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Anthelmintic Activities (*In Vitro* And *In Vivo)* of Some Plant Extracts - A Review

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ABSTRACT

Several plants are found to possess potent medicinal and phytochemical compounds used globally for the treatment of diseases and the discovery of new drugs. Plants with anthelmintic properties have attained a great interest due to their usage in treatment of parasitic (helminthic) diseases that cause major economic loss, resulting to reduced livestock production capacity of farmers. The major impediment in the livestock subsector is the increasing problems of development of resistance to synthetic drugs by the helminths and or high cost of commercially produced anthelmintics and their resultant side effects than the treatment efficacy in the host. Helminthosis is a clinical condition that represents one of the commonly encountered and most important diseases in ruminant farming. This clinical condition is aggravated by indiscriminate use of anthelmintics in an attempt to control the infection, thereby causing resistance of the parasitic helminths to synthetic drugs. This has led to the screening of plant extracts for their anthelmintic properties thereby serving as alternative strategies against gastrointestinal parasitic resistance. However, eighty percent of the world populations use natural plant compounds as anthelmintics for treatment of parasitic infections. Hence, the folkloric claims of the anthelmintic properties of plants extracts for the treatment of helminthes is necessarily important and of great interest. Therefore, this review unveils previous pharmacological and preliminary studies on plants as anthelmintics able to reduce helmintic infections and overcoming helminth parasite resistance.

Keywords: Plants, Extracts, Anthelmintics, Resistance, Helminthes.

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INTRODUCTION

Helminthosis is a disease condition caused by helminth infection. Globally, it is a major constraint in livestock production and chemotherapeutics remain the corner stone for treating these conditions by overcoming certain factors such as chemical residues, toxicity, increased costand non-availability of drugs in the remote areas [1].In Nigeria, diseases such as helminthosis have been implicated as one of the health problems constraining the productivity of ruminant [2].Helminthosis are a problem and a limiting factor in the improvement of livestock resulting in production losses, increased cost of management and treatment and even mortality in severe cases [3]. In tropical Africa, gastrointestinal parasites are regarded as important health problems because, many parasitic infections especially those of helminths are usually asymptomatic or produce only mild symptoms and are often neglected until serious complications or chronic clinical features begin to appear [4].

Diseases due to gastrointestinal parasites have been a challenge, serious threat and a major economic constraint to ruminant livestock production [5, 6]. Routine use of synthetic anthelmintic drugs has led to the development of resistance, whereby the efficacy of drugs against gastro-intestinal nematodes is becoming ineffective in livestock production [7]. The threats of anthelmintic resistance as a result of indiscriminate use, the resultant effect of drug residue and its unavailability to rural farmers of low income in developing countries have led to the notion that sustainable helminths control cannot be achieved with synthetic anthelmintic [8].

Medicinal plants continued to be used globally for the treatments of disease and the discovery of drug entities [9].According to the world health organization (WHO) more than 80% of the world's populations rely on traditional herbal medicine as a means of primary health care [10]. Plants have continued to serve as possible sources for new drugs and chemical compounds. Recently there has been a marked shift towards herbal cures because of the pronounced cumulative and irreversible reactions of synthetic drugs [11]. Previous research have shown that plant natural products have pharmacological and anthelmintic properties that possess some inhibitory effectson gastrointestinal parasites which are useful in ethno-veterinary remedies and the advancement of these plant natural products reveals the efficacy of isolated compounds in the treatment of the gastrointestinal infections [9, 12]. The need to explore medicinal plants usage for the above problem which is more acceptable to the livestock farmer and has been in use from the ancient period having the advantage of sustainable supply and are ecologically acceptable [8].

Therefore, both *in vitro* and *in vivo* studies have employed to explore the potentials of these plants and their folkloric claims.

Plant Extracts and Their Anthelmintic Activities on Parasitic Helminths

Azadirachta indica **(Meliaceae):** Is commonly known as "neem". The Aqueous, methanol and crude extracts of the seed part and leaves inhibits the hatching of egg of *Haemonchus contortus* and Trichostrongylus species in a dose dependent manner [13].

Leonotisocymifolia (Burm. f.) Iwarsson **(Lamiaceae):** An anthelmintic (vermifuge) used in the treatment of diarrhea, stomach pain (colic) and schistosomiasis, the crude aqueous and hydro-alcoholic extracts of aerial parts of this plant tested on the eggs and larvae of *Haemonchus contortus* completely inhibited the egg hatching of *Haemonchus contortus.* The aerial parts of aqueous and hydro alcoholic of this extract induced complete inhibition of

egg hatching [14].

***Trianthema portulacastrum* L (Aizoaceae):** This plant is used widely as anthelmintic vermifuge. The crude aqueous and methanolic extracts were tested on egg hatch and adult motility assay and it showed a dose and time dependent anthelmintic effects on live worms [1, 5].

***Brucea javanica* (Simaroubaceae):** The plant exhibits a significant anthelmintic activity against *D. intermedius* in goldfish [15].

***Tinospora cordifolia* (Menispermaceae):** Commonly named as "Guduchi" possess medicinal properties such as anti-diabetic, anti-spasmodic, anti-inflammatory, anti-oxidant, hepatoprotective, immunomodulatory and anti-neoplastic activities. The aqueous and ethanolic extracts of the stem was tested on *Eisenia foetida* (waterlogged soil) at 100 mg/ml and it exhibited very significant activities as compared to the standard drug piperazine citrate (10 mg/ml) [16, 17].

***Ficus exasperate* Vahl (Moraceae):** The leaf extracts exhibited varying degrees of larvicidal activities against the infective stage larvae of *Heligmosomoides bakeri*at the concentrations of 500 mg/ml and 100% larval mortality [18, 19].

***Irvingia gabonensis* (Aubry-lecomte ex o'rorke) (baill):** The bark has a bitter taste used as purgative for treating intestinal pain. The leaf extracts exhibited larvicidal activities of the infective larval stage of *Heligmosomoides bakeri*, at concentrations of 500 mg/ml and 71.43% larval mortality [18].

***Anogeissus leiocarpus* (African birch; Bambara: ngálăma) (Combretaceae):** The inner bark of the tree is used as a human and livestock anthelmintic for treating worms, and for treatment of a few protozoan diseases in animals, nagana (Trypanosomiasis) and Babesiosis. The extracts of the leaf extracts inhibited the egg hatch hatching and larval development of *Haemonchus contortus*at the concentrations of 1200 and 2400ug/ml and mortality of the larvae (L1) at concentrations of 4 and 8mg/ml [20, 21].

***Daniellia oliveri* (Rolfe) Hutch and Dalz (Caesalpiniaceae):** The gum, stem bark, roots and leaves are widely used in traditional medicine. The stem bark decoction treats intestinal worms. The stem bark extracts inhibited the egg hatching and larval development of *Haemonchus contortus* at the concentrations of 1200 and 2400ug/ml and mortality of the larvae (L1) at concentrations of 4 and 8mg/ml [21, 22].

Chicory (*Cichoriumintybus* L) (Asteraceae): When fed to farm animals as forage supplement, it reduces the helminthic burdens due to its toxic effect on the helminths. The methanolic extracts of chicory (Spadona) has potent activities against *Ascarissuum* third (L3) and fourth (L4) larval stages, as well as *Oesophagostomum dentatum* L4 and adults which shows a significant anthelmintic effect [23, 24].

***Picriafel-terrae* Lour (Curanja) (Linderniaceae):** This plant is an annual herb. The plant extracts has a significant inhibitory effect at a concentrations of 3–5 mg/ml on the larval development of *Haemonchus contortus*. The leaf extract of *Curangafel-terrae* against *Pheretimaposthuma* showed a significant anthelmintic activity when compared to albendazole drug [25, 26, 27].

***Piliostigma thonningii (Schumach.) Milne-Redh.* (Fabaceae):** The various parts of *Piliostigma thoningii* (Root, bark, seed, and fruit) is used for anti-inflammatory, analgesic and anthelmintics activity. The ethanolic extract of the *P. Thoningii* bark, D-3-O-methylchiroinositol induced approximately 60% *Haemonchus contortus* larvae paralysis within 24hrs at 4.4mg/ml concentrate using levamisole [28].

***Artemisia absinthium* (Asteraceae):** An ornamental plant used for treatment of stomach aches and as an anthelmintic. The plant extracts have been tested for their potential *in vitro*

anthelmintic effect against eggs and the third-stage larvae of *Ascaris suum* and *Trichostrongylus colubriformis* at concentrations of 2000 µg/ml. The results show a higher inhibitory effect against the larval stage in comparison with Zentel [29].

***Allium sativum* (Garlic) (Liliaceae):** It is used to treat rheumatism, arthritis, respiratory and reproductive system disorders. The plant extracts have been tested for their potential in vitro anthelmintic effect against eggs and the third-stage larvae of *Ascaris suum* and *Trichostrongylus colubriformis* at concentrations of 2000 µg/ml. The results show a higher inhibitory effect against the larval stage in comparison with Zentel [29].

***Corylus avellana* (Hazelnut) (Bet.ulaceae):** This plant is useful for the prevention and treatment of cancer, cardiovascular, inflammatory and microbial diseases. The extracts of Hazelnut induced the paralysis and structural damage of *Oesphagostomum dentatum* in dose-dependent response with worms exposed to 1 mg/ml of extract and a concentration of ≥ 250 µg/ml [30].

Willow bark (Salicaeae): The willow tree is a medicinal plant used to ease pain and reduce inflammation. The extracts of willow bark at a concentration of 1 mg/ml significantly ($P < 0.01$) induced the migration of L3 stage of *Oesophagostomum dentatum*[31].

***Cleome gynandra*(Capparidaceae):** Oral administration of a decoction of the boiled leaf or juice relieves stomach pain and threats thread-worm infection. The acetone leaf extract ofthe plants had anthelmintic inhibitory effects (68% ± 3%) at a concentration of 2.5 mg/ml on *Haemonchus contortus* egg hatch [32].

***Carissa spinarum*Linn (Apocynaceae):** The leaves, root and bark of *C. spinarum*are used against gastrointestinal tract (GIT) parasites and ring worm. The crude aqueous extracts of the leaves *Carissa spinarum* inhibited the hatching of egg of *Haemonchus contortus* at concentrations less than or equal to 1mg/ml and adult *Haemonchus contortus* mortality raised to the levels of 96.8% and 93.9% at a concentration of 4mg/ml [13].

***Jussiaeahyssopifolia*, G.DON (Onagraceae):** This plant grows in dumpy areas. It is used as an astringent, laxative and diuretic. The methanolic extract of *Jussiaeahyssopifolia* G. Don induced paralysis and death of *Pheretimaposthuma*at the concentration of 300 mg/ml using Albendazole suspension at a dose of 10mg/ml [33].

***Cymbopogon jwarancusa* (Poaceae or Gramineae):** The various parts of the plants are used for treatment such as skin problems, abdominal tumoursand fever. The crude methanolic extracts of the plant had anthelmintic inhibitory effects on *Fasciola gigantica,* and *Paramphistomum cervi*by significantly ($P<0.05$) inhibiting motility and paralysis of these parasites [34, 35].

***Hyamenodictyon pachyantha (*Rubiaceae):** The bark and leaves exhibit broad spectrum medicinal properties and possess pharmacological activities such as antimicrobial, anticoagulant and anti-inflammatory. It also contains scopoletin, hymeselsin, scopolin and 3-*O*-β-D-glucopyranosyl-β-sitosterol. The crude methanolic extracts and fractions of the plant had anthelmintic inhibitory effects on *Haemonchus contortus* when compared to albendazole [36, 37].

Some plant extracts used for *in vitro* and *in vivo* anthelmintic studies

In vitro assay has been one of the methods used in screening for anti-parasitic properties of plants. Some of the advantages of this method include low costs of carrying out the studies and it also gives rapid turnover that allows the screening of plants on a large scale. This assay measures the effect of anthelmintic activity directly on the processes of egg hatching and larval development without interfering with the internal physiological functions of the host

[38]. Several *in vitro* and *in vivo* studies have been carried out globally by some researchers to evaluate the efficacy and anthelmintic properties of medicinal plants on different nematode species of farm animal [39].

Table 1: Some plant extracts used as remedies against helminthes

Plant	Plant Part/extract type	Experimented parasite stage	Type of study	Reference
Piliostigma thoningii	Root bark extracts	*Ascaridia galli*	*in vitro*	Asuzu and Onu. [40]
Persicaria hydropiper	Methanol extract of the aerial part	*Pheritima posthuma*	*in vitro*	Raihan *et al*. [41]
Occimum gratissimum	Leaves essential oil	*Haemonchus contortus* eggs and larvae	*in vitro*	Pessoa *et al*. [42]
Annona sanegalensis	Water extract of stem bark	*Haemonchuscontortus* eggs and larvae	*in vitro*	Alawa *et al*. [43]
Trifolium repens	Aerial shoots extracts	*Hymenolepis diminuta*	*in vivo* in mice	Tangpu*et al*. [44]
Xylopia aethiopica	Crude methanol extract of seeds	*Nippostrongylus braziliensis*	*in vivo* in rats	Suleiman *et al*. [45]
Moringa olifera	Ethanol extract of leaves and stem bark	*Ascaris suum* adult	*in vitro*	Wasswa and Olila. [46]
Euphorbia hirta	Aqueous crude extract of leaves	*Ancylostoma caninum, Toxocara canis, Dipylidium caninum*	*in vivo* in dogs	Adedapo*et al*. [47]
Mimusops elengi	crude alcoholic extracts of bark	*Pheretima posthuma* and *Ascardia galli*	*in vitro*	Mali *et al* . [48]
Combretum molle	Aqueous methanol extract	*Haemonchus contortus* eggs and larvae	*in vitro*	Simon *et al*. [49]
Daniellia oliveri	Stem bark	*Haemonchus contortus* eggs and larvae	*in vitro*	Adama*et al*. [50]
Spigelia anthelmia	Crudeethanol, chloroformandethylacetate extract of plant	*Nippostrongylus braziliensis*	*in vivo* in rats	Jegede *et al*. [51]

Musa paradisiaca	Crude methanol extract of leaves	*Haemonchus contortus* eggs, larvae and adult	*in vitro* and *in vivo*	Hussain *et al*. [1]
Anogeissus schimperi	butanol (BF), ethylacetate (EF) and aqueous (AF)	*Nippostrongylus brazilien sis*	*in vivo* in rats	Jegede *et al*. [52]
Curangafel-terrae	leaf extract	*Pheretima posthuma*	*in vitro*	Huang, [27]
Mucuna pruriens	Leaves	*Haemonchus contortus* adult	*in vivo in lamb*	Huisdena*et al*. [53]
Azadirachta indica	Aqueous and methanol extract of seed	*Haemonchus contortus* eggs and larvae	*in vitro*	Iqbal *et al* . [54]
Schinopsis spp (Quebracho tannin)	Extract of the bark dissolved in water	*Haemonchus contortus* larvae	*in vivo* in mice	Ngongeh and Fakae. [55]
Afzelia africana	Crude methanol, chloroform and n - butanol extract of stem bark	*Nippostrongylus brazilien sis*	*in vivo* in rats	Simon *et al*. [56]
Citrus aurantifolia	Hexane extract (HE), ethylacetate extract (EE) and aqueous methanol extract (AME)	*Heligmosomoides bakeri* eggs and first stage larvae	*In vitro*	Eneojo*et al*. [57]
Citrus aurantifolia	Crude methanol extract (CME), ethylacetate (EE), butanol (BE) and aqueous methanol extract (AME	*Heligmosomoides bakeri*	*In vivo in mice*	Eneojo*et al*. [58]
Chenopodium ambrosoides	Hexane and ethanol extract of leaves	*Heligmosomoides bakeri* eggs and larvae	*in vitro*	Wabo*et al* . [59]
Myrsine africana, Rhus glabrous, Jasminum abysinicum, Rhus vulgaris, *Acokanthera schimperi*	Crude aqueous and methanolic extract	*Haemonchus contortus* eggs and larvae	*In vitro*	Gatachew*et al*. [60]
Annona muricata	The aqueous leaf,root - bark and seed extract	*Haemonchus contortus* eggs and larvae	*in vitro*	Ferreira *et al*. [61]
Carica papaya	benzyl isothiocyanate from leaves	*Ascaris lumbricoides and Ascaridia galli*	*in vitro*	Shifa. [62]
Mucuna pruriens and Canarium schweinfurthii	Macerated extracts	*Ascaris suum* eggs and larvae	*In vitro*	Okoli*et al* . [63]
Prosopis julifora	Ethanolic leaves and root	*Haemonchus contortus* eggs and larvae	*in vitro*	Kipyegon. [39]

Conclusion

The *in vitro* screenings of plant extracts on helminths carried out in the present review are important as they give basis for further *in vivo* studies. The various screening procedures and attempts made by the previous studies are to evaluate and establish the efficacy of anthelmintic medicinal plant species and to discover new anthelmintic molecules and their possible mechanism of action. This will help to reveal the anthelmintic properties of plants and their natural compounds (Extracts) in the treatments of helminth infections. Therefore, further research studies is needed both *in vitro* and *in vivo* to explore more medicinal plants for anthelmintic properties, plant for higher efficiency and lesser side effect, as seen with undesirable side effects in chemically or synthetic anthelmintic drugs on the host, also to reduce problems of drug resistance which will help to reduce the cost of purchase of the synthetic anthelmintic drugs.

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