

Anti-helminthic Activity of Plant Extracts against Gastrointestinal Nematodes in Small Ruminants - A Review

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ABSTRACT

Endoparasites like gastrointestinal nematodes have a deleterious effect on animal health and production as well as have a role in immunity, energy and protein metabolism. There has been appreciable effort in finding alternative remedies to these parasites owing to the problem of resistance and residue in animal body due to anthelmintics. Researchers around the world have experimented with extracts (different parts of plants) utilizing various *in vivo* (FECRT) and *in vitro* tests (AMA, EHA, LDA, LMIT) showing encouraging results against gastrointestinal nematodes especially *Haemonchus contortus* in case of *Annona squamosa*, *Azadirachta indicda*, *Cassia surattensis*, *Chenopodium ambrosioides*, *Jatropha curcas*, *Melia azedarach* amongst other plants. The present review enumerates those several plants that have antinematodal properties, with a view that further research is warranted to develop a cost effective and environment friendly botanical as the way forward in place of traditionally used anthelmintics.

Key words: Antinematodal, *in vitro* test, Plant extract.

INTRODUCTION

Gastrointestinal helminths are common infectious agents in human and animals causing anorexia, anemia, diarrhoea and heavy production losses. The important gastro-intestinal helminth parasites belong to three different classes, nematode (roundworm), trematode and cestodes (flatworm). Amongst these helminthes, gastrointestinal (GI) nematodes like *Haemonchus contortus*, *Bunostomum* sp., *Trichostrongylus* sp., have crucial effect on the food security. GI nematodes have a highly detrimental effect on the small ruminant; some nematodes are blood suckers and cause anemia while many affect the physiological, metabolic and immune system of the body resulting in significant economic losses in meat, milk and wool production as well as in reproduction.^[1] To safeguard our livestock against gastrointestinal nematode infection, usually broad spectrum anthelmintics like ivermectin, albendazole, levamisole are being used. The remnants of these drugs in animal and animal product are the rising cause of resistance along with the toxicities arising out of their use. The recent approach is the use of herbal therapies alone or in combination with traditional anthelmintics.

Researchers have shown herbal anthelmintics remedies comprises of natural plant compounds which are environment friendly. Many researchers have studied plant anthelmintics and their validation as alternative antihelmintics. The ethnoveterinary approach has been started in different part of the world which can be screened by various *in vitro* and

in vivo methods in host and non-host animals. *In vitro* tests like adult mortality test (AMT), egg hatch inhibition assay/test [EHA/EHT], larval mortality assay/test (LMA/LMT), larval development assay/test (LDA/LDT), larval migration inhibition assay (LMIT), Larval feeding inhibition test (LFIT), Larva Exsheathment Assay (LEA) are being utilized for evaluation of anti-helminthic activities of plant extracts and products against gastrointestinal parasites.^[2] The most common tests like AMT and LMT examines the effect of plant extracts on the motility of the adult and larva of nematode respectively, while EHT focuses on the inhibitory effect of the extracts on egg hatching. *In vitro* assays have an edge over *in vivo* methods due to their relative low costing and rapid results that allows large scale testing of plant materials. *In vivo* test includes the faecalegg count reduction test (FECRT) which are not very ideal due to its higher cost, low precision and reproducibility owing to inter animal variation and pharmacodynamics of the drug in the host.^[3]

In this review, medicinal plants effective against gastrointestinal nematodes have been described and tabulated, which can open door for basic pharmacological studies leading to development of new anthelmintics against the conventional ones having the problems of the anthelmintic resistance and high cost.

Since ancient times and folklore, plants have been utilized to treat gastrointestinal helminths of medical and veterinary importance. To validate their

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anthelmintic property, researcher's use the whole/parts of plant extract (aqueous/ethanol/methanol/acetone/ethyl acetate) to conduct various tests as has been described underneath. The screening for phytochemical compounds like alkaloids, tannins etc helps to account for the anthelmintic activity.

Acacia nilotica

Acacia nilotica (Mimosaceae), plant native to India and Africa, used in traditional medicine for the treatment of intestinal parasites and have molluscicidal effects and the antibacterial properties. In rural areas, the barks and pods are used to treat diarrhea, the verminoses and the gastritis.^[4] The anthelmintic effect of trunk barks of *A. nilotica* indicated by the LC₅₀ (Lethal Concentration 50) of adult *Haemonchus* worms was 1.28 mg/ml while LC₅₀ of Levamisole was found to be 3.25 mg/ml. The inhibition of egg hatching was 93.84%. The aqueous extract of the seeds of *Acacia nilotica* also showed 50% reduction in egg hatching.^[5] There was 50% reduction at 0.5mg / ml concentration for the on eggs of *H. contortus*. The phytochemical screening indicated tannins, triterpenes, saponosides which are believed to have anthelmintic property.^[6]

Annona sp.

Annona squamosa belonging to family Annonaceae has its origin from West Indies and is cultivated throughout Asia. The seed extracts from the plant contains acetogenin which has been indicated to have an antiparasitic effect.^[7] A study on methanolic extract of *Annona squamosa* showed inhibition of 100% hatching at concentration of 25 mg/ml with an ED₅₀ value of 3.53 as per Egg Hatch test.^[8] In another study, there was inhibition of 90% egg hatching due to the acetogenin compound isolated from seeds of *A. squamosa* in *H. contortus*.^[9] *Annona muricata* leaf extract showed 84.91% and 89.08% efficacy in EHA and LMT respectively against *Haemonchus contortus*. The AMT test depicted complete immobilization of worms within six hours of exposure to the nematode.^[10] The phytochemical analysis indicated existence of phenols that might be responsible for the anthelmintic effects.

Aloe sp.

Aloe (family Asphodelaceae) is a genus containing flowering succulent plants with a history of folk medication. Aqueous extracts of *Aloe forex* showed an 80 % larval development inhibition at 5mg/ml.^[11] Aqueous extract of *Aloe vera* demonstrated significant egg hatch inhibition at all the concentrations tested and the ED₅₀ value of egg hatch inhibition was 0.57 mg/ml. *In vivo* FECRT depicted reduction in egg per gram count in a dose dependent manner with the highest reduction of 56.36 % at 500 mg/kg.^[12] There is report of utilization of boiled leaves of *Aloe* sp. along with other plants to cure various ailments of livestock.^[13]

Artemisia sp.

The herbaceous plant belongs to Asteraceae and is attributed to have medicinal value against various diseases. *Artemisia herba-alba* flower and aerial part extracts produced a comparable anthelmintic activity with albendazole. A significant egg hatching inhibition effect in a concentration-dependent manner was revealed where methanolic extract (1 mg/ml) of flower and aerial part exhibited 98.67% and 88.3% inhibition, respectively. The crude extracts of the aerial parts of *Artemisia. absinthium* showed significant anthelmintic effects during adult immersion test and *in vivo* test demonstrated faecal egg count reduction (FECR) of 90.46% in sheep (administered with 2.0 g/ kg body weight) 15 days post treatment.^[14] The effect of *Artemisia brevifolia* (whole plant) on live *Haemonchus contortus* was revealed by AMT where there was mortality at 6 hr post exposure. The whole plant was administered as crude powder at the rate of 3 g/ kg body weight to sheep

and there was a reduction (67.2%) in eggs per gram (EPG) of faeces 14 days post treatment.^[15]

Azadirachta indica

Azadirachta indica (Meliaceae) as popularly known as neem has been used extensively in treatment of human ailments as well as a remedy against ecto and endoparasites. The *in vitro* activity of methanolic extract of neem against *H. contortus* larva indicated a 40% mortality at a concentration of 4 mg/ml.^[16] Silver nanoparticles against *Haemonchus contortus* performed with neem leaf extract mediated revealed that a concentration of 6 mg/ml induced 100% egg hatch inhibition. For EHA the IC₅₀ and IC₉₀ values were 0.005mg/ml and 0.066 mg/ml for AgNPs while values were higher [0.665 mg/ml and 3.569 mg/ml] for neem extract. In case of AMT, worms were paralysed within 1-5 min. The neem mediated nanoparticles showed considerable ovicidal activity.^[17] The anthelmintic efficacy of the aqueous extracts of *Azadirachta indica* leaf and stem and root barks was carried out and aqueous extract of leaves and bark inhibited nematode egg hatch.^[18] *In vivo* FECRT test was conducted for crude methanolic extract against *Strongyle* nematode and the result showed significant decrease [$p < 0.05$] in Egg per Gram after day 7 post treatment.^[19]

Cassia sp.

The Cassia plant is documented to possess medicinal properties in ethnobotanical surveys in traditional system of medicine.^[20] Anti nematodal activity was evaluated by using LMI assay on four plant species of Cassia; *Cassia siamea*, *Cassia surattensis*, *Cassia fistula* and *Cassia spectabilis*. *C. surattensis* (200 mg/ml) showed the highest ($p < 0.05$) inhibition of the larvae.^[21] On screening for photochemicals, *Cassiasp* revealed presence of alkaloids, phenol hydroquinone, flavonoid, steroid, triterpenoid, tannin, and saponin. Studies have demonstrated the role of tanins to block through uncoupling the oxidative phosphorylation leading to the death of parasites. Also the binding of tannins to free proteins in the gastrointestinal tract of the animal, or glycoprotein on the cuticle of the helminth's body surface lead to paralysis, and death.^[22] There is also damage to cuticle and digestive tissue of larvae due to tannins.

Chenopodium ambrosioides

Chenopodium ambrosioides (Chenopodiaceae) locally is a strongly aromatic herb, about 1.2 m high and is a common weed of cultivated areas, originated from America, but now it has spread in tropical and subtropical countries. *C. ambrosioides* oil has been traditionally used for treatment of parasitic infection in human beings and animal.^[23] As per a study the hydroalcoholic extract of leaves of *C. ambrosioides* showed 100% inhibition of egg hatching at 0.5 mg/ml and 1 mg/ml concentration while ED₅₀ value were 0.09 and 0.15 respectively.^[24] The adult motility inhibition test showed that 24 hr of exposure of adult *H. contortus* to different concentrations of plant extracts, significant and dose-dependent reduction in motility/mortality was observed for aqueous extracts of *C. ambrosioides*. Phytochemical screening showed presence of saponins, glycoside, polyphenol. Oil of *C. ambrosioides* at concentration of 3.3 µl/ml induced 100% egg hatch inhibition.^[25]

Cissus quadrangularis

C. quadrangularis (Vitaceae) is an edible plant found in Asia and Africa. It has been a traditional medicine in these continents, utilized as anti helminthic and also helpful in case of anorexia, chronic ulcer and swellings. A study using crude extracts of *Cissus quadrangularis* indicated 100% efficacy in adult mortality test while the reduction in egg hatching was

88 % at a concentration of 10mg/ml.^[26] Alkaloid, tannin, flavonoids and phenols were indicated during phytochemical analysis.

Flueggea virosa

The plant *Flueggea virosa* belongs to family Euphorbiaceae having anti-inflammatory, analgesics, haemostatic and wound healing properties and naturally found in tropical Africa, Asia and Japan.^[27] An anthelmintic investigation on leaf and bark extract of *Flueggea virosa* showed a dose dependent activity. As per adult mortality test of nematode, the time for paralysis ranged from 11-29 min and time for death ranged from 19-37 min for leaf extract. For the bark extracts (100 mg/ml) of *F. virosa*, the onset of paralysis time was 8-20 min while death was 13-32 min. Alkaloids, Flavonoids, terpenoids, Cardiac glycosides and reducing sugar were the phytoconstituents obtained during screening.^[28]

Jatropha curcas

Jatropha curcas (Euphorbiaceae) is an ornamental shrub, native to America and later introduced to old world tropics where it is now widely cultivated. The various parts of the plant (root, stem, leaves, seed and fruit) has been profoundly used in folk medicine in parts of Africa and is believed to have purgative and anthelmintic effect.^[29] In Ethiopia *in-vitro* tests was conducted to determine anti nematodal effects on seed extracts of *Jatropha curcas*.^[24] The egg hatch assay revealed 100 % egg hatching inhibition at 1 mg/ml for the aqueous extract of *J. curcas*. Polyphenol was the phytoconstituent recovered from the plant part. In another study, evaluation of anthelmintic activity of ethanol extracts of *Jatropha* seeds utilizing [EHA] and the artificial larval exsheathment inhibition assay [LEIA] was carried out. The ovicidal effectiveness of extract was 91.9% and in 18.9% larva were exsheathed in LEIA.^[30]

Melia sp.

Melia (Family, Meliaceae) is a deciduous tree found in Asia, North and Latin America. The plant has revealed medicinal properties and anti-parasitic activities against many pathogens.^[31] It has been observed that leaves (aqueous extract) of *Melia azedarach* at concentration of more than 0.625 mg/ml caused significant embryonic death and allowed hatching of eggs at a very low level compared to control wells indicating potent ovicidal property of extract. 90 % mortality in larva was observed at concentration of more than 60 mg/ml.^[32] *In vivo* studies with fruit powder of *Melia azedarach* at the dose rate of 30 mg/kg that resulted in 99.4 % reduction in faecal egg count in goats infected with gastrointestinal nematodes, which was higher than caused by morantel tartrate (90.2 %) treatment.^[33] The hexane extract of *Melia azedarach* fruits were evaluated by EHT and LDT against sheep gastrointestinal nematodes showed a LC_{50} of 572.2 l g/ml and 0.7 l g/ml respectively.^[34] The anti-parasitic action of drupe extracts revealed that it better than the standard hexylresorcinol against hookworms.^[35] In EHT, IC_{50} values of acetone extract of *Melia dubia* leaves was 7.752 mg/ml and plant possesses anti nematodal activity may be attributed to high content of phenolics, tannins and alkaloids.^[36]

Schinusmolle

Schinusmolle is domesticated in South America but is now naturalized in many countries. It is used traditionally to treat wounds and its insecticidal properties make it a good candidate for use as a possible substitute to synthetic chemicals in pest control.^[37] The methanolic extract of the plant revealed a 95% adult mortality against *Haemonchus contortus* at 10 mg/ml during a study.^[26] There was 96% inhibition of egg hatching at 10mg/ml and was dose-dependent. Alkaloid and tannins were evident in phytochemical screening.

Terminalia sp.

Terminalia catappa (Combretaceae) has medicinal properties and mostly inhabitates Asia, Africa and Australia. They are used in traditional medicine in India and Philippine to treat dermatitis, helminthiases and hepatitis.^[38] Investigation into anti nematodal activity of dichloromethane and methanol extract of leaves of *Terminalia catappa* displayed 98.94% and 95.77% inhibition of egg hatching at 6.25 mg/ml respectively. At 12.5 mg/ml there was 100% reduction of larva. The preliminary phytochemical screening showed presence of various phytoconstituents like alkaloids, tannins cardiac glycosides, triterpenes, saponins and carbohydrate reducing sugar.^[39] *In vitro* studies on methanolic extract of *Terminalia arjuna* bark by EHA and LDA revealed a LC_{50} of 645.65 and 467.74 mg/ml respectively. *In vivo* test indicated a reduction of 87.3% in sheep treated with crude methanolic extract on 11th day of post-treatment. The antinematodal activity of *Terminalia arjuna* bark might be attributed to its tannin content.^[40]

Numerous studies on use of plant extracts against gastrointestinal nematodes have been carried out in different parts of the world (Table 1) mostly based on putative reports of their use in traditional medicine. The physiological effects of phytochemicals like alkaloids, tannins, cardiac glycosides, saponins, tripeterens elicit its nematocidal mechanism (Figure 1). While most researchers have utilized *in vitro* methods to evaluate the anti nematodal effect of plant extracts, their extrapolation for *in vivo* tests could yield better screening results. The phytoconstituents obtained from different solvent extract can be further analysed through bioassay-guided fractionation and nuclear magnetic resonance spectral analysis for purification of specific compounds responsible for anti-nematodal activity.

LIMITATIONS

Though there are so many accessible medicinal plants that possess anthelmintic property, there are few issues that need to be taken into account, such as whether the selected plants are complaisant to cultivation, their form of administration, their palatability, stability and biodegradability of active compounds in preserved products, their chances/probability of harmful effects/reaction/aftermath. Some plants have high active compound of known direct-acting parasitic ides that may be effective for short-term “curative” purpose whereas some plants should be used along with the other feed for preventive purpose.^[76]

The understanding of some of the herbal anthelmintic is poor; instructions were orally/verbally passed from one to another in which some beneficial/profitable information maybe disoriented/forgotten. Unavailability of standardized dosages may lead to over dosage and may

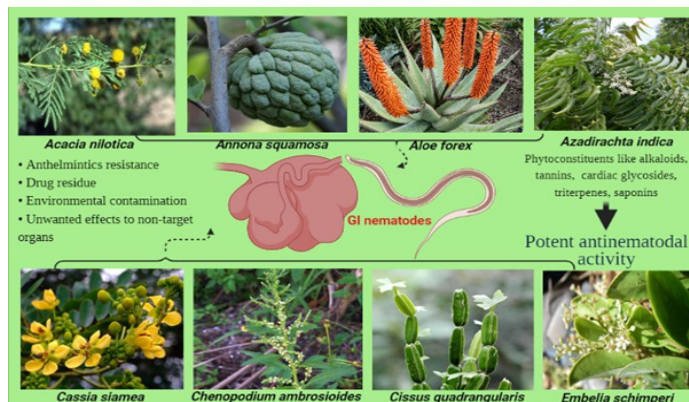


Figure 1: Plants or plant extracts that can be used as potential drug candidates for treatment of nematodes.

Table 1: List plants with activity against gastrointestinal nematodes.

Sl.No.	Name of the plant	Geographical location	Part used	Active principle	Stage	Active against	Tests conducted	References
	<i>Aerva Lanata</i> [Mountain knot grass] Family: Amaranthaceae	Tropical India, Tropical Africa, Saudi Arabia, Sri Lanka	Whole plant	-	Eggs, adult	Mixed nematode species [<i>Haemonchus contortus</i> , <i>Trichostrongylus colubriformis</i> , <i>Oesophagostomum columbianum</i> , <i>Strongyloides papillosus</i> , and <i>Trichuris ovis</i>].	FECRT	Jaswanth et al., 2018 ^[41]
	<i>Acanthus ilicifolius</i> [Holly-leaved acanthus] Family: Acanthaceae	Australia, Australasia, Southeast Asia	Leaves	Alkaloids, flavonoids, tannins, saponins and steroids	Adult	<i>Trichostrongylus axei</i>	AMA	Dadangat et al., 2018 ^[42]
	<i>Achillea millefolium</i> [Common yarrow] Family: Asteraceae	Northern Hemisphere of Asia, Europe, North America	Roots	α -pinene, α -thujene, β -pinene, α -terpene, geraniol	Adult	Mixed species of GI nematodes	FECRT, TWCR	Tariq and Tantry 2012 ^[43]
	<i>Acofantheraschimperi</i> [Round-leaved poison-bush] Family: Apocynaceae	Africa, Yemen	Leaves	-	Eggs, larva	<i>Haemonchus contortus</i>	EHA, LDA	Getachew et al. 2012, ^[44] Kuma et al. 2015 ^[45]
	<i>Adhatodavasica</i> [Vasaka] Family: Acanthaceae	India	Root, aerial parts	Alkaloids Glycosides	Eggs, larva, adult	Mixed nematode infections	EHA, LDA	Tariq 2018 ^[46] Lateef et al., 2003 ^[47]
	<i>Agave sisalana</i> [Sisal] Family: Agavaceae	Southern Mexico Africa, Madagascar, Caribbean, USA	Shredded leaves	Homoisoflavonoid, saponin	Eggs, larva, free-living stages of adult	Nematode parasite	EHA, LMIA, LDA, LFIT AMA	Botraet et al., 2011 ^[48]
	<i>Albizia schimperiana</i> [Forest long-pod Albizia] Family: Fabaceae	East tropical Africa	Stem, bark	Alkaloids, Spermine, Budmunchiamines,	Eggs, larvae	<i>Haemonchus contortus</i> , Guinea-worm	LDA	Egnale et al., 2011 ^[49]
	<i>Anogeissus leiocarpus</i> [African birch] Family: Combretaceae	Tropical central and East Africa, tropical Southeast Asia	Leaf	-	Eggs, adult	<i>H. contortus</i> , gastrointestinal strongly in sheep race	EHA, LDA	Kabore 2009 ^[50]
	<i>Anacardium occidentale</i> [caju] Family: Anacardiaceae	America Caribbean	Shell	-	Eggs, L3 infective larvae, adult	<i>H. contortus</i>	AMA, LMT, EHA	Davuluri et al., 2020 ^[51]
	<i>Calliandra calothyrsus</i> [Calliandra] Family: Fabaceae	Tropics of Central America	Leaves	-	Eggs	<i>Haemonchus contortus</i>	EHA	Florence et al., 2011 ^[52]
	<i>Coriandrum sativum</i> [Coriander] Family: Apiaceae	Southern Europe and Northern Africa to South western Asia	Seeds	-	Eggs, adult	Nematode	FECRT	Egnale et al., 2007b, ^[53]

<i>Caesalpinia cristata</i> L [yellow nicker] Family Fabaceae Caesalpinaceae	India, Sri Lanka and West Indies.	Seeds, whole plant	-	Eggs, adult	Mixed species of gastrointestinal nematodes	AMA, EDA	Jabbaret <i>et al.</i> , 2007 ^[54]
Calotropis procera [Rubber tree] Family Asclepiadaceae	Tropical Africa, Indian Ocean islands, South Africa	LateX, flowers	Anthocyanin, Alkaloids Resins	Adult	Mixed species of gastrointestinal nematodes	FECRT	Iqbal <i>et al.</i> , 2005 ^[55]
<i>Cocos nucifera</i> [Coconut] Family Palmae	Coastal tropical Asia, the Pacific	Fruit	-	Egg, larva	<i>Haemonchus contortus</i> .	EHA, LDA	Egualde <i>et al.</i> , 2011 ^[49]
<i>Combretum mole</i> [velvet bushwillow] Family Combretaceae	South Africa, Namibia, Zimbabwe	Leaves	-	Eggs, larvae	<i>Trichostrongylid</i> nematodes, <i>Haemonchus contortus</i>	EHA, LDA	Oliveira <i>et al.</i> , 2009 ^[56]
<i>Cratylia mollis</i> [amaratu bean] Family Leguminosae	South America	Leaves	-	Egg	Gastrointestinal nematodes of goats	FECRT	Ademola and Eloff 2010 ^[57]
<i>Curcuma longa</i> [common turmeric] Family Zingiberaceae	India, Indonesia, Bangladesh, France, and other Asian countries	Rhizome	Alkaloids, carbohydrate, flavonoids, and saponins	Adult	<i>Haemonchus contortus</i>	AMA	Limaet <i>et al.</i> , 2016 ^[58]
<i>Cymbopogon martinii</i> [lemongrasses, palmarosa] Family Poaceae	India and Indochina	Oil	Geraniol	Egg, larvae	<i>Haemonchus contortus</i> , <i>Trichostrongylus</i> spp.	EHA, LDA, LFIA, LEA.	Pandey <i>et al.</i> , 2018 ^[59]
<i>Cymbopogon schoenanthus</i> [Camel grass] Family Poaceae	Sahara, Sahel, Africa, Arabian Peninsula Iran	Oil	Geraniol	Egg, larvae	<i>Haemonchus contortus</i> , <i>Trichostrongylus</i> spp.	EHA, LDA, LFIA, LEA	Katiki <i>et al.</i> , 2011. ^[60]
<i>Dalbergia sisso</i> [North Indian rosewood] Family Papilionaceae	Indian Sub-continent, Southern Iran, Nepal, Pakistan, Western Asia	Leaves	-	Eggs, adult	<i>Haemonchus contortus</i>	EHA, LDA, FECRT	Katiki <i>et al.</i> , 2011. ^[60]
<i>Daniellia liveri</i> [African Balsam Tree] Family Fabaceae / Leguminosae	Tropical West and Central Africa	-	-	Eggs, adult	<i>Haemonchus contortus</i>	-	Nawazet <i>et al.</i> , 2014 ^[61]
Dryopteris filix-mas [Male wood fern] Family Dryopteridaceae	Temperate Northern Hemisphere, Europe, Asia, North America.	-	-	Eggs	Gastrointestinal nematodes	FECRT	Kabore 2009. ^[50]
<i>Tetradium ruticarpum</i> / <i>Evodia rutaecarpa</i> [Euodia ruticarpa] Family Rutaceae	China, Korea	Dried fruits	Atanine	Larvae	<i>Teladorsagia</i> [ostertagia] <i>circumcincta</i>	LIMIT	Kumaet <i>et al.</i> , 2015 ^[45]

<i>Foeniculum vulgare</i> [Fennel] Family Apiaceae	South-East Asia, East Java	Aerial parts Seeds	-	Egg, larva, adult	<i>Haemonchus contortus</i>	EHA, LDA	Tariq 2018 ^[46]
<i>Gliricidia sepium</i> [Mexican Lilac] Family Leguminosae	Mexico, South America	Leaves	-	Eggs	<i>Haemonchus contortus</i>	EHA	Getachew <i>et al.</i> 2012, ^[44] Kuma <i>et al.</i> 2015 ^[45]
<i>Guazuma umbifolia</i> [Mutamba, guacimo] Family Malvaceae	Caribbean, South and Central America, Mexico, India	Leaves	-	Eggs	<i>Cooperia punctata</i>	EHA	Florence <i>et al.</i> 2011 ^[52]
<i>Hagenia abyssinica</i> [Kossofrican redwood] Family Rosaceae	Africa	Mixed Roots, leaves	-	Eggs, adult	Gastrointestinal parasites	FECRT	Von son de fernex <i>et al.</i> , 2016 ^[62]
<i>Hedera helix</i> [Common ivy] Family Araliaceae	Europe, Western Asia	Ripe fruits	-	Eggs, larva, adult	<i>Haemonchus contortus</i>	EHA, FECRT	Kuma <i>et al.</i> 2015 ^[45]
<i>Iris kashmiriana</i> [Mazarmund] Family Iridaceae	India	Whole plant	-	Eggs, adult	<i>Haemonchus contortus</i>	AMA, FECRT	Egualde <i>et al.</i> , 2007a ^[63]
<i>Illicium verum</i> [Star anise] Family Schisandraceae	Northeast Vietnam, Southwest China, India	Fruit	-	Eggs, larva, adult	<i>Haemonchus contortus</i>	AMA, LMT, EHA	Khan <i>et al.</i> , 2018 ^[64]
<i>Jasminum abyssinicum</i> [Tembelele] Family Oleaceae	Africa	Leaves	-	Adult, L3 stage larvae	<i>Haemonchus contortus</i>	EHA, LDA	Davuluri <i>et al.</i> , 2020 ^[51]
<i>Khaya senegalensis</i> [African mahogany] Family Meliaceae	Africa, India	Bark	-	Eggs, larva, Adult	<i>Haemonchus contortus</i> , Gastrointestinal nematodes	LDA	Getachew <i>et al.</i> 2012, ^[44] Kuma <i>et al.</i> 2015 ^[45]
<i>Leonotis cynifolia</i> [Minaret Flower] Family Lamiaceae	South Africa	Aerial parts	-	Eggs, larvae	<i>Haemonchus contortus</i> , Hookworm infection	EHA, LDA	Ademola <i>et al.</i> , 2004 ^[57]
<i>Leucaena diversifolia</i> [Wild tamarind] Family Leguminosae	Indonesia, Mexico	Leaves	-	Eggs	<i>Haemonchus contortus</i>	EHA	Egualde <i>et al.</i> , 2011 ^[49]
<i>Leucas martinicensis</i> [Whitewort] Family Lamiaceae	Asia, East Africa	Aerial parts	-	Eggs, larvae	<i>Haemonchus contortus</i>	EHA, LDA	Florence <i>et al.</i> 2011 ^[52]

Mallotus philippensis [Kamala tree] Family Euphorbiaceae.	South Asia, Southeast Asia, Afghanistan, Australia	Flower	Tannins, flavonoids, terpenes, phenolic compounds, saponins	Egg, third stage larvae	<i>Haemonchus contortus</i> , <i>Setaria digitata</i>	LMA, LDA, LMIA	Egualé <i>et al.</i> , 2011 ⁽⁴⁹⁾
<i>Mentha piperita</i> [Peppermint] Family Lamiaceae	Europe, the Middle East	Oil	Menthol	Eggs, Larvae	Trichostrongylids <i>Haemonchus contortus</i>	EHA, LDA, LFIA, LEA	Deepa <i>et al.</i> , 2015 ⁽⁶⁵⁾
<i>Momordica charantia</i> [Karolla] Family Cucurbitaceae	Tropical and subtropical Africa and Asia	Fruit, Seed	Tannins, phenolic compounds, steroids, flavonoids	Adult	Gastrointestinal nematodes	AMA	Katiki <i>et al.</i> , 2011 ⁽⁶⁰⁾
<i>Moringa oleifera</i> Family Moringaceae	Asia, Africa	Seed	Tannins	Eggs, L3 infective stage larvae	<i>Haemonchus contortus</i>	EHA, LMT	Sujon <i>et al.</i> , 2008 ⁽⁶⁶⁾
<i>Morus alba</i> [white mulberry] Family Moraceae	China, United States, Canada, South America	Leaves	-	Eggs, adult	<i>Haemonchus contortus</i>	FECRT, AMA, EHA	Cabardoand Portugaliza (2017) ⁽⁶⁷⁾
<i>Musa paradisiaca</i> [Banana] Family Musaceae	Subtropics or tropical highlands	Leaves	Tannins	Eggs, adult	Gastrointestinal nematodes	AMA, EHA	Nawazet <i>al.</i> , 2014 ⁽⁶¹⁾
<i>Nauclea latifolia</i> [Kanluang, Bangkal] Family Rubiaceae	West and Central Africa	Bark, stem	Resin, tannins and alkaloids	Eggs, larva	Mixed nematode infections	FECRT	Hussaimet <i>al.</i> , 2011 ⁽⁶⁸⁾
<i>Nicotiana tabacum</i> [Tobacco] Family Solanaceae	Tropical and subtropical America	Leaves	Tannins	Eggs, adult	<i>Haemonchus contortus</i>	AMA, FECRT	Tariq 2018 ⁽⁴⁶⁾
<i>Ocimum sanctum</i> [Holy basil] Family Lamiaceae	Indian subcontinent, Southeast Asian tropics.	Leaves	Alkaloids, carbohydrates, steroids and tannins	Eggs, Larva	Gastrointestinal nematodes	LDA, FECRT	Iqbal <i>et al.</i> , 2006 ⁽⁶⁹⁾
<i>Ptilostigmathamningii</i> [Camel's foot tree] Family Fabaceae	Tropical Africa	Bark	D-3-O-methyl chiroinositol	L3 larvae	<i>Haemonchus contortus</i>	FECRT	Kanojiya <i>et al.</i> , 2015 ⁽⁷⁰⁾
<i>Phytolacca dodecandra</i> [Soap berry] Family Phytolaccaceae	Sub-Saharan Africa and Madagascar	Leaves, roots, fruits, seeds	-	Eggs, adult	Gastrointestinal nematodes	FECRT	Tariq 2018 ⁽⁴⁶⁾
<i>Prunella vulgaris</i> [Common self-heal] Family Lamiaceae	Europe, Asia, and North Africa, North America	Leaf, stem, flower	-	Eggs, adult	Gastrointestinal nematodes of sheep	AMA, EHA, FECRT	Nalule <i>et al.</i> , 2011. ⁽⁷¹⁾
<i>Punica granatum</i> [Pomegranate] Family Lythraceae	Mediterranean region, Southeast Asia, USA	Peel, root	Tannins	Eggs, adult	<i>Haemonchus contortus</i>	EHA, AMA	Loneet <i>al.</i> , 2017 ⁽⁷²⁾

<i>Rhus vulgaris</i> [Common currant-rhus] Family Anacardiaceae	Southern Africa	Leaves	-	Eggs, larva	<i>Haemonchus contortus</i>	EHA, LDA	Getachew et al. 2012, ^[44] Kuma et al. 2015 ^[45]
<i>Rhus glabrous/ glabra</i> [Kimowhite sumac] Family Anacardiaceae	North America, Canada, and Florida, Arizona in the United States	Leaves	-	Eggs, larva	<i>Haemonchus contortus</i>	EHA, LDA	Getachew et al. 2012 ^[44] , Kuma et al. 2015 ^[45]
<i>Rumex abyssinicus</i> [Spinach Rhubarb] Family Polygonaceae	Tropical Africa, central and eastern Africa, Madagascar	Aerial parts, root, leaf	-	Eggs, larvae	<i>Haemonchus contortus</i>	EHA	Egualie et al., 2011 ^[49]
<i>Saba senegalensis</i> [Weda] Family Apocynaceae	Sahel region of sub-Saharan Africa	Leaves	Tannins	Eggs, adult	<i>Haemonchus contortus</i>	AMA, EHA	Belemiliga et al. 2016 ^[73]
<i>Sapiumgrahamii</i> [Gumtree] Family Euphorbiaceae	Neotropics from Mexico and The Caribbean south to Argentina	Leaves	-	Adult	<i>Haemonchus contortus</i>	AMA	Traore 2014 ^[74]
<i>Senna occidentalis</i> [Coffee senna] Family Fabaceae	Tropical America, Asia, Africa, America	Leaves	-	Eggs, larvae	<i>Haemonchus contortus</i>	EHA	Egualie et al., 2011 ^[49]
<i>Swertia chirata</i> [Chiretta] Family Gentianaceae	Temperate Himalayas	Whole plant	-	Eggs	<i>Haemonchus contortus</i>	EHA	Iqbal et al., 2006 ^[69]
<i>Syzygiumaromaticum</i> [Labanga] Family Myrtaceae	Indonesia, Zanzibar, Madagascar, Sri Lanka and Caribbean.	Flower bud	Eugenol	Eggs, adult	<i>H. contortus</i> , Gastrointestinal nematodes	AMA, EHA	Charitha et al. 2017 ^[36]
<i>Trianthemportulacastrum</i> [desert horsepurslane] Family Aizoaceae	Africa and North and South America	Whole plant	-	Eggs, adult	Gastrointestinal nematodes	AMA, EHA.	Hussain et al., 2011 ^[68]
<i>Vernonia amygdalina</i> [Bitter leaf] Family Asteraceae	Tropical Africa, north-eastern South Africa, Yemen	Mixed roots, leaves	-	Eggs, adult	Gastrointestinal nematodes	FECRT	Nalule et al., 2011. ^[71]
<i>Zingiber officinale</i> [Ginger] Family Zingiberaceae	Tropical Asia, the Caribbean, Central and South America, Australia, Africa	Dried rhizome	-	Eggs	Gastrointestinal nematodes	FECRT	Iqbal et al., 2006 ^[69]
<i>Ziziphus nummularia</i> [Jhar Beri] Family Rhamnaceae	Thar Desert of western India and southeastern Pakistan and South Iran.	Bark	-	Eggs, adult	Trichostrongylid nematodes	AMA, EHA, LDA	Bachaya et al., 2009 ^[75]

Abbreviations, FECRT - Faecal Egg Count Reduction test, AMT - Adult motility test/assay, LDT- Larval development test, LFIT- larval feeding inhibition test, TWCR - Total Worm Count Reduction, EH-, Egg hatch assay, LDA-larval development assay, LEA- larval exsheathment assay.

have injurious effects on the animal. Herbal anthelmintic plants may have many names in local dialects which may lead to confusion in finding the plants moreover; local names may enfold a range of species of plants. The step-by-step process of collection, preparation and administration of the anthelmintic plants may be unfavorable and extensive/laborious. Moreover, there is inadequate information on how to collect and prepare.^[77]

There are some constraints which include insufficient quantity of phytochemical after extraction, low bioavailability of the constituents, lack of standardized quality control systems, improper practices for instances like misidentification, microbial contamination, incorrect packaging, inappropriate maintenance/storage [temperature, light exposure, etc], substitution and adulteration of plants, incorrect preparation and dosage.^[78] Additionally, large number of the herbal anthelmintics do not have research-based knowledge which hinder their utility.

There is variable response when treated with medicinal plants and extracts and this could be due to the amount of phytochemicals/bioactive compounds present in the plants that differ according to the portion of the plant utilized furthermore it also depends on the cultivating manner/technique.^[79] Also, the usage/exploitation of rare species of medicinal plants may wipe out the whole species. Moreover, plants having high content of saponins are not totally safe, they are harmful to fishes.

FUTURE PROSPECTS

Due to problems like resistance to anthelmintics, significant side effects, drug residue in food and on animals, contamination of the environment, unwanted effects to non-target organs, researchers require the search/need for alternative drugs which are safer to animals and environment. The conventional techniques followed/practised by the local traditional healers should be gathered and recorded which may serve as guidelines for veterinary science and pharmacological studies.^[77]

There is requirement of in-depth study of each plant about their chemicals, *in vivo* and *in vitro* experiments and their mechanism of action. Numerous attempts must be conducted to standardize the extracted products and to formulate it.^[80] Further, the farmers should be motivated to cultivate herbal anthelmintics and devise a guidebook to provide treatment techniques.

Many phytochemicals present in the plant extracts may not be safe, biologically active and effective.^[78] Therefore, the bioactive compound present in each plant extract should be inspected by Food and Drug Administration [FDA]. For the effective phytochemical anthelmintic drug delivery to the target organs, nanotechnology-based 'smart' drug delivery systems and nanocarriers can be employed. Nanocarriers have the ability to infiltrate blood-brain barrier and tight epithelial junctions of the skin. Additionally, parameters such as bioavailability, control, facile and efficient release time and precise drug targeting, etc. are also necessary to be investigated. On the other hand, some of the imperative measures for execution and establishment of herbal drugs are toxicological evaluation, regulatory guidelines, quality control and dose standardization. With the latest development of biotechnological and biomedical world at the molecular level, mechanism of action and interaction between large molecules can be interpreted. Also, usage of Nano-level technology can identify small molecules present in the plants or plant extracts that can be used as potential drug candidates for treatment.

The ovicidal and larvicidal property of herbal anthelmintic should be investigated by both *in vitro* and *in vivo* tests. *In vivo* testing of herbal drugs provides good evidence of their anthelmintic property, and if possible, the animals should be slaughtered and must be examined for

worms present in the GI tract. The *in vivo* trials must be standardized as per the host as well as the target parasite characterization.

CONCLUSION

The present review has enumerated indigenous medicinal plants in animals and human having antihelminthic efficacy. Owing to poor economic status of livestock farmers, high cost of antihelminthtics, the highly prevalent helminths in livestock can be combated only by help of ethnoveterinary medicines. The combination with Nanotechnology can also enhance the drug delivery and treatment scenario.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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