of both the innate (eosinophils and basophils) and adaptive (CD4+ T cells that commit to the Th2 pathway) immune systems (Voehringer et al., 2004). Cells of both the innate and adaptive immune systems that are involved in type 2 immunity share the ability to synthesize the core type 2 cytokine IL-4, which mediates directly and indirectly, the reactions that were considered to be symptomatic of helminth infection such as IgE production, eosinophilia, and changes in the physiology of target organs i.e., the intestine and lungs, that are associated with goblet cell hyperplasia and smooth muscle contraction (Finkelman et al., 2004). Research carried on i.e. infections in humans and mouse models of helminth infections, we revealed that, depending on the infection in, type 2 immune responses can prevent the survival of infecting parasites during a homologous secondary infection (Voehringer et al., 2006), expel adult parasites from the gut (Finkelman et al., 2004), allow host survival in a setting where the immune response cannot clear the parasites (Herbert et al., 2004), and/or mediate pathological fibrotic responses (Wynn et al., 2004). Fibrosis has its origins in the wound-healing responses that must be required on an ongoing basis in animals chronically infected with pathogens that cause large amounts of tissue damage by most helminths (Loke et al., 2007). Mode of Action of Herbs having Anthelmintic Activity: Although the plants have the anthelmintic activity mainly due to their phytoconstituents specially due to secondary metabolites it has not be understand clearly the mechanism of action of herbs for their anthelmintic activity. Phytoconstituents, jointly or separately may act by inhibition of tubulin polymerization and blocking glucose uptake (Jain et al., 2011). Any damage to the mucopolysaccharide membrane of worms will expose the outer layer restricting their movement which finally may cause paralysis and ultimately death of parasite (Chandrashekhar et al., 2008). The anthelmintic effects of tannins may be attributed to its capacity to bind free protein available for larval nutrition and thus reducing the nutrient availability resulting in larval starvation or decrease in

Figure 1: Possible mode of action of phytoconstituents as anthelmintic



gastrointestinal metabolism directly through inhibition of oxidative phosphorylation causing larval death (Scalbert., 1991, Athanasiadou et al .,2001). According to (Roy et al., 2010) Alkaloids may act on central nervous system and caused paralysis of the earthworm. The effect can be due to presence of the steroidal alkaloid and oligoglycosides which may suppress the transfer of sucrose from the stomach to the small intestine together with their antioxidant effect which is capable of reducing the nitrate generation which can interfere in local homeostasis that is essential for the development of helminths (Borba et al., 2010). The possible mechanism of phytoconstituents as anthelmintic have been shown in following charts (Patel et al., 2010, John et al., 2009, Roy et al., 2010, Borba et al., 2010). (Figure 1)

Transmission and Clinical Complications caused by helminthes in cattle

Hairworms-(*Nematomorpha*)

Mode of transmission-

Infected cattle pass eggs in manure onto the ground;

Eggs hatch in the manure;

Rain washes the larvae from the manure; and

Cattle swallow larvae on wet grass in moderate temperatures.

Clinical signs -

Clinical signs of wormy cattle include pale mucous membranes, bottle jaw, pot belly, diarrhea, drawled, not grazing, not chewing cud, rough and dry hair coat, thinness, weakness and inability to stand. These signs are similar to those caused by malnutrition and liver flukes.

Control-

The most important way to control hairworms is to maintain good nutrition by:

• Rotating pastures;

• Preventing overcrowding and overgrazing; and

• Providing good quality pasture, hay and supplements.

Lung worms

Large lungworm (*Dictyocaulus* spp.)

Dictyocaulus filaria, the large lungworm of sheep and goats, is a slender, whitish worm 3–10 cm long. Adults live mainly in the airways (bronchi) in the lung. Verminous (worm-related) pneumonia is mainly a disease of cool, moist climates as further development of first stage larvae passed in faeces to the infective third stage requires such conditions. *D. viviparus* occurs in cattle. This is an extremely important parasite in Britain and increasingly so in continental Europe. *D. viviparus* causes parasitic bronchitis, known in Britain as 'husk'. It occasionally causes disease in Australia in young cattle, mainly dairy cattle.

Small lungworm (*Protostrongylus* and *Muellerius* spp.)

Protostrongylus ('small lungworm') and *Muellerius* spp. ('small or nodular lungworm') occur in Australia but are of little importance. *P. rufescens* is parasitic in sheep, goats and deer. Adults are reddish, mainly inhabit bronchioles (small airways) and are 16–35 mm long, smaller than *D. filaria*. Lesions are broadly similar to those produced by *D. filaria* and *M. capillaris*. *M. capillaris* parasitises sheep and goats. Adults live in the lung tissue, rarely the airways, and usually provoke an enveloping inflammatory response, hence the common name, 'nodular lungworm'. There is rarely clinical evidence of disease in affected sheep.

Diagnosis and treatment

Diagnosis is based on clinical signs, post-mortem findings and laboratory testing (detecting lung worm larvae in faeces).

Most modern drenches are effective against lung worm.

Liver flukes (*Clonorchis sinensis, Fasciola hepatica)*

Transmission-Infected cattle, deer and rabbits pass eggs in manure and drop the manure in water; Eggs hatch in water and larvae develop in snails; and Cattle swallow cysts on grass or hay.

Clinical signs: Clinical signs of digestive inefficiency are evident in young cattle with acute liver disease and in older cattle with chronic liver disease. Fluky cattle show signs similar to those with malnutrition and hair worms.

Strategic worming: Wormers are administered to cattle not only as a treatment to kill internal parasites and to stop damage caused by parasites, but also to prevent pasture contamination and reinfection of the cattle. Strategically administering drugs reduces environmental contamination and infection of cattle and snails.

Coccidia (*Hepatozoon, Toxoplasma)*

Transmission-Infected cattle pass cysts in manure onto the ground; Rain washes the cysts from the manure; the cysts develop under moist and moderate tem per a true conditions; and

Cattle swallow cysts on moist ground.

External parasites

(a) Horn flies
(b) Lice
(c) Grubs

Conventional modes and treatment/ Drugs for tackling helminthes problem Anthelmintics: Anthelmintic drugs are used to eradicate or reduce the numbers of helmintic parasites in the intestinal tract or tissues of the body. These parasites have many biochemical and physiological processes in common with their human hosts, yet there are subtle differences that are beginning to yield to pharmacological investigation. Most of the drugs were discovered by traditional screening methods, they act through affecting the energy metabolism or by paralyzing the parasite.

Drugs used as Anthelmintics: The following are the drugs which are used as anthelmintic which have various mechanisms of actions:

- Albendazole: A broad-spectrum oral anthelmintic albendazole, is a drug of choice and its mechanism of action is through inhibiting microtubule synthesis in nematodes, thus irreversibly impairing glucose uptake. As a result, intestinal parasites are immobilized or die slowly (Jay et al, 1979).
- Mebendazole: It is a broad spectrum anthelmintic which selectively and irreversibly blocks glucose uptake by adult intestinal-dwelling nematodes and cestodes and their tissue-dwelling larvae. Inhibition of glucose uptake appears to lead to endogenous depletion of glycogen stored within the parasite. The lack of glycogen results in a decreased formation of adenosine triphosphate, required for survival and reproduction of the helminth. As mebendazole acts by affecting the entire energy metabolism, it is used as a standard drug for anthelmintic activity (Jay et al, 1979).

Transmission and Clinical Complications caused by helminths in men

Large Intestine	**Transmission**	**Disease/ Metabolic disorder**
Trichuris (Whip-worm)	Oral	Hemorrhagic colitis
Enterobius (Pin-worm)	Oral	Perianal itch
Small intestine		
Ascaris (Round-worm)	Oral	Small intestine obstruction
Strongyloides (Thread-worm)	Percutaneous and autoinfection	Duodenitis, Cutaneous larva currens, Hyperinfection in immune compromised
Ancylostoma & *Necator* (Hook-worm)	Percutaneous	Iron deficiency anemia

Transmission and Clinical Complications caused by helminthes in cattle

Worm	**Transmission**	**Disease/ Metabolic disorder**
Trichinella spiralis or *native*	Raw pork, Bear, Walrus	Myositis, Diarrhoea, Eosinophilia, Raised CPK
Toxocara canis (Visceral larva migrans)	Oral	Eosinophilia, Hepatomegaly, Cough, Fever
Wuchereria bancrofti or Brugia malayi (Lymphatic filariasis)	Mosquito vector	Elephantiasis, Chyluria or Hydrocoele
Onchocera volvulus (River blindness)	Black fly vector	Itchiness, Persistant skin nodules, Blindness
Loa loa (Eye worm)	Horse fly vector	Calabar swellings (3-4 days), Eye worm

Helminths infection: Humans are the primary (definitive) hosts for most, helminth infections; In other words, most worms reproduce sexually in the human host, producing eggs or larvae that pass out of the body and infect the secondary (intermediate) host. There are two clinically important types of worm infections – those in which the worm lives in the host's alimentary canal and those in which the worm lives in other tissues of the host's body.

- Praziquantel: It is a broad-spectrum anthelmintic drug. Which acts by altering calcium homeostasis in the parasite cells causing contraction of the musculature and eventually results in paralysis and death of the worm (Rang and Dale, 2003)?
- Piperazine: Piperazine can be used to treat infections with the common round worm and the threadworm. It reversibly inhibits neuromuscular transmission in the worm, probably by acting like GABA, on GABA-gated chloride channels in nematode muscle. As a result paralysed worms are expelled alive (Rang and Dale, 2003).
- Pyrantel Pamoate: A derivative of tetrahydropyrimidine that act by depolarizing the helminth neuromuscular junction, causing spasm and paralysis. It also has some anticholinesterase activity (Rang and Dale, 2003).
- Niclosamide: Niclosamide was the drug of choice for tapeworm infections and which inversely damage proximal segment separating worms from the intestinal wall and thus expelling them out of the host body. (Rang and Dale, 2003).
- Diethylcarbamazine: A piperazine derivative, it is active in filarial infections. It has been suggested that it modifies the parasite so that it becomes susceptible to the host's normal immune responses. It may also interfere with the parasite's arachidonate metabolism (Rang and Dale, 2003).
- Levamisole: A drug effective in common roundworm infection, acts by stimulating and subsequently blocking the neuromuscular junctions. Thus paralysing the worms to be expelled out (Rang and Dale, 2003).
- Ivermectin: A semisynthetic agent, obtained from an actinomycete, is thought to paralyse the worm by opening chloride channels and increasing chloride conductance (Rang and Dale, 2003).
- Oxamniquine: Active against *Schistosoma mansoni*, it affects both mature and immature forms of parasite. Its mechanism of action may involve intercalation in the DNA and its selective action may be related to the ability of the parasite to concentrate the drug (Rang and Dale, 2003).
- Metriphonate: Its action is thought to be due to an inhibitory effect on cholinesterases in the helminth, causing paralysis (Rang and Dale, 2003).

Drugs used in helminths infection

Helminth	Drugs used
Round worm: *Ascaris lumbricoides*	Mebendazole, Albendazole, Pyrantel
Hook worm: *Ancylostoma duodenate*, *Necator americanus*	Pyrantel, Mebendazole, Albendazole, Mebendazole, Albendazole
Thread worm: *Enteriobius (oxyuris) vermicularis*	Pyrantel, Mebendazole, Albendazole
Strongyloides stercoralis	Ivermectin
Whip worm: *Trichuris trichiura*	Mebendazole
Trichinella spiralis	Albendazole
Filaria: *Wuchereria bancrofti, Brugia malayi*	Diethyl carbamazine, Ivermectin
Guinea worm: *Dracunculus medinensis*	Metronidazole
Tape worms: *Tanenia saginata*, *Tanenia solium, Hymenolepis nana*, *Neurocysticercosis*	Praziquantal, Niclosamide, Praziquantal Praziquantal, Albendazole
Hydatid disease: *Echinococcus granulosus*, *E.multilocularis*	Albendazole

Side effects/toxicity/limitation of modern anthelmintic therapy

Although synthetic molecules are effective in the treatment/management of parasitic infections, they suffer from limitations of side effects or toxicity

- Albendazole- It produces few side effects when used for short-term therapy of gastrointestinal helminthiasis. Transient mild GI symptoms are epigastric pain, diarrhea, nausea, and vomiting, dizziness, and headache (Horton, 2000). Some times allergic phenomena such as edema, rashes and urticaria also occur. In children with asymptomatic trichuriasis, albendazole reportedly impaired growth in childrens. The most common side effect is

an increase in serum aminotransferase activity; rarely jaundice or chemical cholestasis may be noted. A recent pharmacoepidemiologic analysis concluded that long-term treatment of echinococcosis or cysticercosis with high-dose albendazole accounted for most of the adverse drug reactions attributed to anthelmintic therapy (Bagheri et al, 2004).

- Mebendazole- Transient symptoms of abdominal pain, distention, and diarrhea have occurred in cases of massive infestation and expulsion of gastrointestinal worms. Rare side effects in patients treated with high doses of mebendazole include allergic reactions, alopecia, reversible neutropenia, agranulocytosis, and hypospermia. Reversible elevation of serum transaminases is not uncommon in this population. Mebendazole treatment may be associated with occipital seizures (Wilmshurst et al, 1998). Mebendazole is a potent embryotoxin and teratogen in laboratory animals; effects may occur in pregnant rats at single oral doses as low as 10 mg/kg. Thus, despite a lack of evidence for teratogenicity in humans, it is advised that mebendazole not be taken by pregnant women or to children less than 2 years of age.
- Praziquantel- Abdominal discomfort, particularly pain and nausea, diarrhea, headache, dizziness, and drowsiness may occur shortly after taking praziquantel; these direct effects are transient and dose-related. Indirect effects such as fever, pruritus, urticaria, rashes, arthralgia, and myalgia are noted occasionally. Such side effects and increases in eosinophilia often relate to parasite burden. In neurocysticercosis, inflammatory reactions to praziquantel may produce meningismus, seizures, mental changes, and cerebrospinal fluid pleocytosis (Adam et al, 2004).
- Pyrantel pamoate- Transient and mild GI symptoms occasionally are observed in humans, as are headache, dizziness, rash, and fever. Pyrantel pamoate has not been studied in pregnant women. Thus, its use in pregnant patients and children less than 2 years of age is not recommended
- Diethylcarbamazine- Reactions typically are most severe in patients heavily infected with O. *volvulus*, less serious in *B. malayi* or *L. loa* infections, and mild in bancroftian filariasis, but the drug occasionally induces retinal hemorrhages and severe encephalopathy in patients heavily infected with *L. loa*. In patients with onchocerciasis, the *Mazzotti reaction* typically occurs within a few hours after the first dose and includes intense itching, enlargement and tenderness of the lymph nodes, and sometimes a papular rash, fever, tachycardia, arthralgias, and headache. Ocular complications include limbitis, punctate keratitis, uveitis, and atrophy of the retinal pigment epithelium (Dominguez et al, 1983, Rivas et al, 1981).
- Ivermectin- In animals, signs of CNS toxicity, including lethargy, ataxia, mydriasis, tremors, and eventually death, occur at very high doses (Campbell, 1993). In infected humans, ivermectin toxicity nearly always results from Mazzotti-like reactions to dying microfilariae; the intensity and nature of these reactions relate to the microfilarial burden and the duration and type of filarial infection (Campbell, 1984).

Herbal drugs used as anthelmintic:

Helminthes infections are the most common infections in man affecting the large proportions of the world's population. The synthetic anthelmintics used are not very safe as they suffer from the problem of side effects and toxicity and many of them are not recommended for young children and pregnant ladies. In the treatment of parasitic diseases, the anthelmintic drugs are used indiscriminately. Recently the use of anthelmintic produces toxicity in human beings. Hence the development and discovery of new substances acting as anthelmintic are being derived through plants. Various plants were used in veneral diseases, to promote healing of wounds, swellings, abscesses, rheumatism and treating pain in lower extremities, skin diseases, leucorrhoea, dysentery, dysuria and fever (Anisuzzaman et al, 2007, Vijayan et al, 2007). Anthelmintics are those drugs that are used in expelling out the worms that are parasitic in nature by either stunning them or by killing them. They are also known as

Natural anthelmintics:

Name of Plants	Part used	Effective against	Target	Reference
Allium sativum (Lillaceae)	Bulb	Round-worms	Cattle, goat, sheep	Iqbal *et al.,* 2001b
Annona senegalensis (Annonaceae)	Leaf, bark, root	*Nippostrongyllus braziliensis*	Rat	Ibrahim *et al.,* 1984
Acacia albida (Fabaceae)	Seeds	Sheep, goat	Sheep, goat	Nwude and Ibrahim,1980
Adhatoda vesica (Acanthaceae)	Roots	Mixed GI nematodes	Sheep	Lateef *et al.,* 2003
Ageratum conyzoides (Asteraceae)	Leaves, flowers	Tape-worms	Not reported	Sharma *et al.,* 1979
Alangium lamarckii (Alangiaceae)	Roots and bark	Hook-worms, ascarids	Dogs, poultry	Dubey and Gupta, 1968
Albizia anthelmintica (Fabaceae)	Bark	Anthelmintic	Cattle, goat, sheep	Minja, 1989; ITDG and IIRR, 1996
Azadirachta indica (Meliaceae)	Cake and leaves	Anthelmintic	Small ruminants	Gowda,1997; Mostofa *et al.*,1996
Artemisia mesatlantica (Asteraceae)	Flavonoids and sesquiterpene lactones	Anthelmintic	Not reported	Holeman *et al.,* 1991
Bixa orellana (Bixaceae)	Seeds	*Ascaridia galli, Ascaris suum*	Chicken, pig	Fernandez, 1991
Butea frondosa (Fabaceae)	Seeds	Anthelmintic, *ascaridia galli, Ascaris lumbricoides*	Chicken (*In vitro*), canine, human	Kalesaraj and Kurup, 1962, 1968; Joshi, 1970; Narayana *et al.,* 1976; Lal *et al.,* 1976, 1978; Shilaskar and Parashar, 1989
Butea frondosa (Fabaceae)	Seeds	*Ascaridia galli*	*In vitro*	Lal *et al.,*1976
Butea monosperma (Fabaceae)	Seeds	Anthelmintic, GI nematodes	Sheep and others	Kalesaraj and Kurup,1968; Chandra and Sabir,1978; Lal *et al.,*1978; Prashanth *et al.*, 2001; Iqbal *et al.* 2006b

Contd.

Butea superba (Fabaceae)	Not reported	Anthelmintic	Not reported	Charka, 1948; Chopra *et al.,* 1958
Calliandra calothyrsus (Fabaceae)	Legume	*Haemonchuscontortus*, *Trichostrongylus*, *Strongyloides papillosus*	Sheep	Parker and Palmer, l991
Calliandra portoricensis (Leguminosae)	Roots, leaves, flowers	*Toxocaracanis*, Gastrointestinal nematodes, *Haemonchus contortus*	Dog, Sheep	Adewunmi and Akubue,1981; Garg and Atal, 1963; Jain *et al.,* 1996; A1-Qarawi *et al.,* 2001; Iqbal*et al.,* 2005
Capillipedium foetidum (Poaceae)	Oil, grass	*Pheretima posthuma* (earthworms), *Taenia solium* and *Ascaris lumbricoides*	*In vitro*	Siddiqui and Garg, 1990
Carum copticum (Umbelliferae)	Seeds	*Ascaris lumbricoides*	Human	Krantz and Carr, 1967; Kalesaraj, 1974
Cassia spectalis (Fabaceae)	Roots	Round-worms	Cattle, goat, sheep	ITDG and IIRR, 1996
Chenopodium album (Chenopodiaceae)	Leaves	Nematodes	Sheep	Akhtar*et al.,* 1999
Chenopodium spp. (Chenopodiaceae)	Oil	Ascaris spp., Toxocara, Strongylus spp.	Horses, pigs, dogs, horses	British Veterinary Codex, 1953, 1965
Commiphora mukul (Burseraceae)	Oleo-gum resin	Tape-worms, hook-worms	Not reported	Kakrani and Kalyani, 1984
Cucurbita rnexicana (Cucurbitaceae)	Seeds	Moniezia expansa, Fascialopsis buski, Ascaris lumbricoides, Hymenolepis diminuta	Not reported	Shrivastava and Singh, 1967
Cucurbita moschata (Cucurbitaceae)	Seeds	Cestodes	Human	Xiao and Lin, 1986
Cyathocline lyrata (Asteraceae)	Essential oil	Tape-worms, hook-worms	In vitro	Shrivastava, 1979
Datura quercifolia (Solanaceae)	Fruit	Ascaridia galli	In vitro	Kaushik et al.,1981
Diospyros scabra (Ebenaceae)	Seeds	Fasciolosis, lung-worms	Cattle, goat, sheep, camel	ITDG and IIRR,1996
Dodonea viscose (Sapindaceae)	Leaves	Intestinal-worms	Not reported	Sharma and Singh, 1989

Contd.

Dryopteris filixmas (Dryopteridaceae)	Male fern	Moniezia, tape-worms, *Dicrocoeliu dendriticum*, *Fasciola hepatica*	Not reported	British Veterinary Codex,1953
Embelia kilimandschiraca	Roots	Anthelmintic	Not reported	Minja,1989
Embelia ribes (Myrsinaceae)	Seeds	Tape-worms	Poultry	Qureshi and Sabir, 1979
Eupatorium triplinerve (Asteraceae)	Flowers	*Ascaris lumbricoides* and *Taenia solium*	Not reported	Garg and Nakhare, 1993
Evodia rutaecarpa (Rutaceae)	Not reported	Ascarid nematodes, L4 of *Ostertagia circumcincta*	Pig (*in vitro*), sheep (*in vitro*)	Perrett and Whitfield, 1995
Feruia foetidissima (Rubiaceae)	Not reported	Haemonchus, Bunostomum, Chabertia, Nematodirus	*in vitro* Sheep	Pustovoi, 1968
Ficus religiosa (Moraceae)	Not reported	Anthelmintic	*In vitro*	Iqbal *et al.,* 2001b
Fumaria parviflora (Fumariaceae)	Plant powder	*Tricho strongylus*, Haemonchus, Trichuris, Fasciola spp.	Sheep, buffalo	Akhtar and Javed, 1985; Kailani *et al.,* 1995
Gardenia lucida (Rubiaceae)	Essential oil	Tape-worms, earth-worms	Not reported	Girgune *et al.,*1979
Hagenia abyssainicia (Rosaceae)	Fruit	Round-worms	Cattle, goat, sheep	ITDG and IIRR, 1996
Helleborus niger (Ranunculaceae)	Stem	*Ascaris lumbricoides*	Humans	Kalesaraj, 1974
Hyoscyamus niger (Solanaceae)	Seeds	Mixed nematode infection	*In vivo*	Akhtar and Ahmad, 1990
Inula racemosa (Asteracea)	Essential oil	Earth-worms, tape-worms	Not reported	Mishra *et al.,* 1979
Khaya senegalansis (Meliaceae)	Bark	Fasciola spp.	Not reported	Bizimana, 1994
Lagenaria siceraria (Cucurbitaceae)	Seeds	Cestodes, moniezia, avitelina spp.	Sheep	Akhtar and Riffat, 1987

Contd.

Lantana trifolia (Verbenaceae)	Fruit	Fasciolosis, lung-worms	Cattle, goat, sheep	ITDG and IIRR, 1996
Lawsonia inermis (Lythraceae)	Leaves	Fasciolosis	Sheep, goat	Nwude and Ibrahim, 1980
Mangifera indica (Anacardiacea)	Seeds	*Ascaris lumbricoides*	Humans	Kalesaraj, 1974
Melia toosendan (Meliaceae)	Not reported	Ascarids	Not reported	Xiao and Lin, 1986
Mitragyna stipulosa (Rubiaceae)	Roots	Guinea-worm	Humans	Sofowora, 1982
Moringa olelfera (Moringaceae)	Seeds	*Ascaris suum*	Pig	Fernandez, 1991
Nicotiana tabacum (Solanaceae)	Nicotine sulphate	Moneizia, Ascaridia, Cooperia, Haemonchus, Nematodirus, Ostertagia, Trichoslrogylus spp.	Not reported	British Veterinary Codex, 1953, 1965
Peganum harmala (Zygophyllaceae)	Seeds	Mixed GI infection, cestode infection	Goats	Akhtar and Ahmed, 1991
Piper betle (Piperaceae)	Not reported	Earth-worms	*In vitro*	Ali and Mehta, 1970
Quisqualis indica (Combretaceae)	Seeds	*Haemonchus contortus*	Goat	Xiao and Lin, 1986
Randia dumetorum (Rubiaceae)	Seeds	Earth-worms, tape-worms	Not reported	Mishra *et al.,* 1979
Rhus vulgaris (Anacardiaceae)	Roots	Round-worms	Cattle, goats, sheep	ITDG and IIRR, 1996
Senecio lyratiparitus (Asteraceae)	Leaves	Anthelmintic	Not reported	Minja, 1989
Swertia chirata (Gentianaceae)	Whole plant	*Ascaridia galli*	Not reported	Shilaskar and Parashar, 1989
Terminalia avicennoides (Combretaceae)	Leaves, roots	*Nippostrongylus braziliensis*	Rats	Ibrahim *et al.,* 1984
Trichilia emetic (Meliaceae)	Bark	Fasciolosis, lung-worms	Cattle , goats, sheep, camels	ITDG and IIRR, 1996
Uvaria hookeri (Annonaceae)	Root bark	*Haemonchus contortus*	Not reported	Padmaja*et al.,* 1993
Vernonia amygdalina(Asterac)	Stem bark	*Haemonchus contortus*	*In vitro*	Alawa *et al.*, 2003

vermifuge or vermicides. Natural anthelmintic includes the following components:

Tobacco, Walnut (Dun 1892), American wormseed (Hall,1924), Clove, Kalonji seeds, Garlic, Male-fern, Pine-apple, Diatomaceous earth, Soya and other legumes, Honey, water and vinegar are mixed with warm water, Aconite (Dun 1892), Valerian (Dun 1892), Calomel(Ludow, 1860), Jalap (Dun 1892), Kamala (Dun 1892), kuosso, kosin (Dun 1892), mucuna beans, cowhage (Ludow, 1860) oil of chenopodium (Hall,1924), pink root (Ludow, 1860), podophyllin (Dun 1892), quassia wood (Dun 1892), santonica(Hall,1924), stavesacre seeds(Dun 1892), turpentines, wormwood.

Plus points of use of herbal anthelmintics-

- There is an increased awareness among medical and scientific communities that the importance of medicinal plant studies should go beyond mere anthropological curiosity. Plant anthelmintics have been in the forefront of this growing awareness (Mccorkle et al, 1995). Studying herbal medicine can serve to validate and enhance existing local anthelintics uses and can give clues to remedies with further potential. Although locally produced plant anthelmintics is their relative cheapness compared to synthetic molecules (Anjaria, 1986).
- All medicinal plants have anthelmintic properties.
- Ethno veterinary sources are always accurate.
- All medicinal plants will directly kill the parasites.
- Medicinal plants are safe to ingest.
- The activity of the medicinal plants is consistent.
- If it works in one host species or for one parasite species it will work for all.
- Expelled worms are always visible after plant ingestion.
- The method of preparation used traditionally is the best.

Future scope of developing anthelmintic agent/formulation from herbal drugs: In the recent years, the importance of Herbal drugs in Medicine has tremendously increased because of their fewer side effects. Consequently, the demand for the herbal formulation is increasing day by day. The phytochemical constituents and their standardization are accelerated with the development of instrumental analysis and this field becomes important and new for investigation.

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