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Medicinal plants and its activity against helminth: A review

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Abstract

The therapeutic value of Indian medicinal plants is known since the ancient ages. Ayurveda, the oldest system of medicine recommends use of remedies, mainly based on medicinal herbs, for the treatment of a variety of diseases in man and animals. The herbal remedies are economical and within the reach of common man. It has been pointed out that about three-fourths of world's population cannot afford the expensive products of western pharmaceuticals (Handa, 1996). Therefore, about 80 per cent of people living in developing countries are almost completely dependent on traditional means for their primary healthcare needs (Fransworth, 1990; Pushpagandan, 1996). The therapeutic value of Indian medicinal plants is well recognized and acknowledged all over the world. There has been an ever enhancing awareness globally to rely on natural remedies in place of the chemical drugs. More recently, the western multinational drug companies, taking leads from ayurveda and Indian folklore medicines, are diverting their R and D activities on Indian medicinal plants to find out the active principles, isolate and patent them. Anthelmintic resistance in the parasites is spreading and the inefficacy of chemical anti-parasitic compounds is threatening animal health. New plants with medicinal properties against parasites of ruminants are being investigated around the world with promising results. In the near future natural products obtained from plants extracts seems that likely will become a viable alternative of control of parasitizes of veterinary importance.

Keywords: Medicinal plants, phytochemical, anthelminthics resistance, ethanopractices

Introduction

Plants are a source of large amount of drugs comprising to different groups such as antispasmodics, emetics, anti-cancer, antimicrobials, antihelmintics etc. A large number of the plants are claimed to possess the antibiotic properties in the traditional system and are also used extensively by the tribal people worldwide. It is now believed that nature has given the cure of every disease in one way or another. Plants have been known to relieve various diseases in Ayurveda. The use of chemical anthelmintics drugs for controlling animal parasite is rapidly losing popularity due to a number of disadvantages. Anthelmintic resistance in the parasites is spreading and the inefficacy of chemical anti-parasitic compounds is threatening animal health. New plants with medicinal properties against parasites of ruminants are being investigated around the world with promising results. In the near future natural products obtained from plants extracts seems that likely will become a viable alternative of control of parasitizes of veterinary importance. WHO has recently estimated that 80% of the populations of the developing countries rely on traditional medicine, mostly plant drugs, for their primary health care needs. In India, the history of medicinal uses of plants dates back to 3500-1800 B.C. where in the Rig-Veda mentions a number of plants with different healing practices. A large part of the population depends even at the present time on the indigenous systems of medicine, ayurveda, Unani and Sidha. Now days a number of plant showing antiparasitic properties and use as potent antiparasitic agent. The aqueous and alcoholic extracts of Ananas sativus (Bromeliaceaea), Embellia ribes, Macuna prurita (Leguminosae) and Melia azedarach have been found to bear significant activity against Taenia canina and Paramphistomum cervi; *M. prurita*, in particular, has been found to be more effective against trematodes. The plant extract of papaya posses a dose dependedent effect on larva and adult worm of T. colubriformis (Hounzangbe et al., 2005)^[29]. The aqueous, etheral and alcoholic extracts of Cucurbita mexicana (Cucurbitaceae) seeds have exhibited significant anthelmintic activity against Moniezia expansa, Fasciolopsis buski, Ascaris lumbricoides and Hymenolepis diminuta. Fumaria parviflora ethanol extract eliminated fecal eggs and caused 72 and 88% mortality of adult Haemonchus contortus and Trichostrongylus colubriformis, respectively. The anthelmintic activity of ethanolic extract of Melia azedarach Linn. (Meliaceae) was found to be better against *T. solium* than that of piperazine phosphate

(Szewczuk *et al.*, 2003) ^[71]. Recent surveys in developing countries have identified many plants that are intended have the potential to be used as anthelmintics.

 Table 1: Ethan veterinary sources on plants identified with potential antihelmintics activity

Origin of survey	No. of plants	References	
SE asia	23	Anon.1994 ^[10]	
Kenya	19	Anon.1996 ^[11]	
Eastern and Southern Africa	>100	Watt and Breyerwijk, 1962 [78]	
East Africa	>100	Kokwaro, 1993	
West Africa	18	Ibrahim <i>et al.</i> , 1984 ^[30]	
Zaire	11	Kasonia et al, 1991	
Nigeria	15	Nwude and Ibrahim,1980 ^[58]	
Africa	>50	Bizimania,1994	
World wide	100	Tagbota and townson, 2001 [73]	
Indo-Pakistan subcontinent	>50	Akhtar, et al, 2000 ^[7]	

Advantage of Plant based anthelmintics over chemicals anthelmintics

- 1. Synthetics anthelmintics are expensive whereas plant based anthelmintics are less expensive.
- 2. Synthetics anthelmintics cause drug residues problem while plant based anthelmintics are free from drug residues.
- 3. There is chance of drug resistance after prolonged use of synthetics anthelmintics whereas in plant based anthelmintics have less chance of drug resistance.
- 4. Synthetics drugs are unavailable in rural areas whereas it is easily available.
- 5. Synthetics drugs cause environment pollution whereas plant based anthelmintics are eco-friendly and promote biodiversity.

Common phytochemicals found in plant containing potent anthelmintic activity

- a. Alkaloids e.g. Palasonin
- b. Isoflavones e.g. Genistein
- c. Triterpenoids e.g. Ursolic acid
- d. Polyphenols (Tannins and flavonoids), simple phenols (Phenolic acids)
- e. Saponins
- f. Organosulfides- Allicin, Isothiocyanates,
- g. Thymoquinone
- h. Cysteine proteinases.

Method of extraction of phytochemicals

The basic principle is to grind the plant material (dry or wet) finer, which increases the surface area for extraction thereby increasing the rate of extraction. Earlier studies reported that solvent to sample ratio of 10:1 (v/w) solvent to dry weight ratio has been used as ideal (Das *et al*, 2010) ^[22].

Extraction procedures

a. Plant tissue homogenization

Plant tissue homogenization in solvent has been widely used by researchers. Dried or wet, fresh plant parts are grinded in a blender to fine particles, put in a certain quantity of solvent and shaken vigorously for 5 - 10 min or left for 24 h after which the extract is filtered. The filtrate then may be dried under reduced pressure and redissolved in the solvent to determine the concentration. Some researchers however centrifuged the filtrate for clarification of the extract (Das *et al*, 2010) $^{[22]}$.

b. Serial exhaustive extraction

It is another common method of extraction which involves in volves successive extraction with solvents of increasing polarity from a non-polar (hexane) to a more polar solvent (Methanol) to ensure that a wide polarity range of compound could be extracted. Some researchers employ soxhlet extraction of dried plant material using organic solvent. This method cannot be used for thermo labile compounds as prolonged heating may lead to degradation of compounds (Das *et al*, 2010)^[22].

c. Soxhlet extraction

Soxhlet extraction is only required where the desired compound has a limited solubility in a solvent, and the impurity is insoluble in that solvent. If the desired compound has a high solubility in a solvent then a simple filtration can be used to separate the compound from the insoluble substance. The advantage of this system is that instead of many portions of warm solvent being passed through the sample, just one batch of solvent is recycled. This method cannot be used for thermo labile compounds as prolonged heating may lead to degradation of compounds (Nikhal *et al*, 2010) ^[57].

d. Maceration

In maceration (For fluid extract), whole or coarsely powdered plant-drug is kept in contact with the solvent in a stoppered container for a defined period with frequent agitation until soluble matter is dissolved. This method is best suitable for use in case of the thermo labile drugs (Ncube *et al*, 2008)^[54].

e. Decoction

This method is used for the extraction of the water soluble and heat stable constituents from crude drug by boiling it in water for 15 minutes, cooling, straining and passing sufficient cold water through the drug to produce the required volume (Remington, 2008)^[64].

f. Infusion

It is a dilute solution of the readily soluble components of the crude drugs. Fresh infusions are prepared by macerating the solids for a short period of time with either cold or boiling water (Remington, 2008)^[64].

g. Digestion

This is a kind of maceration in which gentle heat is applied during the maceration extraction process. It is used when moderately elevated temperature is not objectionable and the solvent efficiency of the menstrum is increased (Remington, 2008)^[64].

h. Percolation

This is the procedure used most frequently to extract active ingredients in the preparation of tinctures and fluid extracts. A percolator (A narrow, cone-shaped vessel open at both ends) is generally used. The solid ingredients are moistened with an appropriate amount of the specified menstrum and allowed to stand for approximately 4 h in a well closed container, after which the mass is packed and the top of the percolator is closed. Additional menstrum is added to form a shallow layer above the mass, and the mixture is allowed to macerate in the closed percolator for 24 hr. The outlet of the percolator then is opened and the liquid contained therein is allowed to drip slowly. Additional menstrum is added as required, until the percolate measures about three-quarters of the required volume of the finished product. The marc is then pressed and the expressed liquid is added to the percolate. Sufficient menstrum is added to produce the required volume, and the mixed liquid is clarified by filtration or by standing followed by decanting (Handa, *et al*, 2008)^[26]

i. Sonication

The procedure involves the use of ultrasound with frequencies ranging from 20 kHz to 2000 kHz; this increases the permeability of cell walls and produces cavitation. Although the process is useful in some cases, like extraction of rauwolfi a root, its large-scale application is limited due to the higher costs. One disadvantage of the procedure is the occasional but known deleterious effect of ultrasound energy (more than 20 kHz) on the active constituents of medicinal plants through formation of free radicals and consequently undesirable changes in the drug molecules (Handa, *et al*, 2008) ^[26].

Screening of phytochemicals

Phytochemical examinations were carried out for all the extracts as per the standard methods.

- **1. Detection of alkaloids:** Extracts were dissolved individually in dilute Hydrochloric acid and filtered.
- a. **Mayer's Test:** Filtrates were treated with Mayer's reagent (Potassium Mercuric Iodide). Formation of a yellow coloured precipitate indicates the presence of alkaloids.
- b. **Wagner's Test:** Filtrates were treated with Wagner's reagent (Iodine in Potassium Iodide). Formation of brown/reddish precipitate indicates the presence of alkaloids.
- c. **Hager's Test**: Filtrates were treated with Hager's reagent (saturated picric acid solution). Presence of alkaloids confirmed by the formation of yellow coloured precipitate.

2. Detection of glycosides

Extracts were hydrolysed with dil. HCl, and then subjected to test for glycosides.

- a. **Modified Borntrager's Test:** Extracts were treated with Ferric Chloride solution and immersed in boiling water for about minutes. The mixture was cooled and extracted with equal volumes of benzene. The benzene layer was separated and treated with ammonia solution. Formation of rose-pink colour in the ammonical layer indicates the presence of anthranol glycosides.
- b. **Legal's Test:** Extracts were treated with sodium nitropruside in pyridine and sodium hydroxide. Formation of pink to blood red colour indicates the presence of cardiac glycosides.

3. Detection of Saponins

- a. **Froth Test:** Extracts were diluted with distilled water to 20ml and this was shaken in a graduated cylinder for 15 minutes. Formation of 1 cm layer of foam indicates the presence of saponins.
- b. **Foam Test:** 0.5 gm of extract was shaken with 2 ml of water. If foam produced persists for ten minutes it indicates the presence of saponins.

4. Detection of tannins

Gelatin Test: To the extract, 1% gelatin solution containing

sodium chloride was added. Formation of white precipitate indicates the presence of tannins.

5. Detection of flavonoids

- **a.** Alkaline Reagent Test: Extracts were treated with few drops of sodium hydroxide solution. Formation of intense yellow colour, which becomes colorless on addition of dilute acid, indicates the presence of flavonoids.
- **b.** Lead acetate Test: Extracts were treated with few drops of lead acetate solution. Formation of yellow colour precipitate indicates the presence of flavonoids.

Mode of action of different phytochemicals Saponins

Affect the permeability of the cell membrane of the parasites and cause vacuolization and disintegration of teguments (Melzig *et al*, 2001)^[47].

Benzyl isothocyanate

Inhibiting energy metabolism and affecting motor activity of the parasites

Cysteine proteinases

Plant cysteine proteinases papain and chymopapain have high proteolytic activities that are known to digest nematode cuticles.

Isoflavones

Inhibiting the enzymes of glycolysis and glycogenolysis and disturbing the Ca2+ homeostasis and NO activity in the parasites (Das *et al.* 2004) $^{[20]}$.

Artemisinin

The mechanism of action of artemisinin involves cleavage of end peroxide bridges by iron producing free radicals (hypervalent iron-oxo species, epoxides, aldehydes, and dicarbonyl compounds) which damage biological macromolecules causing oxidative stress in the cells of the parasite (Cumming *et al*, 1997) ^[80].

Common indigenous plant having activity against helminth Carica papaya

- Common name: Papita, Pawpaw
- Active principle: Papain, Chymopapain, Benzyl isothiocynate
- Plant parts used: leaves, Fruits,

Antiparasitic activity

Papaya has antihelmintic activity against natural infection of *A. suum* in pigs and found 100% efficacy at the dose rate of 8g/kg b. wt. (Satrija *et al.*, 1994) ^[66]. The plant extract of papaya posses a dose dependent significant effect on egg, infective larvae and adult worm of *T. colubriformis* (Hounzangbe *et al.*, 2005) ^[29]. The cold macerated aquous extract of matured papaya seed shown anti amoebic activity against *E. histolytica* (Tona *et al.*, 1998) ^[76]. Aqueous extract of the seeds of Carica papaya showed over 90 % efficacy against Oesophagostomum, Trichuris and trichostrongylus. (Fajimi, *et al.*, 2001) ^[81].

Butea monosperma

- Common name: Palash, Dhak, Khakara, Chichra, Bastard Teak, Bengal Kino,
- Active principles: Palasonin,
- Plant part used: seed

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Anti parasitic activity

The anthelmintic activity of different Butea has been reported against *Ascaridia galli, Ascaris lumbricoides, earthworms, Toxocara canis, Oxyurids, Dipylidium caninum* and Taenia (Iqbal *et al.*, 2006) ^[32]. Pipali Rasayana, an Ayurvedic herbal medicine, prepared from *Piper longum* (Pippali) and *Butea monosperma* (Palash) in which ash of stem, root, flower and leaves of *Butea monosperma* is used, has significant activity against Giardiasis It produced up to 98% recovery from the infection.

Terminalia arjuna

- Common name: Arjuna Tree
- Active principle: Tannins
- **Plants part used :** Barks (methanolic extract)

Effective against

Terminalia arjuna bark exhibited anthelmintic activity both *in vitro* (eggs, larvae & adult of *H. contortus* and *in vivo* studies against mixed gastrointestinal trichostrongylid nematodes of sheep (Bachaya *et al.*, 2009) ^[82].

Fumaria parviflora

- Common name: Papara, Pit papra
- Active principle: Alkaloids (Protopine, fumarizine, Papraine, Papracine papracinine and Tannins (Heidari *et al.*, 2004; Rao *et al.*, 2007)^[27, 63]
- Plants part used: Barks

Antiparasitic activity

Water and ethanol extracts of *Fumaria parviflora* posses significant anthelmintic efficacy against *Trichostrongylus, Haemonchus and Trichuris infections in sheep* (Akhtar and Javed, 1985)^[5].

Allium sativum

- Common name: Lahsun, lasum, lassan
- Active principle: Oxygenated sulphur compound Allicin.
- **Plant part used:** Bulb

Antiparasitic activity

Allicin (30 µg/mL) very efficiently inhibited the growth of protozoan parasites such as *Giardia lamblia, Leishmania major, Leptomonas colosoma, and Crithidia fasciculata* (Mirelman *et al.*, 1987)^[49]. Oil of *A. sativum has also been reported to* possess anthelmintic activity and discards all injurious parasites in the intestine (Nadkarni, 1976)^[51]. *A. sativum* has shown been anthelmintic action against *H. gallinae, A. galli* (Nagaich, 2000)^[69], *H. contortus* (Iqbal *et al*, 2001)^[84], and eggs of *A. suum* (Chybowski, 1997)^[85] *in vitro. In vivo* it is also effective against strongyloids in donkey (Sutton and Haik, 1999)^[17].

Cucurbita máxima

- Common name: pumpkin, Kaddu
- Active principle: Cucurbitin
- Plant part used: Seed

Antiparasitic activity

The aqueous, etheral and alcoholic extracts of C. mexicana seeds have exhibited good anthelmintic activity *against Moniezia expansa, Fasciolopsis buski, Ascaris lumbricoides* and *Hymenolepis diminuta* (Shrivastava & Singh, 1967)^[68].

Therapeutic efficacy of *Cucurbita maxima* against clinical cases of nematodiasis in calves has been documented (Pradhan *et al.*, 1992)^[61].

Z. officinale

- Common name: Ginger, Adrak, Ada, Sonth
- Active principle: zingiberene and bisabolene, gingerols and shogaols
- Plant part used: Rhizomes

Antiparasitic activity

The anthelmintic activity of alcoholic extracts of rhizomes of *Z. officinale* against human *Ascaris lumbricoldes* is appreciable (Kalesaraj, 1974; 1975) ^[38, 39]. Antifilarial effect of *Z. officinale* against *Dirofilaria immitis* is reported by Datta and Sukul, 1987 ^[23]. *Z. officinale* also have Molluscicidal and Antischistosomal activities (Adeewunmi *et al.*, 1990) ^[2].

Nigella sativa

- **Common name:** black cumin, kali jeera kolajeera, kalo jeeray
- Active principle: Thimoquinone, dithimo quinone-Cymen α-pinane
- Plant part used: seed

Antiparasitic activity

The essential oils of *Nigella sativa* exhibit good anthelmintic activity against earthworms, tapeworms, hookworms and nodular worm (Agarwal *et al.*, 1979) ^[3]. Kailani *et al.* 1995 ^[37] evaluated antifasciolic efficacy of powdered *Nigella sativa* seeds.

Flemingia vestita

- **Common name:** Benth,
- Active principle: Genistein
- Plant part used: Root Tuber peel extract

Antiparasitic activity

Genistein was subsequently demonstrated to be highly effective against intestinal parasites such as the poultry cestode *Raillietina echinobothridia* (Tandon *et al.*, 1997) ^[74] the pork *trematode Fasiolopsis buski* (*Kar et al.*, 2002) ^[40] and the sheep liver fluke *Fasciola hepatica* (Toner *et al.*, 2008) ^[77]. Genistein and its derivatives, Rm6423 and Rm 6426, are potent cestocides against *E. multiloculoris* and *E. granulous* metacestodes (Naguleswaran *et al.*, 2006) ^[83].

Melia azedarach

- Common name: Bakain, Vilayati neem, Ghoda neem
- Active principle: Mliacaprin, Scopoletin, Meliartenin
- Plant part used: leaves and seed.

Antiparasitic activity

Melia azedarach extracts have larvicidal and ovicidal activity on the helminthus *Haemonchus contortus*. (Maciel *et al.*, 2006) ^[45]. the anthelmintic activity of ethanolic extract of *Melia azedarach* Linn. (*Meliaceae*) was found to be better against *T. solium* than that of piperazine phosphate (Szewczuk *et al.*, 2003) ^[71]. *M. azedarach* extracts was viable in reducing the viability of *Trichmonas vaginalis*. (Lee *et al.*, 2007) ^[86]. Extracts of *M. azedarach* showed efficacy against the *tick Boophilus micoplus*, the malarial vector *Anopheles stephensi*, the dengue vector, *Aedes aegypti* and the human lice *Pediculus humanus capitis*.

Ocimum sanctum

- Common name: Sacred basil, Tulsi
- Active principle: Eugenol, β caryophyllene, urosilic acid
- **Plant part used:** leaves and seed.

Antiparasitic activity:

Singh and Nagaichi (2002) ^[69] evaluated the antiparasitic effects of ethyl alchohol extract of *Ocimum sanctum against A. galli in vitro*. Various essential oils and eugenol isolated from *Ocimum sanctum* have shown potent anthelmintic activity against *C. elegans* (Asha *et al.*, 2001) ^[82].

Azadirachta indica

- Common name: Neem
- Active principle: Azadirachtin
- Plant part used: leaves, flowers

Antiparasitic activity

Alcoholic extract effective against *Fasciola gigantica* (Kushwaha *et al.*, 2004) ^[88]. Aqueous and alcoholic extracts of flowers show anthelmintic activity against *Setaria cervi* (Mishra *et al.*, 2005) ^[50]. Aqueous and Methanolic extract of leaves is effective against *Haemonchus contortus* (Singh *et al.*, 2008, Arora *et al.*, 2010) ^[69] *Azadirachta indica* (neem) possesses larvicidal activity against *C. felis* and *Xenopsylla brasiliensis* (Kilonzo, 1991) ^[42]. *A. indica* seed showed very high level of efficacy (80%) after 5 h of treatment against *B. microplus* (Srivastava *et al.*, 2008) ^[89].

Calotropis procera

- Common name: Milkweed Aak, Mudar,oak,
- Active principle: calotropin, calactin
- Plant part used: Root, leaves and flower.

Antiparasitic activity

Calotropain (Proteolytic enzyme isolated from the latex of *Calotropis procera*) have potent anthelmintic activity against *Oesophagostomum columbianum* and *Bunostomum trigonocephalum* of sheep origin (Garg and Atal, 1963) ^[28]. The latex has been shown to possess anthelmintic activity against *H. contortus* infection in sheep (Shivkar and Kumar, 2003) ^[67]. It is also effective against Osetertagia, nematodirus, Dictyocaulus, Teania, Ascaris and Fasciola. (Al-qarawi *et al*, 2001) ^[1].

Artemisia annua

- **Common name:** Sweet wormwood, annual wormwood, Nagdona, Daman
- Active principle: Artemisinin, Quercetin
- **Plant part used:** leaves and twigs

Antiparasitc activity

Artemisinin-derived drugs have shown effects on a variety of parasites such as *Fasciola hepatica* and gastrointestinal nematodes in small ruminants. *Plasmodium* spp., *Coccidia* spp., *Babesia* spp., *Leishmania* spp., *Neospora caninum* and

Schistosoma spp (Tariq *et al.*, 2009)^[75]. Artemisinin and its derivatives are used for both uncomplicated and severe *P*. *falciparum* malaria. *Artemisia annua tea* was also effective against *Toxoplasma gondii*, although *artemisinin* was only present at 0.2% in the tea (Oliveira *et al.*, 2009)^[87].

Achyranthes aspera

- Common name: Prickly Chaff-flower, Latjeera, Chirchira
- Active principle: Calotropin, Calactin
- Plant part used: Dried leaf, flower and seed extract

Antiparasitic activity

Ethyl acetate extracts of *A. aspera* shows antiparasitic activity against the larvae of cattle tick *Rhipicephalus, Boophilus microplus* and sheep internal parasite *Paramphistomum cervi* (Zahir *et al.*, 2009) ^[79]. Acetone, chloroform, ethyl acetate, hexane and methanol leaf extracts of *Achyranthes aspera* cause mortality of the early fourth-instar larvae of *Aedes aegypti* and *Culex quinquefasciatus* within 24 hrs (Bagavan *et al.*, 2008) ^[13].

Limitation of plant based anthelminthics

- Seasonal availability of certain plants.
- Some plants has to be found in special habitats.
- Collecting, preparing and administering the ingredients, which is very time consuming.
- Ethanomedicine does not follow western paradigms of scientific proof of efficacy.

Future prospects

- There is need to screening of medicinal plants with reference to the phytoconstituents on the basis of research problem in livestock.
- The 80% population of developing countries depends upon herbal medicine so marketing is too good
- To explore indigenous Traditional knowledge through medicine plants needs government support and establishment of biotechnology industry for proper implementation of herbal medicine
- Need of establishment and implementation of policy frame work for the regulation and standardization of herbal medicines.

Conclusion

- Plant medicine are used as alternative methods to control livestock parasitism
- Plant anthelmintics have good efficacy against helminthes
- The chance of development of resistance against phytoanthelmintics is lesser than in comparison to chemical anthelmintics
- Plant based anthelmintics are safe, economical, easily available in surrounding and it will be helpful for poor farmers or livestock rearer.
- It is eco-friendly and promotes biodiversity.

Table 1: Medicinal Plants and their activity	against different classes of Helmith
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Medicinal Plants	Active Principle	Effective against	References
Vernonia anthelmintica	Anthraquinone	Nematodes	Hordegen <i>et al.</i> 2003 ^[28]
C. ambrosioides	Benzyl isothiocynate	Nematodes	British Vet. Codex 1965
Azadirachta indica	Azadirachtin	Nematodes	Hogade et al. 2014
C. cinerariaefolium	Pyrethrin	Nematodes	Mbaria et al. 1998 ^[46]
Macuna prurita	Alkaloids	Cestodes	Neogi et al. 1964 [55]

Lagenaria siceraria	Terpenoids	Cestodes	Akhtar <i>et al</i> . 1987 ^[6]
Zanthoxylum alatum	Tannin, Saponin	Cestodes	Singh et al. 1982 ^[70]
Albizia anthelmintica	Tetra hydroharmine	Cestodes	Atta et al. 2003
Embelia schimperi	Benzoquinone	Trematodes	Bagh et al. 1996 [15]
Albizia anthelmintica	Tetra hydroharmine	Trematodes	Koko et al. 2003 ^[43]
Nigella sativa	Thimoquinone	Trematodes	Shalaby et al. 2012
Artemisia annua	Artemisinin	Trematodes	Tariq et al. 2009 ^[75]

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