**Anthelmintic activity of plant extracts and synthesized green metal nanoparticles against gut helminths of ruminants**

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**Abstract**

India's economy is heavily dependent on its livestock industry. It improves the financial situation of rural impoverished people. It is a key agricultural source that boosts household income in rural regions and benefits the economy by generating jobs. Goats, cows, and buffaloes are raised for a number of purposes, including the production of leather, meat, and milk. Helminths are known for infecting humans, goats, cows, and buffaloes. The country's economy is impacted by these illnesses since they result in serious livestock ailments. Various kinds of synthetic drugs like albendazole, mebendazole, etc. are easily available in the local market, widely used for helminth control. However, long-term use of these synthetic medications reveals significant toxicity and adverse clinical side effects to both target and non-target species, including loss of appetite, nausea, vomiting, headaches, stomach discomfort, diarrhoea, and hepatotoxicity. It is therefore imperative to find anthelmintic medications that are more effective, less toxic, and have few to no adverse effects. The current review effort compiles research on medicinal plants' effectiveness against various cattle helminths conducted in vitro and in vivo. The development of efficient anthelmintic drugs with minimal side effects and non-resistance to parasitic helminths is expected to be possible using these plant-based herbal remedies. Recently, various types of plant synthesized-metal nanoparticles have proved highly effective in controlling helminth diseases, they have been examined in broad range of research field because they are safe, cost-effective, and easily available having simple biosynthesis process. This review paper also emphasises the therapeutic applications of diverse biologically produced metal nanoparticles, which presents a new avenue with pharmacological support for the successful treatment of numerous helminth illnesses.

**Keyword**: Anthelmintic activity, plant extract, synthesized green nanoparticles, parasitic helminth

**Introduction**

Worldwide, helminth parasite diseases affect billions of people as well as ruminants (WHO 2010), with the majority of cases occurring in tropical and sub-tropical nations with low per capita incomes and unhygienic living conditions (Hotez et al., 2007). India is responsible for about 25% of all helminth infections worldwide. In the livestock industry, this infectious agent causes anorexia, anaemia, diarrhoea, weight loss, and significant production losses (WHO, 2017). The three groups of helminth parasites are cestodes (flatworm), trematodes (flukes), and nematodes (roundworms). Gastrointestinal (GI) nematodes, such as Haemonchus contortus, Bunostomum sp., and Trichostrongylus sp., are among these helminths and have a significant impact on the security of the food supply. All types of ruminants are adversely affected by helminths; some helminths are bloodsuckers and cause anaemia, while many others affect the body's physiology, metabolism, and immune system, leading to significant economic losses in the production of meat, milk, and wool as well as in reproduction (Suarez et al., 2009). Since a decade, broad spectrum synthetic anthelmintic medications like ivermectin, albendazole, and levamisole have been utilised to protect our animals against gastrointestinal helminth infections. The main source of resistance as well as the toxicities growing out of their use is the residue of all these dangerous synthetic medications in animals and animal products (Kundu et al., 2015). According to Devi et al. (2009), these sorts of dangerous medications exhibit high levels of toxicity and severe clinical symptoms such as loss of appetite, nausea, vomiting, headaches, abdominal discomfort, diarrhoea, and hepatotoxicity. The most recent strategy involves using herbal treatments either by alone or in conjunction with conventional anthelmintics. Researchers have shown that herbal anthelmintics contain natural plant components that are safe for the environment, non-toxic, cost-effective, and have very few or no side effects. Numerous researchers have examined plant anthelmintics and established their efficacy as complementary anthelmintic treatments. The majority of in vitro studies concentrated on how plant extracts and their fractions affected helminths while they were in their free-living phases. Animal feed was the main source of medicine for in vivo research, which revealed poorer efficacy than in vitro tests. To assess the anthelmintic effects of plant extracts and products, in vitro anthelmintic tests such as the egg hatch inhibition assay/test (EHIA/EHIT), adult mortality inhibition assay/test (AMIA/AMIT), larval development inhibition assay/test (LDIA/LDIT), larval mortality inhibition assay/test (LMIA/LMIT), larval migration inhibition assay/test (LMIA/LMIT), larval feeding inhibition assay. The most common tests, such as LMIT and AMIT, evaluate different plant extracts' abilities to affect helminth larvae and adult motility, and EHIT evaluates their ability to prevent egg hatching. Due to their quicker turnaround times and comparable cost-effectiveness, in vitro procedures are preferred to in vivo methods for testing plant materials on a wide scale. The faecal egg count reduction test (FECRT) and the controlled efficacy test (CET) are two in vivo anthelmintic tests that aren't the best due to their higher cost, lack of precision, and reproducibility due to inter-animal variation and the drug's pharmacodynamics in the host (O'Craven et al., 1999; Santos et al., 2019).

Botanical anthelmintics are known to be abundant in the plant kingdom (Satyavati et al., 1985). For primary healthcare and other health benefits, almost 80% of the world's population still uses our traditional medicines made from plant extracts (WHO, 2008). According to Temjenmongla and Yadav (2005), traditional medicines have a lot of potential as sources of easily accessible efficient anthelmintics drugs. In poor nations like India, China, Bangladesh, etc., helminthiasis is historically treated with a variety of folklore medicinal herbs (Choudhary et al., 2015). The anthelmintic efficacy of several fabled medicinal plants against liver fluke and other parasites has been investigated (Tandon et al., 1997; Mehlhorn et al., 2011). In order to cure parasite infection, plant-derived medications and herbal remedies are becoming increasingly popular (Mehlhorn et al., 2010; Dehuri et al., 2021). These herbal medications are appealing since they are easily accessible, affordable, have few to no adverse effects, and do not result in resistance (Wakayo and Pewo, 2015).

Recently, efficient green chemistry techniques for the synthesis of metal nanoparticles, which is of special interest to researchers, have been developed. They have done extensive research and have discovered a method for producing well-characterized nanoparticles that is both secure and environmentally benign. The use of organisms to produce metal nanoparticles is one of the approaches that is most frequently discussed. Among these creatures, plants seem to be the most appropriate and best option for the mass synthesis of nanoparticles. Compared to microbes, plants create nanoparticles that are more stable and synthesise them at a faster rate. In addition, the nanoparticles differ from those made by other animals in form and size (1-100 nm). Due to the advantages of employing plants and products made from plants for the biosynthesis of metal nanoparticles, researchers are investigating the mechanisms of metal ions uptake and bio-reduction by plants as well as the potential mechanisms of metal nanoparticle formation in plants. Typically, diverse biomolecules, particular medications, nucleic acids, peptides, and antibodies are carried by metal nanoparticles made of gold, silver, platinum, iron, silica, copper, zinc, and some lanthanides. For a variety of illness types, such as cancer, microbial infections, parasitic infections, cardiovascular disease, and neurological disorders, they can serve as diagnostic and therapeutic agents (Zhang et al., 2020). Metal nanoparticles derived from plants offer hope for new therapies for the management of parasitic illnesses.

Studies are done both in-vitro and in-vivo to determine the efficacy of plants with anthelmintic activity. Various medicinal plants and artificial green nanoparticles that may be effective against various gastrointestinal helminths (cestode, trematode, and nematode) have been described and tabulated in this review. These findings may pave the way for basic pharmacological studies that will result in the development of new anthelmintics to replace the traditional ones that suffer from anthelmintic resistance and high cost.

**Objectives**

The purpose of this review of the literature is to compile and update information on crude extracts and green metal nanoparticles created from medicinal plant extracts that have been suggested to have potential anthelmintic activities (ovicidal, larvicidal, and adulticidal) against various types of ruminant's gut helminth.

**Material and methods**

The review of literature has been made by following various research articles including 8 databases (5 English databases: PubMed, Elsevier, Research Gate Google scholar, Science Direct) And (3 Persian databases: Scientific Information Database or SID, Magiran, and ISC) through the years between 2002 – 2022, where Anthelmintic activity of plants extracts and green synthesis of Metal Nano particles were reported. The combination of the words “Herbal medicine,” “Plant extract,” “In vitro,” “In vivo,” “Anthelmintic”, “Ruminant”, “Green synthesis”, and “Nano particles” were used for searching. I have collected those data from the relevant papers and enlisted them in this review of literature.

**General concept about helminth**

Helminth means parasitic worm in general term. They are invertebrates characterized by flat, elongated or round bodies. Flukes and tapeworms are examples of platyhelminths, sometimes known as flatworms (the word "platy" is derived from the Greek for "flat"). Nematodes are roundworms; the term nemato means "thread" in Greek. These categories are further separated into the host organs that each group inhabits, such as intestinal roundworms, extraintestinal tapeworms, and lung flukes. The internal and exterior morphology of the egg, larval, and adult stages form the basis for the final classification. Aschelminthes and Platyhelminthes are the two phyla in which helminths are classified. In the Phylum Platyhelminthes, parasitic helminths largely belong to the two classes Trematoda and Cestoda, however in the Phylum Aschelminthes, there is only one class Nematoda that has parasitic helminth. These intestinal and blood endoparasites are the source of a number of illnesses referred to as helminthiasis.

**Cestodes (Tapeworms)**

They are commonly known as tapeworms. The body of the cestode is divided into several segments known as proglottids and lacks cilia and an epidermis. Scolex is present on the front end and has hooks and suckers. They are always hermaphrodites. Adult tapeworms inhabit in the intestinal lumen and larva are cystic or solid, they inhabit in extraintestinal tissues. Some of the most widespread diseases caused by cestodes are Taeniasis *(Taenia saginata* and *Taenia solium),* Hymenolopiasis (*Hymenolepis nana*), Echinococcosis or Hydatid cyst disease *(Echinococcus* sp.), diphyllobothriasis *(Diphyllobothrium latum), Hymenolepis dimimita* etc.

**Trematodes (Flukes)**

Flukes are flatworms with a leaf-like form that are adults and have distinct oral and ventral suckers that aid in maintaining posture. With the exception of blood flukes, all parasites are hermaphroditic. A snail serves as an intermediary host during the life cycle. Some of the most common and widespread diseases caused by trematodes are Schistosomiasis *(Schistosoma mansoni, Schistosoma japonicum* and *Schistosoma haematobium),* Opisthorchiasis or clanorchiasis *(Opisthorchis* sp.), paragonimiasis *{Paragonimus* sp.), Fasciolopsiasis *(Fasciolopsis buski),* Fascioliasis *(Fasciola hepatica).*

**Nematodes (Roundworms)**

They are frequently referred to as roundworms because of their cuticle-covered body wall, lack of cilia, cellular or syncytial epideris, and longitudinal muscles in four bands. In most cases, internal fertilisation happens in dioecious animals. Both the larva and the adults have a cylindrical form and are bisexual. They reside in both intra- and extraintestinal locations. The most common widespread diseases caused due to infestation with the nematodes are Ascariasis (*Ascaris* sp.), Ancylostomiasis (*Ancylostoma duodenale*), Enterobius (*Enterobius vermicularis*), Trichuriasis (*Trichuris trichura*), Trichinosis (*Trichinella* sp.), Filariasis (*Wucheraria bancrofti*), Loiasis (*Loa loa*), Onchocerciasis (*Onchocerca volvulus*).

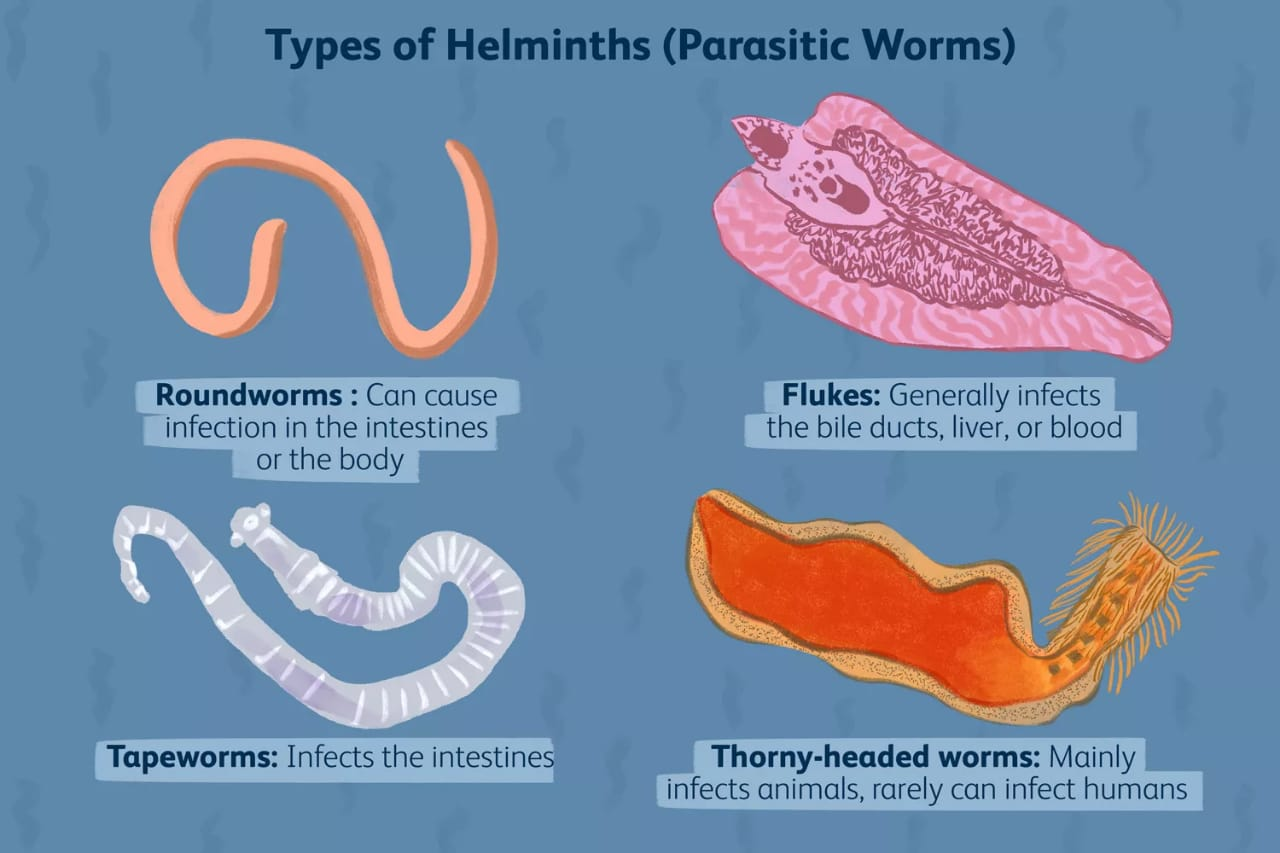


Figure 1: **Types of helminths (parasitic worms)**

(Source: https://www.verywellhealth.com/helminths-5207511)

**About nanoparticles**

The word nanoparticles come from the Greek word “nano”. Nano is a very small size. According to Horikoshi and Serpone (2013), nanoparticles are particles with sizes between one and one hundred nanometers. Any unit can have it as a prefix to denote a billionth of that unit. The active substances are dispersed, trapped, encapsulated, adsorbed, or connected to micromolecular components that make up these products. It is a colloidal particle that is solid.

Green synthesis is a method for creating nanomaterials that is clean, safe, economical, and ecologically beneficial. The green synthesis of nanomaterials uses microorganisms like bacteria, yeast, fungi, algal species, and some plants as substrates. The green synthesis method offers quick, inexpensive, and repeatable methods for producing metallic nanoparticles that are environmentally benign.

Metal-based nanoparticles are widely used in engineering and medicinal sciences. Their market has expanded considerably over the past few years, and it is not expected to decline. AgNPs, CuONPs, AuNPs, and ZnONPs are a few examples of the several types of nanoparticles that are frequently utilised in pharmaceutical and medical applications (such as antibacterial, antifungal, antiviral, antiamebic, anticancer, and anti-angiogenic drugs).

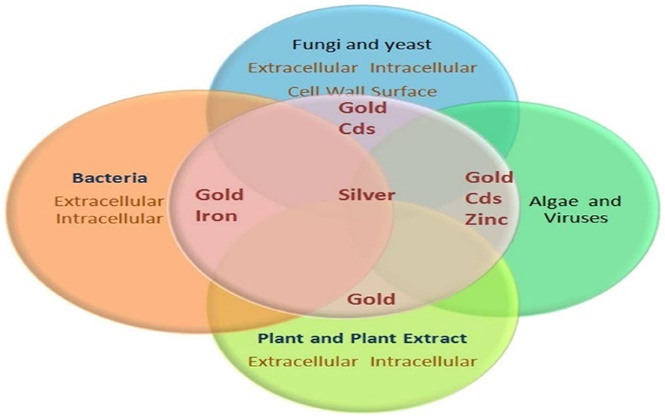


Figure 2: **Different metal Nanoparticles (Gold, Silver, Zinc, Cadmium, Iron)**

(Source: https://www.frontiersin.org/articles/10.3389/fchem.2020.00799/full)

**Mode of action of plant as an anthelmintics**

According to the WHO (2002), two-thirds of the world's population rely on plants as their main source of medical treatment. According to Newman and Cragg (2016), between 50,000 and 70,000 plant species are employed in both traditional and Western medical practises, and 25% of prescription drugs are made from plants or secondary metabolites obtained from them (Hammond et al., 1997; Akhtar et al., 2000; Githiori et al., 2006). Even today, at least 25% of medications are still derived from plants, and many more are semi-synthetic and constructed on plant-derived prototype chemicals (Kalia, 2005). All plant anthelmintics essentially kill helminth by paralyzing or starving them to death. If a paralysed parasite loses their ability to hold their position in the stomach for a while, they will also die (Schoenian, 2010). Scanning electron micrograph (SEM) showed that plant Anthelmintic mostly causes tegumental damages, sucker disruption, scolex and entire body shrinkage in helminth and transmission electron micrograph (TEM) showed loss of parenchymal layer and chromatin clumped in nucleus occurs in helminth in most cases. Phytoconstituents showing anthelmintic effect includes tannins, alkaloids, polyphenols, saponins, flavonoids etc.

i) Alkaloids operate on the CNS, which causes paralysis, reduce the support of glucose to the helminths, and inhibit the transfer of sucrose from the stomach to the small intestine (Roy, 2010).

ii) According to Wang et al. (2010), saponins cause vacuolization and the disintegration of teguments by interfering with the permeability of the helminths' cell membrane.

iii) According to Tiwari et al. (2011), Sutar et al. (2010), and Mali et al. (2007), polyphenols and tannins increase the supply and absorption of digestible proteins by forming protein complexes in the rumen, which dissociate at low pH in the abdomen and release more protein for metabolism. They also suppress energy generation by uncoupling oxidative phosphorylation and reduce gastro-intestinal metabolism, which causes helminth paralysis and death.

iv) By linking through H-H bonds, tannins bind to free proteins in the GI tract of the host animal or to the glycoprotein in the cuticle of helminths. This reactivity results in toughness in the skin, which renders worms immobile and non-functional. Tannins also reduce nutrient availability, which causes starvation in the larvae or reduced GI metabolism, which causes paralysis and then death (Vidyadhar et al., 2010). According to several reports, improving the availability of digestible protein helps sheep be more resilient and resistant to gastrointestinal nematodes. It also causes physiological changes in the host's gut, which leads to the rapid secretion of mucous and chemicals that are toxic to the helminths (Bachaya et al., 2009).

v) Steroidal alkaloid oligoglycosides prevent sucrose from being transferred from the stomach to the small intestine while decreasing the support of glucose in helminths and its antioxidant function. which inhibits the production of nitrate (which might be used in protein synthesis) and any potential inflammatory effects on the gastric and intestinal mucosa that might disrupt local homeostasis, both of which are necessary for the growth of helminths (Cruz, 2008).

vi) According to Laverack (1963), ethanol extract can lower pH, which has the effect of starving the worms or causing osmotic anomalies.

vii) On adult parasites, hydro-alcoholic extracts typically perform better than aqueous extracts. Recent research suggests that it may have occurred because hydroalcoholic extracts were more easily absorbed through the skin into the helminth's body than aqueous extracts. Hydroalcoholic plant extracts frequently include specific non-polar chemical components with lower polarity than aqueous extracts for improved anthelmintic activity. As a result, they are lipid soluble in comparison to aqueous extracts (Kumar et al., 2010).

Here some Medicinal plants list with proven anthelmintic effects are given below (in table 1).

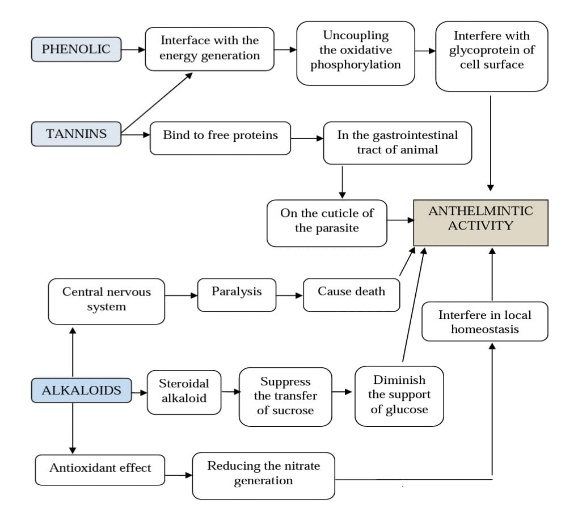


Figure 3: **Different phytochemical’s mode of action in Anthelmintic activity**

(Source: Kumar et al., 2010)

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| Table 1: **Medicinal plants list with proven anthelmintic effects** | | | |
| **Plant name** | **Family** | **Plant part used** | **Reference** |
| *Tamarindus indica* | Caesalpiniaceae | Bark | Das et al., 2011 |
| *Tephrosia purpurea* | Fabaceae | Leaves | Manjula et al., 2013 |
| *Terminalia arjuna* | Combretaceae | Bark | Bachaya et al., 2009 |
| *Uncaria gambier* | Rubiaceae | Leaves | Patil et al., 2012 |
| *Mimuosops elengi* | Sapotaceae | Bark | Mali et al., 2007 |
| *Murraya koenigii* | Rutacae | Root | Pagariya et al., 2013 |
| *Nicotiana tabacum* | Solanaceae | Leaves | Iqbal et al., 2006 |
| *Albizia schimperiana* | Fabaceae | Stem and root | Githiori et al., 2003 |
| *Paederia foetida* | Rubiaceae | Leaves | Pal, 2011 |
| *Pajanelia longifolia* | Bignoniaceae | Bark | Asha et al., 2013 |
| *Portulaca oleracea* | Portulacaceae | Leaves | Rao et al., 2013 |
| *Saraca indica* | Leguminosae | Leaves | Sharma et al., 2011 |
| *Spermacoce ocymoides* | Rubiaceae | Leaves | Parhi et al., 2012 |
| *Strobilanthes discolor* | Acanthaceae | Leaves | Tangpu et al., 2006 |
| *Curcuma amada* | Zingiberaceae | Rhizome | Rakh et al., 2014 |
| *Diplazium esculentum* | Athyriaceae | Rhizome | Amit and Singh, 2012 |
| *Drypetes sepiaria* | Euphorbiaceae | Leaves | Gadamsetty et al., 2013 |
| *Ficus bengalensis* | Moraceae | Fruit | Sawaskar et al., 2011 |
| *Flacourtia sepiaria* | Flacourtiaceae | Leaves | Sreejith et al., 2013 |
| *Gymnema sylvestre* | Asclepiadaceae | Leaves | Raj et al., 2012 |
| *Hedychium spichatum* | Zingiberaceae | Rhizome | Goswami et al., 2011 |
| *Helicteres isora* | Sterculiaceae | Fruit | Amit et al., 2011 |
| *Heliotropium indicum* | Boraginaceae | Leaves | Mahato et al., 2014 |
| *Physalis minima* | Solanaceae | Leaves | Ahmed et al., 2022 |
| *Cotyledon orbiculate* | Crassulaceae | Shoots | Mofele et al., 2013 |
| *Achyranthes aspera* | Amaranthaceae | Stem | Naga et al., 2013 |
| *Croton bonplandianium* | Euphorbiaceae | Leaves | Hapse et al., 2012 |
| *Baliospermum montanum* | Euphorbiaceae | Root | Mali and Wadekar, 2008 |
| *Bambusa vulgaris* | Bambusoideae | Leaves | Ikechukwuogu, 2012 |
| *Juglans regia* | Juglandaceae | Stem bark | Kale et al., 2011 |

**Mode of action of green synthesis metal nanoparticles as an anthelmintics**

The majority of research studies on the use of metal-based nanoparticles in the treatment of infectious diseases are built on preclinical analysis. In the treatment of helminth infections, combining metal nanoparticles with plant extract increased the anthelmintic activity. The nanoparticles that are currently being used have better cell interaction and uptake, and some of them even exhibit good selectivity when given specific functional modifications.

**1. Silver nanoparticles**

Plant extracts and silver nanoparticles combined to produce effective anthelmintic action. Rashid et al. used fruit extract to show that polyaniline-coated silver nanoparticles have anthelmintic properties. While the plant extract contains phytochemicals that attach with the free proteins in the gastrointestinal system on the helminth's cuticle, causing paralysis and death, the +ve charge on the Ag ion was attracted to the -ve charged cell membrane of microorganisms by electrostatic interaction (Rashid et al., 2016).

**2. Gold nanoparticles**

Gold nanoparticles, in addition to silver nanoparticles, have the potential to be anthelmintic agents. Kar et al. evaluated the anthelmintic activity of gold nanoparticles. Gold nanoparticles were produced by mixing gold chloride with a mycelia-free culture filtrate of the phytopathogenic fungus. The gold nanoparticles caused the helminth's paralysis and eventual death by directly affecting its physiological processes. The helminth's enzyme activity considerably changed following treatment with gold nanoparticles, illuminating the potential of these particles (Kar et al., 2014).

**3. Metal oxide nanoparticles (Zinc and iron oxide)**

Nanoparticles made of iron oxide and zinc oxide, for instance, have an antihelmintic impact on helminth parasites. Khan et al. (2015) revealed that zinc oxide nanoparticles have an anthelmintic effect on the helminth parasite that affects Indian livestock. By causing the helminths to create ROS, low nanoparticle concentrations caused oxidative stress. The flukes showed signs of a survival strategy by increasing the activity of antioxidant enzymes to scavenge the ROS. When they were treated with a high quantity of nanoparticles, the survival effort was hampered. The detoxification process was rendered ineffective because the worm's antioxidant enzymes were saturated. The antioxidant enzymes of the worm were saturated, rendering the detoxification process ineffective. It is hypothesised that the increased intracellular ROS level will change the contractile activity, interfere with the electron transport chain and make the cell membrane more permeable in helminths (Khan et al., 2015). Zinc oxide and iron oxide nanoparticles were tested for their anthelmintic properties against helminth by Dorostkar et al. (Dorostkar et al., 2017). Iron oxide nanoparticles were shown to be more effective than zinc oxide nanoparticles due to the nature of the nanoparticles. Superoxide Dismutase activity (SOD) was increased following treatment with low doses of both nanoparticles. Because the enzyme was saturated at high nanoparticle concentrations, there was a noticeable decrease in SOD activity in helminths. High concentrations of the oxidative stress caused by the nanoparticles overwhelm ATP production and cause structural damage. According to Dorostkar et al. (2017), the anthelmintic action of metal oxide nanoparticles is caused by the development of oxidative stress.

Metal-based nanoparticles have beneficial biological interactions with biomolecules located within and on the surfaces of cells. They can also be modified to have improved therapeutic efficacy at the diseased site by introducing potent biological components with specific binding activity to choose target cells.

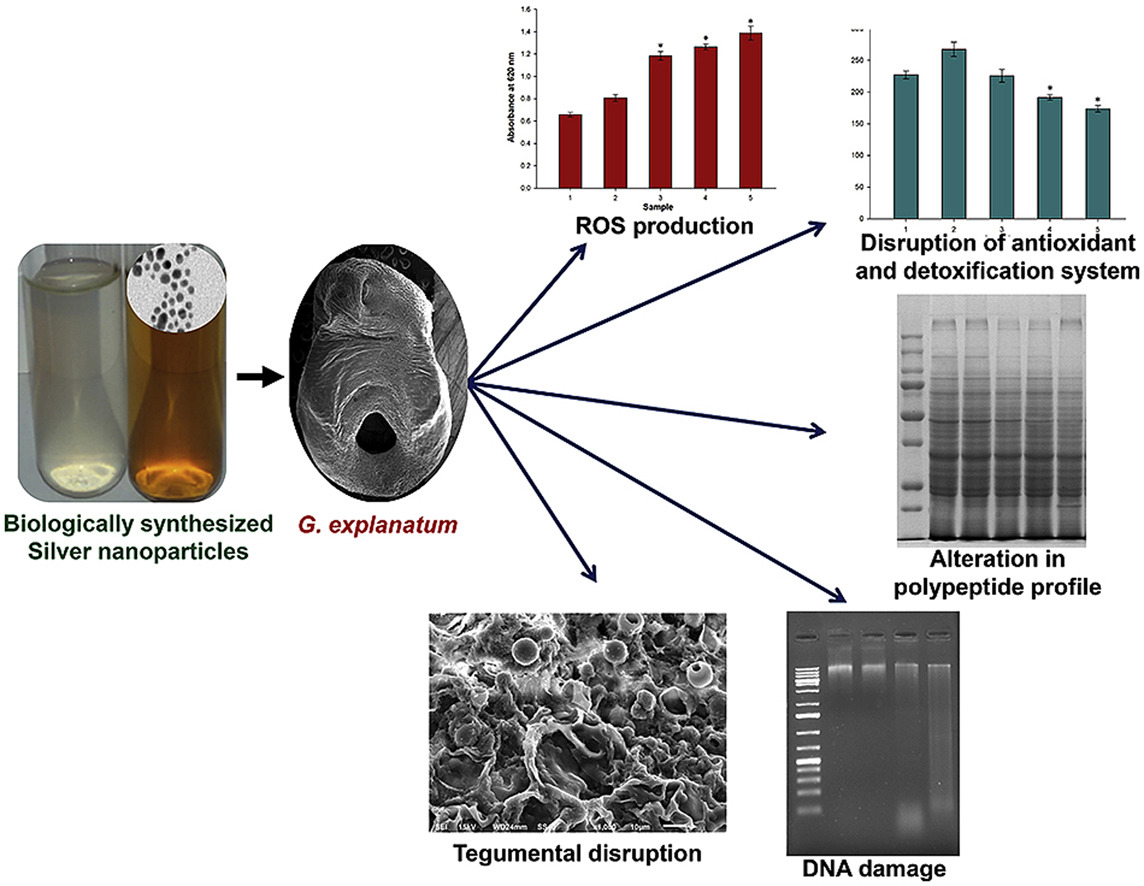


Figure 4: **Morphological alternation in *Gigantocotyle explanatum* (Trematode) due to application of biologically synthesized silver nanoparticles.**

(Source: Rehman et al., 2019)

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| --- | --- | --- | --- | --- | --- | --- | --- |
| Table 2: **Plants reported for having Anthelmintic activity against cestode** | | | | | | | |
| **Name of the helminth** | **Name of the plant** | **Plant part used** | **Solvent used** | **Stage of helminth** | **Test conducted** | **Result /LC50 values** | **Reference** |
| *Hymenolepis diminuta* | *Oroxylum indicum* | Stem,  Bark | Methanol | 2nd stage of Juvenile & Adult in Albino rat | In vitro and in vivo | In vitro, juveniles died after being exposed to 30 mg/ml of extract for the first time (0.25 ± 0.00 hrs.)  of the extract reduced EPG counts by 79.3% and worm numbers by 70.8% in vivo. | Deori et al., 2016 |
| *Cynodon dactylon* | Whole plant | Methanol | Adult,  EPG in Wister rat | In vitro and in vivo | The 40 mg/ml conc. resulted in worm paralysis and mortality in an in vitro test after 4.12 ± 0.55 and 5.16 ± 0.34 hrs. respectively. 800 mg/kg administered orally for 5 days in vivo showed up to 77.64% and 79.00% reductions in EPG counts. | Yadav and Nath, 2017 |
| *Cyperus compressus* | Root | Methanol | Adult in Wister rat | In vitro and in vivo | In vitro, mortality at 8.3 ± 0.05 hrs. at the of 30 mg/ml. Studies conducted in vivo showed a 61.74% decrease in the number of eggs per gram (EPG). | Soren and Yadav,  2020 |
| *Pinus sp., Corylus avellana* and *Trifolium repens* | Pine bark hazelnut Pericarp  White clover flowers | Acetone/water  (7:3; v/v) Condense tannin | Cysticercoids in beetle | In vitro and in vivo | In vitro, condense tannin from all three plant extracts had dose-dependent inhibitory effect, In vivo, hazelnut extract was most effective on cysticercoid development. | Dhakal et al. 2014 |
| *Acorus calamus* | Rhizomes | Methanol | EPG in rat | In vivo | 800 mg/kg of rhizome extract for 5 days causes a 62.30% decrease in the EPG of faeces and an 83.25% decrease in the number of worms. | Nath and Yadav,  2016 |
| *Psidium guajava* and  *Lasia spinosa* | Leaves | Aqueous | Adult in rat | In vitro | 40 mg/ml of aqueous extract showed best result. | Temjenmongla et al., 2015 |
| *Caesalpinia bonducella* and  *Croton joufra* | Leaves | Methanol | 2nd stage of Juvenile and adult in Wister rat | In vitro | 30 mg/ml of methanol extracts showed best result. | Gogoi et al., 2022 |
| *Caesalpinia bonducella* | Leaves | Methanol | Egg,  Adult in mice | In vitro and in vivo | In vitro, 30 mg/ml of methanol extract caused mortality in 2.5 ± 0.2 hrs. In vivo 85% worm load reduction in rats. | Gogoi et al.,  2016 |
| *Raillietina tetragona* and *Ascaridia galli* | *Imperata cylindrica* | whole underground  parts | Chloroform | Adult in fowl | In vitro | Chloroform extract 20 mg/ml took time for *R. tetragona* 36.53 ± 2.66 hrs. to kill and took 81.56 ± 1.71 hrs. took for *A. galli* to kill respectively. | Lalthanpuii and  Lalchhandama, 2020 |
| *Raillietina tetragona* | *Cassia alata, Cassia angustifolia and Cassia occidentalis* | Leaves | Alcohol | Adult from fowl | In vitro | At 40 mg/ml, *C. alata* took less time (1.68 ± 0.27 hrs) to be paralysed combination with any of this plant took shorter time to be paralyzed. | Kundu and Lyndem, 2012 |
| *Iiex khasiana* | Leaves | Methanol | Adult in fowl | In vitro | 20 mg/ml of the methanolic extract took 20.40 ± 2.55 h to kill all the adults. | Lalnunfela et al., 2020 |
| *Raillietina echinobothrida* | *Lysimachia ramose* | Leaves | Crude & N- butanol | Adult in fowl | In vitro | At a dosage of 6 mg/ml of PBS, crude leaf extract and N-butanol fraction caused adults' glycogen conc. to drop by 26–51%. . | Dey and Roy, 2020 |
| *Acmella*  *Oleracea* | Aerial parts | Methanol | Adult in fowl | In vitro | 20 mg/ml the plant extract took 18.42 ± 0.95 hrs to kill the adults. | Lalthanpuii et al.,  2020 |
| *Spilanthes acmella* | Aerial parts of the plant | Chloroform | Adult in fowl | In vitro | Plant extract was effective at all conc. | Lalthanpuii et al., 2020 |
| *Carex baccans* | Root | Aqueous | Adult in fowl | In vitro | 50 mg/ml of the plant extract caused paralysis and death after 3.59 ± 0.02 hrs and 4.13 ± 0.06 hrs. of incubation respectively. | Challam et al., 2012 |
| *Moneizia expansa* | *Abutilon indicum* | Leaves | Methanol | Adult,  Egg in  sheep | In vitro | At 100 mg/ml conc. the paralysis and death time were recorded at 66.3 ± 0.03 and 93.2±0.09 minutes respectively. | Thooyavan et al., 2018 |
| *Tephrosia purpurea* | Root | Methanol | Adult in goat | In vitro | Methanolic extract of 125 mg/ml showing 1.29 ± 0.17 hrs. and 2.63 ± 0.36 hrs. for paralysis and death, respectively. | Ghaywat et al., 2021 |
| *Taenia saginata* | *Gongronema latifolium, Piper guineense and*  *Ocimum gratissimum* | Leaves | Ethanol | Ova in cow | In vivo | 8 hrs. of exposure to 50% conc. of O. gratissimum resulted in 100% death for each ovum. | Daniel et al., 2015 |
| *Hymenolipes nana* | *Punica granatum* | Peel | Methanol | Eggs in rat | In vivo | Methanolic extract with doses of 0.5 ml, 1.0 ml and 1.5 ml decreased the number of worms at 15.6 ± 2.6, 8.4 ± 2.1 and 5.7 ± 2.5 in treated groups respectively. | Al-Megrin et al., 2016 |
| *Ferula*  *Assa-foetida* | Aerial parts | Methanol | Eggs in rat | In vitro | When compared to the control, the highest conc. of methanolic extract significantly reduced the number of eggs and helminths. | Farhadi et al., 2016 |
| *Taenia tetragona* | *Acmella*  *Oleracea* | Aerial parts | n-Hexane | Adult | In vitro | Lethal conc. (LC50) of the n-Hexane extract was 5128.61 ppm. | Lalthanpuii and  Lalchhandama, 2020 |

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| Table 3: **Plants reported for having Anthelmintic activity against trematode** | | | | | | | |
| **Name of the helminth** | **Name of the plant** | **Plant parts used** | **Solvent used** | **Stages of helminth** | **Test**  **Conducted** | **Result /lc5o values** | **References** |
| *Carmyerius spatiosus* and *Paramphistomum sp.* | *Cassia siamea,*  *Plumbago zeylanica,*  *Plumbago indica* and *Terminalia catappa* | Leaves, Heartwoods, Roots and Flowers | Ethyl acetate,  n-butanol,  Hexane and Water | Adult in Cattle and  Buffalo | In vitro | Most effective extract was hexane having LC50 value 34.38 ppm and LC90 value 64.09 ppm. | Minsakom et al.,  2019 |
| *Fasciola hepatica* | *Acacia* *farnesiana, Acacia cornigera, Artemisia absinthium, Bocconia frutescens, Artemisia* *Mexicana, Cajanus cajan, Hibiscus rosasinensis, Cordia spp, Leucaena diversifolia, Lantana camara, Melia azedarach,*  *Mentha sp, Piper auritum, Ocimum basilicum* and  *Teloxys ambrosioides* | Leaves | Hexane,  Ethyl acetate and  Methanol | Newly excysted flukes in ruminant | In vitro | *C. cajan*, *L. camara,* and *P. auritum* all demonstrated 100% efficacy at a dose of 500 mg/l, whereas *B. frutescens* and *A. Mexicana* demonstrated 100% efficacy at a level of 125 mg/l. | Mercado et al., 2015 |
| *Schistosoma mansoni* | *Corydalis crispa* and  *Pleurospermum amabile* | Whole plant | Methanol | Adult in mice | In vitro | IC50 value is 8.6 µg/ml | Wangchuk et al., 2016 |
| *Eryngium triquetrum* | leaves | Essential oil | Larva | In vitro | 0.1 ppm had a prevalence of 3.3%, which was less infectious than untreated, which had a prevalence of 44%. | Augusto al., 2020 |
| *Teclea nobilis* | Leaves | Essential oil | Eggs | In vitro | Essential oil showed LC50 and LC90 values of 196.29 and 367.24 ppm respectively after 30 mins. | Njogu et al., 2014 |
| *Ficus carica* and *Olea europaea* | Leaves | Alcohol | Adult in mice | In vitro | The LC50 about both extracts might have been 21. 35 and 47.98 after 120 hrs. of exposure. | Reda et al. 2016 |
| *Foeniculum vulgare* | Fennel | Essential oil | Adult in mice | In vitro | Conc. of 100 μg/ml, was more effective against adult. | Wakabayashi et al., 2015 |
| *Crocus sativus* | Flower | Aqueous | Egg from mice | In vivo | Significant reduction in overall worm burden (7.00 ± 1.00) and significant increase in the number of dead ovules (13.11 ± 1.68). | Shaaban et al., 2019 |
| *Mentha x villosa huds* | Leaves | Essential oil | Adult in Swiss webster mice | In vitro | Essential oil caused the death of all worms at 500 μg mL-1 after 24 hrs. | Rocha et al., 2016 |
| *Cotylophoron cotylophorum* | *Nigella sativa* | Seeds | Ethanol | Adult in small ruminant | In vitro | After 8 hrs. of treatment, the highest motility inhibition was seen at 0.5 mg/ml conc. | Selvaraju et al., 2019 |
| *Acacia concinna* | Pods | Aqueous | Adult in small ruminant. | In vitro | Effective at 0.5 mg/ml after 8 hrs. of exposure. | Priya and Veerakumari, 2017 |
| *Syzygium aromaticum* | Clove buds | Ethanol,  Hexane, Chloroform and  Ethyl acetate | Adult in small ruminant | In vitro | Ethanolic extract showed maximum inhibition in the motility at highest conc. 86.86%. | Dhanraj and Veerakumari, 2014 |
| *Allium sativum* | Bulb | 70%  Ethanol | Adult in cattle | In vitro | Alcoholic extract showed highest mortality rate at a conc. of 1 mg/l after 8 hrs. exposure. | Radwan et al.,  2012 |
| *Gastrothylax indicus* | *Azadirachta indica, Calotropis procera* and *Punica granatum* | Flower,  Leaves and Fruit peel | Aqueous  Ethanol | Adult in ruminant | In vitro | LC50 values were 12.05 mg/ml ± 3.24 and 23.52 mg/ml ± 6.4 for *C. procera* for ethanolic and aqueous extracts respectively. | Aggarwal et al.,  2016 |
| *Fasciola gigantica* | *Curcuma aeruginosa* | Rhizome | Methanol | Adult in cattle | In vitro | 50% of *C. aeruginosa* extract showed highest mortality. All flukes died after 48 mins. of treatment. | Vanda et al., 2020 |
| *Terminalia catappa* | Leaves | Ethanol | Adult in cattle | In vitro | Maximum efficacy was observed in ethanolic extract of 1000 µg/ml, where 100 % death occur after 3 hrs. of incubation. | Anuracpreeda et al., 2017 |
| *Veitchia merrillii* | Nut | 96% methanol | Adult in cattle | In vitro | 50% of extract showed highest mortality. All flukes died after 30 mins. of treatment. | Vanda et al., 2021 |
| *Dioscorea bulbifera L.* | Bulbils | Methanol | Adult in cattle | In vitro | The median lethal conc. values for liver fluke were 61.73 and 41.79 mg/ml for the meat and peel extracts, respectively. | Adeniran and Sonibare, 2013 |
| *Dregea volubilis* | Leaves | Methanol | Adult in cattle | In vitro | With a conc. of 100 mg/ml, the maximum fasciocidal activity was discovered at 38.83 3.41 minutes. | Hossain et al., 2013 |
| *Fasciola* spp | *Cantharellus cibarius* and *Ganoderma applanatum* | Mushroom fruiting bodies | Ethanol | Eggs and Miracidia stage in gall bladder of cattle | In vitro | *G. applanatum* ethanolic extract (GEE) tested at 8 mg/ml with 91.3% ovicidal activity was significant. higher than *C. cibarius* ethanolic extract (CEE) at the same conc. | Nwofor et al., 2019 |
| *Gastrothylax crumenifer* | *Microlepia*  *Speluncae* | Leaves | Methanol | Adult in sheep | In vitro | LC50 value was 3.666 with a 95% confidence interval of 1.508-4.046. | Devi et al., 2018 |
| *Spilanthes*  *Acmella* | Leaves | Hexane Ethyl acetate Methanol and  Aqueous | Adult in sheep | In vitro | Most effective in aqueous extract of callus at 5 mg/ml conc., caused onset of paralysis in 45.7 min and death in 87 mins. | Singh et al. 2013 |
| *Fasciola hepatica* | *Eugenia uniflora,*  *Harpagophytum procumhens,*  *Psidium guajava* and  *Stryphnodendro nadstringens* | Leaves,  Roots and  Bark | Alcohol | Eggs | In vitro | 100% effective at 0.10% (*E*. *uniflora)* and 100 % effective at 0.25% *(H. procumbens).* | Marques et al., 2020 |
| *Paramphistomum*  *Microbothrium* | *Balanites aegyptiaca* | Fruits | Methanol | Adult | In vitro | The fruit's 200 g/ml methanolic extract demonstrated the maximum potency. | Shalaby et al., 2016 |
| *Paramphistomum explanatum* | *Drega volubilis* | Leaves | Methanol | Adult from buffalo | In vitro | 100 μg/ml of methanolic extract took 10.67±0.61 mins. for death. | Hossain et al., 2012 |
| *Bombax malabaricum* | Leaves | Methanol | Adult from buffalo | In vitro | 100 μg/ml of methanolic extract took 22.17±0.48 mins. for death. | Hossain et al., 2012 |
| *Jatropha gossypifolia* | Root | Petroleum ether extract (60- 80°C) (PEJG) | Adult in cattle | In vitro | PE extract of *J. gossypifolia* (PEJG) at 25 mg/ml killed the trematodes within 158.83 ± 4.94 mins. | Lahiri et al., 2016 |
| Mixed trematodes in bird | *Punica gramatum* | Bark | Acetic acid | Adult in fowl | In vitro | 100 % mortality observed at 5 % conc. after 360 mins. of exposure. | Hai et al., 2014 |
| *Paramphistomum* sp | *Clerodendrum viscosum, Eryngium foetidum, Lippia Javanica,* and *Murraya koenigii* | Leaves | Methanol | Adult in cattle | In vitro | Paralysis and death time were recorded at 0:56 ± 0:09 hrs. and 1:35 ± 0:07 hrs. *for L. javanica* at 50 mg/ml conc. | Swargiary et al.,  2016 |
| *Paramphistomum cervi* | *Physalis minima* | Leaves and Stem | Ethanol | Adult in cattle | In vitro | Paralysis took 10.5 mins. for leaves and 11.3 mins for stem and mortality took 28.8 mins. for leaves and 20 mins. for stem of worms by an ethanolic extract at 100 mg/ml. | Ahmed et al., 2022 |
| *Carica papaya* L. | Leaves | Ethanol | Adult in cattle | In vitro | Higher conc. (100 mg/ml) of ethanolic extracts of the leaves responsible for the paralysis and death. | Haque, 2019 |
| *Balanites aegyptica* | Fruit, leaves and  seed | Alcohol | Adult in buffalo | In vitro | Alcoholic extract at 125 mg/ml conc. showed total mortality at 5 hrs. | Swarnakar et al., 2015 |
| *Ananas sativus, Erythrina variegata and Alocasia indica* | Leaves,  Bark and  Rootstock | Crude aqueous and Hydro-alcoholic extracts | Adult in cattle | In vitro | The hydroalcoholic leaf extract of A. sativus showed paralysis in all three conc. (25, 50, and 100 mg/ml), with death times ranging from 7.26 to 26.76 and 15.40 to 35.55 minutes, respectively. | Islam et al., 2015 |
| *Faciola gigantica and*  *Schistosama sp.* | *Gongronema latifolium, Piper guineense and Ocimum gratissimum* | Leaves | Ethanol | Ova in ruminant, mice | In vitro | *P. guineense* at 75% conc. showed mortality after 2 hrs. of exposure to *F. gigantica O. gratissimum* at 75% conc. showed mortality after 4 hrs. of exposure to  *Schistosoma* *sp.* | Daniel et al., 2015 |

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| Table 4: **Plants reported for having Anthelmintic activity against nematode** | | | | | | | |
| **Name of helminth** | **Name of plant** | **Plant parts** | **Solvent used** | **Stages of helminth** | **Test**  **Conducted** | **Result/ lc50 values** | **References** |
| *Meloidogyne sp.* | *Asteriscus imbricatus, Lavendula dentata, Pulicaria mauritanica* and *Globularia alypum* | Aerial parts | Petroleum ether Chloroform  Distilled water | Egg and  Larva in plant root | In vitro | At 2000 ppm, 89, 31 % and 92, 71% of mortality observed in A. imbricatus PE and chloroform extracts respectively. | Senhaji et al. 2018 |
| *Meloidogyne incognita* | *Raphanus raphanistrum L.,*  *Peganum harmala L.,*  *Taxus baccata L. Ricinus communis L.*  and  *Sinapis arvensis L.* | Seed,  Root and Aerial parts | Aqueous and  Ethanol | Eggs and 2nd stage Juvenile in plant root | In vitro and  In vivo | The extract of R. communis had the highest LC50 of all methanolic extracts in vitro, which was 0.75 ml/ml, whereas the extract of T. baccata had the lowest LC50 of all aqueous extracts, which was 0.51 ml/ml. After the application of methanolic extracts of the three plants, there was a decrease in the quantity of galls on the roots and the infestation rate in vivo. | Zaidat et al., 2020 |
| *Abrus precatorius* Linn., *Bunium persicum* Boiss., *Amaranthus virdis* Linn., *Dioscorea deltoidea* Wall. Ex Griseb*., Teraxacum officinale* Weber., *Malva neglecta* Wall., *Robina pseudoacacia* Linn. and *Podophylum hexandrum* Royle | Seed | Chloroform and methanol (50:50, v/v) | Eggs and 2nd stage Juvenile in plant root | In vitro | The highest rates of death were seen in seed extracts from T. officinale (93.67%) and B. persicum (89.66%) after 72 hrs. | Nengroo et al., 2021 |
| *Azadirachta indica, Ocimum tenuiflorum, Arthemisia pallens, Ficus hispida* and *Hibiscus rosasinensis* | Leaves | Methanol | Eggs and 2nd stage Juvenile in plant root | In vitro | The methanolic extracts of five plant species decreases the viability of nematodes as the conc. of the extracts increases. | Akshaya et al., 2020 |
| *Curcuma longa* | Root | Crude extract, Methanol, Chloroform Ethyle acetate and Hexane | Eggs and 2nd stage Juvenile in plant root | In vitro | The chloroform extract showed maximum mortality at highest  Conc.  . | Rashid et al., 2021 |
| *Lantana camara* L*.* | Leaves | Aqueous | 2nd stage Juvenile in plant root | In vitro | The highest mortality (98.6%) was recorded in 100%  Conc. of leaf extract at 48 hrs of exposure period. | Ghimire et al., 2015 |
| *Jatropha curcas* | Leaves and Root | Distilled water | Eggs in root | In vitro | The highest % of nematode mortality was achieved by application of alkaloids (94.73%). | Ogwudire et al., 2022 |
| *Vernonia colorata,*  *Searsia lancea,*  *Pelargonium sidoides*  and  *Cucurbita maxima* | Leaves | Methanol | Eggs and  2nd stage Juvenile in plant root | In vitro | 100% of root gall growth was inhibited in seedlings given the methanolic extract of *V. colorata.* At 0.8 mg/ml, all 8 plant extracts demonstrated positive nematicidal action. | Sithole et al., 2021 |
| *Catharanthus roseus* and  *Solidago virgaurea* | Leaves | Aqueous, Ethanol | Eggs and  2nd stage juvenile | In vitro | Inhibition of egg hatching by *C. roseus* extracts was higher than *S. virgaurea* extracts. LC90 was found to be achieved by a conc. of almost 1 g D. Wt./L in *S. virgaurea.* | Kesba et al., 2021 |
| *Amaranthus viridis, Solanum nigrum, Chenopodium album, Euphorbia hirta* and *Carica papaya* | Leaves, Stem and  Fruit | Aqueous | Eggs and Larva in root | In vitro | Maximum reduction (24.3%) in egg hatching while using 2% concentrated *C. album* stem extract. Maximum larval mortality (33%) was noted in *C. album* leaf extract at 10% conc. after 48 hrs. of exposure. | Afzal et al., 2021 |
| *Tagetes erecta, Tithonia diversifolia, Chromolaena odorata* and *Occimum gratissimun* | Leaves | Aqueous extract | Second stage  of juveniles | In vitro | Within 24 hrs. of exposure, *T. erecta* resulted in 100% juvenile mortality.  . | Taiwo et al., 2018 |
| *Aloe vera* | Leaves | 70%  Ethanol | 2nd stage of Juvenile, Adult male and adult female | In vitro | Highest efficacy was found at 80 mg/ml treatments. | Chinaka et al. 2017 |
| *Mentha piperita,*  *Mentha spicata* and  *Mentha pulegium* | Leaves | Aqueous and Essential oil | 2nd stage of Juvenile | In vitro | The aqueous extract exhibited the EC50/72 hrs. | Caboni et al.  2013 |
| *Meloidogyne javanica* | *Ochradenus baccatus* | Seedling,  Stem,  Flower, Root core and Root bark | Aqueous | Eggs and 2nd stage Juvenile in plant root | In vitro | After 48 hrs. of exposure to the highest conc. (16%) in both trials, the aqueous extracts of stem and flower immobilised 40-7-100% of juveniles. | Oka et al., 2014 |
| *Myrtus communis* | Leaves | Methanol and Ethanol | 2nd stage of Juvenile stage and eggs in root | In vitro | Methanol or ethanol extracts showed the highest nematicidal activity among all extracts tested. | Oka et al., 2012 |
| *Haemonchus contortus* | *Caesalpinia coriaria* | Fruit | Hydro-alcoholic and aqueous | Infective larval stage | In Vivo and in vitro | The in vitro findings demonstrated a clear larvicidal efficacy. In the in vivo trial, there was a 78.6% reduction in the elimination of EPG of faeces. | Hernandez et al., 2022 |
| *Anacardium occidentale, Illicium verum*, and  *Artocarpus heterophyllus* | Shell,  Seed and  Fruit | Hydro-alcohol | Eggs,  Infective larva and  Adult in sheep  EHA, AMA | In vitro | *A. Occidentale* shell caused adult worm mortality (LD50 = 1.0365 mg/mL) at a lower conc. (LD50), larval paralysis (LD50 = 0.196 mg/mL), and 50% egg hatch inhibition (LD50 = 0.0255 mg/mL). | Davuluri et al., 2020 |
| *Artemisia herba-alba,*  *Balanites aegyptiaca,* and  *Allium sativum* | Stem,  Leaves,  Fruits and Cloves | Ethanol | Eggs and  Larva in sheep | In vitro and in vivo | Clove ethanolic extract (CEE) of *B. aegyptiaca* demonstrated the greatest anthelmintic effect on adult worms in vitro. At 7 days after treatment, the CEE of *B. aegyptiaca* achieved faecal egg removal (100%) in vivo. | Hassan et al., 2021 |
| *Artemisia herba- alba* and  *Punica granatum* | Flower, Aerial parts,  Peel and  Root | Methanol | Eggs and  Adult | In vitro  AMA and EHIA | In vitro EHIA, flower methanolic extract of *A. herba-alba* exhibited 98.67% inhibition and 94.63 % at 1 mg/ml conc. of peel extracts of *P. granatum* respectively. In AMA, all helminths were dead within 5 hrs. at a conc. of 0.25 mg/ml. | Ahmed et al., 2020 |
| *Chenopodium ambrosioides* and  *Castela tortuosa* | Aerial parts, Leaves and Stem | n-Hexane | Larvae in | In vitro and in vivo | The E-Cham extract produced an in vitro impact (96.3%) after 72 hrs. At 40 mg/ml, the maximum combined effect (98.7%) was attained after 72 hrs. Individual treatment of the E-Cato and E-Cham extracts decreased the parasite by 27.1% and 45.8%, respectively, in an in vivo experiment. | Zamilpa et al., 2019 |
| *Allium sativum* and  *Tagetes erecta* | Bulb and Flower | Aqueous | Larva in ruminant | In vitro and in vitro | Larvicidal activity% in vitro was 68% with *A. sativum* and 36.6% with *T. erecta* at a conc. of 40 mg/ml. Mortality was induced by the mixture by 83.3%. *A. sativum* and *T. erecta* extracts at a conc. of 40 mg/ml reduced the parasite burden in living organisms by 68.7% and 53.9%, respectively. | Landin et al., 2015 |
| *Annona muricata* and *Arachis pintoic* | Leaf | NP/PEG,  Dragendroff Kedde reagents, Acetic acid, Methanol | Eggs  Larva,  Adult in ruminant | In vitro | Egg hatch test (EHT) and larval motility test (LMT) results at higher doses of *A. muricata* extract demonstrated 84.91% and 89.08% efficacy, respectively. | Ferreira et al.,  2013 |
| *Caesalpinia coriaria* | Fruits | Methanol | Eggs and Infective  Larvae in ruminant | In vitro | The highest activity of the extract at the highest conc. (with LC50 are 8.38 and 0.00064 mg/ml and LC90 % are 235.63 and 0.024 mg/ml, respectively, for larvae and eggs. | Martinez  et al.,  2018 |
| *Caesalpinia coriaria* | Foliage | Acetone-water, Methanol-water,  Acetone-water-dichloromethane and methanol-water-dichloromethane | Eggs and Larva in sheep | In vitro  EHT,  LEIT | For MWD, MW, AW, and AWD, the in vitro EC50 for EHT were 2947.0, 3347.0, 3959.6, and 4538.7 g/ml, respectively. For AWD, AW, MWD, and MW, the EC50 for LEIT were 2883.4, 5927.4, 9876.3, and 9955.4 g/ml, respectively. | Morales et al., 2021 |
| *Caesalpinia pyramidalis* | Leaves | Distilled water | Adults of either sex | In vivo | All groups treated with this extract had a positive FECR of 54.61% for G3 (2.5 mg/kg body weight) and 71.21% for G4 (5.0 mg/kg body weight). | Santos et al., 2012 |
| *Haemonchus placei* | *Ocimum gratissimum* and *Cymbopogon citratus* | Leaves | Acetone | Adult in cattle | In vivo  AMIA | For *C. citratus* and *O. gratissimum*, the best-fit LC50 values were substantially different (alpha 0.0001), coming in at 17.70 mg/ml and 56.04 mg/ml, respectively. | Aderibigbe  and Idowu, 2020 |
| *Toxocara canis* | *Balanites aegyptiaca* | Fruit | Methanol | Adult in dog | In vitro | The most effective treatment used BAE methanolic extract at 120 g/ml. | Shalaby, 2018 |
| *Toxocara vitulorum* | *Balanites aegyptiaca* | Fruit | Methanol | Eggs and  Adult in  ruminant | In vitro | The highest value, which was 240 g/ml in conc., achieved 100%. | Shalaby et al., 2012 |
| *Trichinella spiralis* | *Lasia spinosa* | Leaves | Crude | Adult,  Migrating larva and  Encysted muscle larvae in rat | In vivo | 800 mg/kg of plant extract administered orally resulted in a 75.30% decrease in adult worms. | Yadav and Temjenmongla, 2012 |
| *Trichostrongylus sp. and*  *Haemonchus contortus* | *Cymbopogon citratus* | Leaves | Aqueous, Methanol | Eggs and Infective larva (L3) in sheep | In vitro | At 1000 g/ml, six fractions of *C. citratus* exhibited high ovicidal activity, and two fractions exhibited high activity at all tested conc. | Rocha et al., 2020 |
| *Strongyloides sp.* | *Piper tuberculatum, Lippia sidoides, Mentha piperita, Hura crepitans* and *Carapa guianensis* | Leaves | Crude aqueous | Eggs and Adult in sheep | In vitro and in vivo  EHT,  LDH | For EHT, the LC50 and LC90 of the extracts were 0.031 and 0.09 mg/ml for *P. tuberculatum.* For LDT, the LC50 and LC90 were 0.02 and 0.031 mg/ml for *P. tuberculatum.* | Carvalho et al., 2012 |
| *Mangifera indica* L. | Unripe fruit | Aqueous | Larva and Adult in sheep | In vitro  LMIA | 100 mg/ml of immature fruit aqueous extract completely inhibited the growth of larvae. | Sherbini and Osman, 2013 |
| *Ascaridia galli* | *Areca catechu* L. | Leaves | Crude aqueous | Eggs in fowl | In vitro and  in vivo  EPG | In vitro, the *Areca catechu* L. aqueous extract (AAE) damaged the morphology. The average EPG in vivo reduced from 1485386.62 to 00.00 over the course of 14 days of 79 mg/ml AAE treatment. | Mubarokah et al., 2019 |
| *Tagetes erecta Linn*. | Leaves | Ethanolic and aqueous | Adult in  fowl | In vitro | When compared to the aqueous extract, the ethanol extract at 100 mg/mL conc. had more significant activity. | Goswami and Singh, 2018 |
| *Schleichera olesa* | Leaves | Ether  Water  Ethanol  Chloroform  Acetone | Adult in  fowl | In vitro | Alpha-amylase was significantly inhibited by ethanolic and aqueous extracts, with IC50 values of 36.63 and 73.94 g/ml, respectively. | Goswami and Singh, 2018 |
| *Ocimum sanctum* L. | Ethanol | Ethanol | Adult in fowl | In vitro | *O. sanctum* Linn. leaf ethanol extract had LC50 values of 14.8% at 6 hrs., 4.8% at 12 hrs., 3.0% at 24 hrs., and 9.1% at 24 hrs. | Kharisma et al., 2019 |
| *Maytenus emarginata* | Stem,  Bark | Methanol,  Aqueous and Hydroalcohol | Adult in fowl | In vitro | At a conc. of 50 mg/ml, methanolic, aqueous, and hydroalcoholic extracts all displayed significant anthelmintic efficacy. | Joshi and Wagh, 2019 |
| *Acmella oleracea* | Whole plant | Methanol | Adult in fowl | In vitro | At the conc. of 20 mg/ml plant extract killed all worms at 112.17 ± 0.88 hrs. | Lalthanpuii et al., 2020 |
| Curcuma longa  Zingiber officinale | Methanol | Crude  aqueous | Eggs and Adult in fowl | In vitro and  in vivo | The effectiveness of the extracts was demonstrated in vitro in a consistent time-dependent way. Compared to the in vitro study, the in vivo investigation with ginger and curcumin showed lower fatality rates. | Bazh and El-Bahy, 2013 |
| *Oesophagostomu mcolumbianum,*  *Haemonchus contortus* and  *Bunostomum spp* | *Cucurbita pepo* | seeds | Aqueous  Ethanol | Eggs,  larva in ruminant | In vitro  EHA, LMIA | ED50 value of EHA was 3.5 mg/ml. Larval migration was inhibited by aqueous and ethanolic extracts, and the LM50 values were 1.75 and 0.32 mg/ml, respectively. | Meenakshisudaram et al., 2017 |
| *Syphacia obvelata* | *Caesalpinia*  *bonducella* | Leaves | Methanol | Adult in mice | In vitro and in vivo  EPG | In vitro, 30 mg/ml conc. of methanolic extract caused mortality in 3.57 ± 0.16 hrs. 800 mg/kg dosage in mice showed a 93% reduction in worm load in vivo. | Gogoi et al., 2016 |
| *Ascaris suum* and *Ascaridia* sp. | *Punica gramatum* | Bark | water with previous soak in CH3COOH 5 %, (2) water with previous soak in NaOH 5 % | Adult in pig and fowl | In vitro | *Ascaris summ,* 50 % died at 20% cone, of extract (Acid-DW solvent) after 1.30±2.3 mins of exposure while in *Ascaridia sp.* 50 % died at 20% cone, of extract (Acid-DW solvent) after 1.20±5.1 mins of exposure. | Hai et al., 2014 |
| *Ascaris suum* | *Rhoicissus*  *tridentata* | Root-Tuber | Ethanol  Water | Adult in fowl | In vitro | Median effective doses of ethanol and water extract were 12.3 and 23.5 mg/ml respectively. | Nalule et al.,  2012 |
| *Euphorbia heterophylla* | Aerial whole plant parts | Ethanol  water | Adult in pig | In Vitro | In a dose-dependent manner, both crude extracts reduced worm motility by 100% in the 48 hrs. following treatment, with the median effective doses being 26.85 mg/ml, 4.60 mg/ml, and mg/ml, respectively. | Naluale et al., 2013 |
| *Pinus sylvestris, Onobrychis viciifolia, Ribes nigrum, Ribes rubrum* and *Trifolium repens* | Bark, Whole parts, Bushes, Flower | Condense tannin | Eggs, L3, L4 larva and Adult in pig | In vitro  EHA,  LMIA | All larvae subjected to 1 mg/ml of tannins died, and against the L3 and L4 stage, motility was seen at the lowest conc. of 111 g/ml. | Williams et al., 2014 |
| *Ascaris lumbricoides* | *Gongronema latifalium, Piper guineense,* and *Ocimum gratissimum* | Leaves | Ethanol | Eggs in faeces | In vitro | 100% mortality at 75% conc. of *P. guineese* after 4 hrs. of exposure and 50% mortality at 25% cone. of *O. gratissimum* after 8 hrs. of exposure. | Daniel et al.,  2015 |
| *Cooperia*  *punctata* | *Leucaena leucocephala, Gliricidia sepium, Guazuma ulmifolia* and *Craty lia argentea* | Leaves | Aqueous,  Acetone water, Acetonic and  polyethylene glycol (PEG) | Eggs in faces of cattle | In vitro | The best-fit LC50 values for *G. sepium*-AC and *L. leucocephala*-AQ were 1.03 0.17 and 7.90 1.19 mg/ml, respectively. | Fernex et al.,  2016 |
| *Trichuris muris* | *Corydalis crispa* and  *Pleurospermum amabile* | Whole plant | Methanol | Eggs and Adult in mice. | In vitro and in vivo | The IC50 range in vitro is 9.7–20.4 g/ml. One oral dose of 100 mg/kg was considerably (27.6%) better in vivo than the control group. | Wangchuk et al., 2016 |
| *Heterakis*  *gallinarum* | *Cassia alata*  *Cassia angustifolia* and  *Cassia occidentalis* | Leaves | Crude and Ethanol | Adult in fowl | In vitro | With *C. angustifolia, C. alata,* and *C. occidentalis*, respectively, at a conc. of 40 mg/ml, the animals lost their motility at 5.71, 6.60, and 13.95 hrs. | Kundu et al.,  2014 |
| *Ascaridia perspicillum* | *Acmella oleracea* | Aerial parts | Hexane | Adult in fowl | In vitro | The lethal conc. (LC50) of the plant extract was 8921.50 ppm. | Lalthanpuii et  al., 2020 |
| Mixed species of gastro-intestinal nematode | *Cratylia mollis* | Leaves | Leaf decoction extract | Eggs in sheep | In vivo  FECRT | Significant faecal egg reduction (FEC) 61.1%. | Lima et al., 2016 |
| *Ananas comosus, Allium sativum, Aloe ferox, Warburgia salutaris* and *Lespedeza cuneata* | Leaves | Ethanol | Eggs in Sheep | In vivo EPG | *A. comosus* and *L. cuneata* treatments had the highest efficacies of 58% and 61%. | Ahmed et al., 2014 |
| *Prunella vulgaris* | Leaves,  Stem and  Flower | Aqueous, Methanol | Eggs and Adult in sheep  EHA,  AMA and FECRT | In vitro | The highest value for AMA caused 75% mortality after 8 hrs. of exposure at 50 mg/ml. Crude methanolic extract shows stronger inhibitory effects on EHA (LC50 = 2.48 mg/ml). Methanolic extract produced FECRTs of 81.47% and 92.86% in vivo at dosage levels of 1 g/kg body weight and 2 g/kg body weight, respectively. | Lone et al., 2017 |
| *Strongylus spp.* | *Ferula asafoetida* and *Allium sativum* L. | Leaves | Hydro-alcohol | Larva in horse | In vitro | Hydroalcoholic extract of *A. Sativum* extract at the conc. of 50 and 100 mg/ml killed over 95% of larvae (p<0.05). | Tavassoli et al., 2018 |
| Protoscoleces of *Echinococcus granulosus* | *Salvadora parsica* | Root | 70% Ethanol | Larva in sheep | In vitro | *S. persica* extract at a conc. of 50 mg/ml, killed 100% of protoscolices after 30 mins. | Abdel-Baki et al., 2016 |
| *Nigella sativa* and *punica granatum* | Essential oil and Peel | Cold-macerated petroleum ether (40-60) %  Aqueous | Larva in camel | In vitro | After 120 minutes of exposure, *N. sativa* oil at 100 mg/ml conc. showed a 100% maximum mortality rate for protoscolices. | El-Bahy et al., 2019 |
| *Setaria cervi* | *Terminalia bellerica*  *Terminalia chebula* and  *Terminalia catappa* | Leaves | Hexane  Chloroform  Methanol Acetone | Microfilari | In vitro | After 4 hrs. of incubation, larger doses (at higher doses of 5 and 10 mg/m)l after of *T. Bellerica, T. Chebula,* and *T. Catappa* demonstrated a decrease in the worms' motility in vitro. | Behera and Bhatnagar, 2018 |
| *Heligmosomoides bakeri* | *Saba Senegalensis* | Leaves | Aqueous decoction (AD)  hydroethanolic macerate (HEM) | Eggs | In vitro | Emax = 100% and an LC50 = 900 µg/ml. | Belemlilga et al., 2019 |
| *Cucurbita pepo* L. | Seed | Hot and cold aqueous extract,  Ethanol | Adult and  Eggs | In vitro and  In vivo | In vitro, all seed extracts exhibited a nematicidal activity. The dose of 8 g/kg that produced the maximum FECR was measured (IC50 against H. bakeri = 2.43; 95% Cl = 2.01-2.94). | Grzybek et al., 2016 |
| *Setaria digitata* | *Azadirachta indica* | Leaves | Diethyl ether, Chloroform, Ethanol and Methanol | Eggs,  Third stage larvae | In vitro  LMA, LDA,  LMIA | After 135 minutes of incubation, the methanol and ethanol extracts showed the maximum mortality rate of microfilariae at a conc. of 200 g/ml. | Kausar, 2017 |
| *Haemonchus contortus* | *Curcuma longa* | Rhizome | Ethanol | Infective larva (L3) in sheep | In vitro | Within 24 hrs. of exposure, the highest dose rate of 200 mg/ml resulted in a 78% worm mortality rate. | Nasai et al., 2016 |
| *Iris kashmiriana* | Rhizome | Aqueous and Methanol | Eggs and Adult in sheep | In vitro and in vivo AMIA, FECRT | In vitro, LC50 values of methanolic extracts of rhizome on adult worms was 16.66 mg/ml. In vivo, ECR in sheep treated with methanolic extracts at 1 g kg−1 body weight on day 15 after treatment (33.17% ECR). | Khan et al., 2018 |
| *Rhus glutinous, Syzygium guineensa* and  *Albizia gumifera* | Leaves | Condense tannin extract | Eggs and Larva in sheep | In vitro  EHA, LDA | According to IC50 and IC90 values, the condensed tannin-enriched extracts are the most effective at inhibiting EHA and LHA for R. glutinosa in in vitro tests. | Birhan et al., 2020 |
| *Saba senegalensis* | Leaves | Aqueous | Eggs and  Adult | In vitro,  AMA,  EHA | LC50 on adult worms was 6.79 mg/ml for the leaves. Inhibition of EHA showed a conc. dependent inhibition of 93.63% at the conc. of 15.00 mg/ml. | Belemlilga et al., 2016 |
| *Indigofera tinctoria L* | Leaves | Aqueous | Eggs and Adult | In Vitro and in vivo  AMA,  FECRT | Adults were dead at a dose of 220 mg/ml (93.33% mortality) after 8 hrs. of treatment in vitro, whereas in vivo, the treatment group's maximum FECRT value occurred at a dose of 62 mg/ml on the 14th day following treatment. | Muda et al., 2021 |
| *Camellia sinensis L.* and  *Albizia lebbeck L*. | Leaves | Ethanol | Adult | In vitro  AMA | Following an 8 hrs. of treatment period, both ethanolic extracts showed 88% and 95% mortality at 6 and 8 mg/ml of doses. | Zaheer et al., 2019 |

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| Table 5: **Anthelmintic activity of synthesized metal nanoparticles from the plant parts** | | | | | | | |
| **Helminth species** | **Plant part used** | **Plant name** | **Stages** | **Size & shape of nanoparticle** | **Test**  **Conducted** | **Results** | **References** |
| *Haemonchus contortus*  (Nematoda) | Leaf  Aqueous extract | *Azadirecta indica*  (Neem tree)  Meliaceae family | Egg and Adult in small ruminant | Silver nanoparticles (AgNps)  15-25 nm and Sphericalshape | In vitro EHIA and AMIA | For AgNps the IC50 value for EHI was at 0.001 μg/ml, and AMI was produced at 7.89 μg/ml (LC50). | Tomar and Preet, 2017 |
| Leaves  Aqueous extract | *Ziziphus jujuba*  (Common Jujube)  Jujube family | Egg and Adult in small ruminant | Silver nanoparticles (AgNps)  28-44 nm and Spherical shape | In Vitro  EHA and Adulticidal | The greatest conc. of AgNPs inhibited egg hatching by 91 1.76%. EHA had IC50 and IC90 values of 0.007 ppm and 7.71 ppm, respectively. | Preet and Tomar,  2017 |
| Fruit Aqueous extract | *Lansium parasiticum*  (Schisandraceae family) | Eggs, Adult and L3 stage of larva in small ruminant | Silver nanoparticles (AgNps)  ~16 ± 5 nm and Spherical shape | In vitro | Silver nanoparticles (LAgNPs) showed LD50values of 65.6 ± 32.8 nM (12 hrs.), 139.6 ± 39.9 nM (12 hrs.) against adult male, female, and L3 larvae, respectively. EHA with an IC50 value of 144.4 ± 3.1 nM at 48 hrs. of exposure. | Goel et al., 2020 |
| *Gigantocotyle explanatum*  (Trematode) | Seed  Ethanolic extract | Tribulus terrestris  caltrop family  (Zygophyllaceae) | Adult in water buffaloes | Silver nanoparticles (AgNps)  ∼8 nm and Qausi-spherical shape | In Vitro  Adulticidal | AgNPs resulted in pronounced tegumental damages, complete deformities with deep lesions. | Rehman et al., 2019 |
| *Raillietiina sp.*  (Cestode) | Mycelia-free culture filtrate | *Nigrospora oryzae*  (Trichosphaeriaceae family) | Adult in fowl | Gold nanoparticles (AuNps)  ∼6 nm to -18 nm and Cubic shape | In vitro  Adulticidal | Paralysis time of 1.47 hrs. and death time of 2.55 hrs., for dose of 1.0 mg/ml. | Kar et al., 2014 |
| *Ancylostoma caninum*  (Nematode) | *Duddingtonia flagrans*  Fungus  Orbiliaceae family | | Larva L3 stage in dog | Silver nanoparticles (AgNps)  14.51±3.25 nm and Spherical shape | In vitro  Larvicidal | Penetrates the larvae's cuticle, altering the tegument and ultimately leading to the nematode's death. | Barbosa et al., 2019 |
| *Strongylus* sp.  (Nematode) | Seed  Aqueous extract | *Moringa oleifera*  (Moringa)  Moringaceae family | Eggs in small ruminant | Silver nanoparticles (AgNps)  10-30 nm and Cubic shape | In vitro  EHA | At 8 mg/ml conc., AgNPs from *M. oleifera* seeds generated a maximum 80.59 ± 5.65% inhibition of egg hatching. | Ilavarashi et al., 2019 |
| *Marshallagia marshalli*  (Nematode) | Seed | *Rhus coriaria*  (Anacardiaceae family) | Adult in small ruminant | Silver nanoparticles (AgNps)  60 nm and Spherical shape | In vitro  AMA, EHA | The anthelmintic effects grew as the conc. of nanoparticles and the incubation period rose. | Mirzaei et al., 2022 |
| *Meloidogyne incognita*  (Root-knot nematodes) | Whole part | *Colpomenia sinuosa* and *Corallina mediterranea*  (Marine algae)  Scytosiphonaceae family and Corallinaceae family | Eggs and 2nd stage Juvenile in plant root | Silver nanoparticles (AgNps)  20-70 nm and spherical shape | In vitro | 100% mortality after 24 and 72 hrs. of exposure, and 87.5% mortality after 12 hrs. | Ghareeb et al., 2021 |
| Leaves | Conyza dioscoridis, Melia azedarach and Moringa oleifera  (Asteraceae family, Meliaceae family and Moringaceae family) | Eggs and 2nd stage Juvenile in plant root | Silver nanoparticles  30-100 nm and Spherical | In vitro | Ag-essential oil nanoparticles of three plants had significant nematicidal activity. | Abbassy et al., 2017 |

**Discussion**

Infections with helminth parasites are regarded as neglected tropical diseases. Helminths are parasitic worms with elongated, rounded, or flat bodies that are an invertebrate (Hotez et al., 2008; Headly et al., 2017). The most common helminths include intestinal nematodes, schistosomes, and filarial worms. In the past, it was calculated that the sheep, goat, and cow industries suffered a significant loss of Rs. 31.43 million annually (Iqbal et al., 2014). Along with livestock, it primarily affects kids and can weaken nutritional status, leading to stunted growth and memory impairment. Helminth infections are treated with enhanced hygiene, a combination of medications, and health education. Antihelmintic medications are used to treat helminthic disorders, however some of these infections are drug-resistant and have serious side effects. Nearly 80% of the global population uses traditional medicines made from plant extracts for primary healthcare and health benefits (WHO, 2008). In developing nations like India, China, and Bangladesh, helminthiasis is historically treated with a variety of folklore medicinal herbs. In order to effectively cure parasite illness, plant-derived medications are therefore receiving a lot of research (Neogi et al., 1964; Dehuri et al., 2021). There are several medicinal plants and their different crude products, solvent extracts and active components have been reported, which are analysed for helminthic infection control (Kozan et al., 2006). Plants have been widely used to treat gastrointestinal helminths of medical and veterinary value since ancient times and in folklore in order to test and validate their anthelmintic properties. Researcher’s use the whole/parts of plant extract (aqueous/ethanol/methanol/acetone/ethyl acetate) to conduct various tests which has been described underneath (Tandon et al., 1997; Dehuri et al., 2021). Condensed tannins, alkaloids, saponins, phenol, and flavonoids are a few of the secondary metabolites found in plants that are typically linked to their anthelmintic effects (Rawani and Gope, 2021). The development of efficient anthelmintic drugs with minimal side effects and non-resistance to parasitic helminths is expected to be possible using these plant-based herbal remedies. The better anthelmintic action and new herbal anthelmintic medicine are partly explained by the screening for phytogenic chemical components like tannins, alkaloids, phenol, saponin, flavonoids, etc. Silver, gold, and metal-based oxide nanoparticles including zinc oxide and iron oxide have all been investigated for their potential to treat a variety of diseases. Recent research state that they work as very effective larvicides and adulticides against many helminth species that are significant in medical science and veterinary medicine (Zhang et al., 2020).

**Conclusion**

According to the study, medicinal plants have been employed as a part of traditional medicine from the beginning of time. The study reported that, whole plants or plant parts in crude form, solvent extract, and artificial green nanoparticles all have the potential to be effective against parasitic helminth. Although some metal nanoparticles shown lesser biological activity due to their design, metal composition, and lack of selectivity for the target cells, it has been demonstrated that metal nanoparticles have the potential to be therapeutically useful. When the metal compounds were included into particular drug delivery methods, these restrictions were overcome in those instances.

There is an urgent need for developing metal-based nanoparticles that are affordably priced and have outstanding therapeutic outcomes because there are few publications on the use of metal-based nanoparticles for the treatment of parasite infections in comparison to other infectious diseases. Research is also needed on the pharmacokinetics and toxicological properties of medications based on different metals nanoparticles. Metal-based nanoparticles may be able to circumvent drug resistance, which is characteristic for most organic molecules. Metal-based nanoparticles are without a doubt promising future treatments for the management of various infectious illnesses. However, it is important to understand the detailed mode of action of herbal products through in vivo studies as they will be used for further commercial purpose.

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