**Recent advances of plant extracts and synthesized green metal nanoparticles against gut helminths of ruminants**

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**Abstract**

Livestock is an important pillar of India’s economy. It elevates the economic standing of rural poor people. It is a significant source of agriculture and supports the economy by creating jobs and raising household income in rural areas. Goats, cows, and buffalos are being reared for variety of items like leather, meat and milk production. Helminths are notorious for causing infections in goats, cows, buffalos, and human beings. 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, but long-term utilization of these synthetic drugs shows much toxicity and harmful clinical side effects as loss of appetite, dizziness, nausea, vomiting, headache, abdominal pain, diarrhoea, and hepatotoxicity etc. to target and non-target organisms. Thus, it is the high time to look for more efficient and less toxic anthelmintic drugs with minimum or zero side effects. The present review work summarizes the in vitro and in vivo studies of medicinal plants including their activity against different helminths of livestock. These plant-based herbal medicines are thought to be promising sources for developing effective anthelmintic drug with minimum side effects and non-resistance to parasitic helminths. 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 work also focuses on the therapeutic uses of biologically synthesized different metal nanoparticles which opens a new door with pharmacological basis for effective treatment of various helminth diseases.

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

**Introduction**

Helminth parasites diseases are one of the major and critical health problem affecting billions of people as well as ruminants all over the world (WHO 2010), especially it is mostly found in tropical and sub-tropical countries with low income per capita and unhygienic conditions (Hotez et al., 2007). India contributes approximately 25% to the total global cases of helminth infections. That infectious agent manifest anorexia, anemia, diarrhea, weight reduction and heavy production losses in livestock industry (WHO, 2017). Helminth parasites belong to three different classes cestodes (flatworm), trematode(fluke) and nematode (roundworm). Among these helminths, gastrointestinal (GI) nematodes like *Haemonchus contortus, Bunostomum sp., Trichostrongylus sp*. have crucial effect on the food security. Helminths have a highly detrimental effect on all kinds of ruminants, some helminths are blood suckers and cause anemia while many affect the physiological, metabolic, and immune system of the body resulting in significant economic losses in meat, milk and wool production as well as in reproduction (Suarez et al., 2009). To protect our livestock against gastrointestinal helminths infection, usually broad spectrum synthetic anthelmintic drugs like ivermectin, albendazole, levamisole is being used for decade. The remnants of all these harmful synthetic drugs in animal and animal product are the major cause of resistance along with the toxicities enhancing out of their use (Kundu et al., 2015). These types of harmful drugs show much toxicity and severe clinical symptoms as loss of appetite, dizziness, nausea, vomiting, headache, abdominal pain, diarrhoea, and hepatotoxicity (Devi et al., 2009). The recent approach is the use of herbal therapies alone or in combination with traditional anthelmintics. Researchers have shown herbal anthelmintics remedies comprises of natural plant compounds which are eco-friendly, non-toxic, cost-effective with very less or zero side effects. Many researchers have studied plant anthelmintics and their validation as alternative anthelmintic medicine. The majority of in vitro investigations focused on the effects of plant extracts and their fractions on helminths in their free-living stages. In vivo studies were conducted mainly using medicinal plants in animal feed, which showed lower effectiveness than in vitro assays. In vitro Anthelmintic tests include 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/test (LFIA/LFIT), Larva ensheathment inhibition assay (LEIA) are being utilized for evaluation of anthelmintic activities of plant extracts and products against gastrointestinal helminths (Tariq et al., 2009; Ronaldo et al., 2013). The most popular tests, such as LMIT and AMIT, assess the effectiveness of various plant extracts on the motility of helminth larvae and adults, respectively, whereas EHIT assesses the inhibitory effect of plant extracts on egg hatching. In vitro methods have an edge over in vivo methods due to their relative cost-effective and rapid results which leads large scale testing of plant materials. In vivo Anthelmintic tests include the fecal egg count reduction test (FECRT) and the controlled efficacy test (CET) which are not very ideal due to its higher cost, low precision and reproducibility owing to inter animal variation and pharmacodynamics of the drug in the host (O’Craven et al., 1999; Santos et al., 2019).

The plant kingdom is known to provide a rich source of botanical anthelmintics (Satyavati et al., 1985). In ethnomedicine, nearly, 80% of the world’s population keep relies on our traditional medicines from Phyto extracts for primary health care and health benefits (WHO, 2008). Traditional medicines hold great promise as sources of readily available effective anthelmintics agents (Temjenmongla and Yadav, 2005). Many folklores medicinal plants are traditionally uses to cure helminthiasis in developing countries like India, China, Bangladesh etc. (Choudhary et al., 2015). several folklore medicinal plants have been tested for their anthelmintic efficacy against liver fluke and other parasites (Tandon et al., 1997; Mehlhorn et al., 2011). So, plant derived drugs and herbal medicines are gaining lot of attention for treatment of parasitic infection (Mehlhorn et al., 2010; Dehuri et al., 2021). These herbal drugs are a point of attraction due to their easy availability, are cost-effective, having minimum or zero side effects, and also do not cause any resistance (Wakayo and Pewo, 2015).

For the synthesis of metal nanoparticles, which is of particular interest to researchers, effective green chemistry methods have recently been devised. They have investigated thoroughly and find a safe and eco-friendly technique for production of well-characterized nanoparticles. One of the most considered methods is production of metal nanoparticles by using organisms. Plants appear to be the most suitable and best choices among these organisms for large-scale production of nanoparticles. Nanoparticles produced by plants are more stable and its rate of synthesis is faster than in the case of microorganisms. Also, the nanoparticles are various in shape and size (1-100 nm) in comparison with those produced by other organisms. Researchers are looking into the mechanisms of metal ions uptake and bio-reduction by plants as well as the potential mechanisms of metal nanoparticle creation in plants due to the benefits of using plants and materials produced from plants for the biosynthesis of metal nanoparticles. Generally, metal nanoparticles comprised of gold, silver, platinum, iron, silica, copper, zinc, and some lanthanides are used as carriers of different biomolecules, specific drugs, nucleic acids, peptides, and antibodies. They can act as diagnostic and therapeutic agents for various disease models, including cancer, microbial infections, parasitic infection, cardiovascular disease, and neurodegenerative diseases (Zhang et al., 2020). So, plant-based metal nanoparticles are promising future therapeutics for the treatment of parasitic diseases.

Both in-vitro and in-vivo studies are carried out to find the effectiveness of plants having Anthelmintic activity. In this review, various medicinal plants and synthesized green nanoparticles are reported which are potentially effective against different types of gastrointestinal helminths (cestode, trematode and nematode) have been described and tabulated, which can open door for basic pharmacological studies leading to development of new anthelmintics against the conventional ones having the problems of the anthelmintic resistance and high-cost issue.

**Objectives**

The aim of this present review of literature is to collate and update the Crude extracts and synthesized green metal nanoparticles from medicinal plant extracts which are reported to have potential Anthelmintic activities (ovicidal, larvicidal and adulticidal) against various kinds 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 definitive classification is based on the internal and external morphology of egg, larval, and adult stages. Helminth belongs to the two phylum Platyhelminthes and Aschelminthes. In Phylum Platyhelminthes, primarily two-class Trematoda and Cestoda, in which parasitic helminths belong, and in phylum Aschelminthes, there is only one class Nematoda which possess parasitic helminth. These are the endoparasites of the gut and blood and cause various diseases collectively called helminthiasis.

**Cestodes (Tapeworms):**

They are commonly known as tapeworms. The body of the cestode is without epidermis and cilia but covered with cuticles, body divided into many segments known as proglottids. Anterior end bears scolex, which is provided with 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. Flukes are hermaphroditic except blood flukes, they are bisexual. The life-cycle includes a snail intermediate host. 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 commonly known as roundworms body wall with cuticle, cellular or syncytial epideris, and longitudinal muscles in four bands, no cilia, circulatory and respiratory system absent. They are generally dioecious internal fertilization occurs. Adult and larval roundworms are bisexual, cylindrical worms. They inhabit intestinal and extraintestinal sites. 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).*

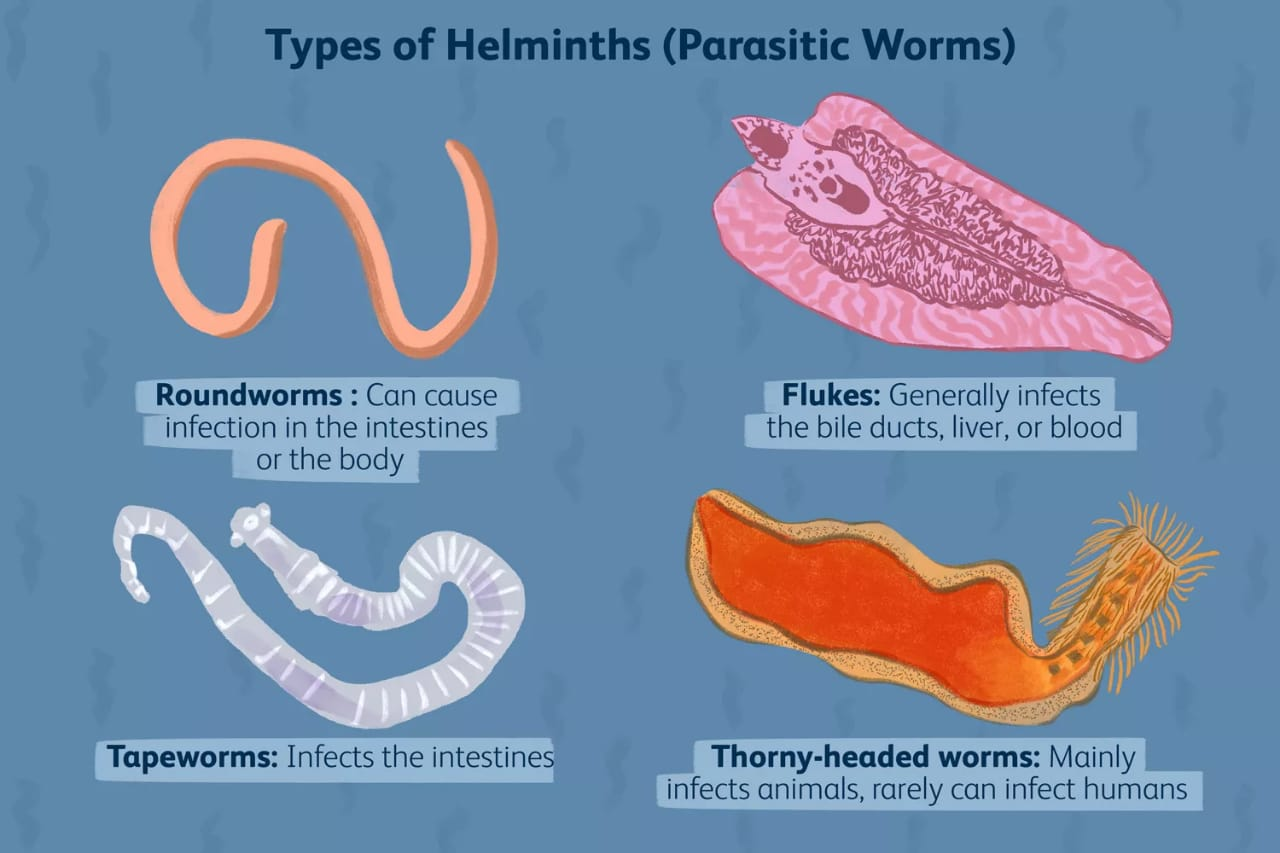


Figure 1: **Types of helminths (parasitic worms)**

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

**About nanoparticles**

Nanoparticles is derived from the greekword nano. Nano means extremely small. Nanoparticle are particle which lie in dimensions between 1-100 nm (Horikoshi and Serpone, 2013). It can be used as a prefix for any unit mean a billionth of that unit. They consist of micromolecular materials in which the active ingredients are dissolved, entrapped, encapsulated, adsorbed, or attached. It is a solid colloidal particle.

Green synthesis employs a clean, safe, cost effective and environmentally friendly process of constructing nano materials. Micro-organisms such as bacteria, yeast, fungi, algal, species and certain plants act as substrates for the green synthesis of nano materials. Green synthesis method provides a faster metallic nanoparticles production by offering an environmentally friendly simple, economical are reproducible approaches.

Engineering and biomedical sciences both make substantial use of metal-based nanoparticles. Their market has grown significantly in recent years, and it is not anticipated to shrink. There are various types of nanoparticles such as AgNPs, CuONPs, AuNPs, and ZnONPs, which are frequently used in pharmaceutical and medical applications (such as as antibacterial, antifungal, antiviral, antiamebic, anticancer, and anti-angiogenic medicines).

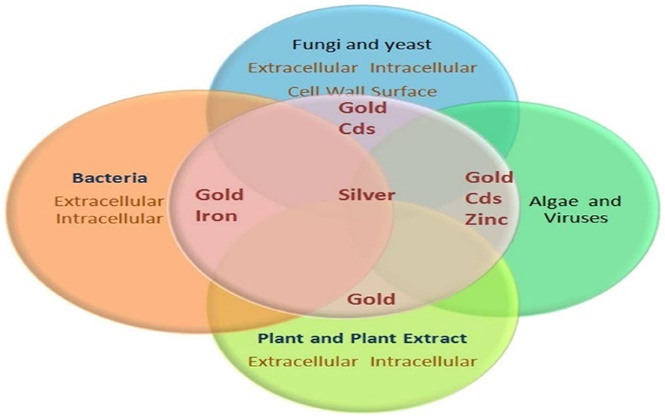


Figure 2: **Different metal Nanoparticles (Gold, Silver, Zinc, Cadmium, Iron)**

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

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

Two-thirds of the world’s population depend on plants as primary agents to resolve health issues (WHO, 2002). Approximately, 50,000 to 70,000 plant species are used in both traditional and Western medicine approaches (Newman and Cragg, 2016) and 25% of prescription medicines are derived from plants or plant-derived secondary metabolites (Hammond et al., 1997; Akhtar et al., 2000; Githiori et al., 2006). Even the modern pharmacopoeia still contains at least 25% of drug derived from plants and many others which are semi-synthetic, built on prototype compounds isolated from plants (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 suppress the transfer of sucrose from stomach to small intestine, diminish the support of glucose to the helminths, and act on CNS which leads to paralysis (Roy, 2010).

ii) Saponins disrupt the permeability of the cell membrane of the helminths and causes vacuolization and disintegration of teguments (Wang et al., 2010).

iii) Polyphenols and tannins increase the supply and absorption of digestible proteins via forming protein complexes in rumen, which dissociate at low pH in the abdomen and release more protein for metabolism, it suppresses energy generation by uncoupling oxidative phosphorylation, cause gastro-intestinal metabolism reduction which leads to paralysis and death of helminths (Tiwari et al., 2011; Sutar et al., 2010; Mali et al., 2007).

iv)Tannins bind to free protein in GI track of host animal or to glycoprotein of cuticle of helminth by linking through H-H bonding, this reactivity causes toughness in the skin, it makes worms immobile and non-functional, then it also reduces nutrient availability resulted in larval starvation or GI metabolism reduction which leads to paralysis followed by death (Vidyadhar et al., 2010). Several reports suggested that, enhancement of digestible protein supply improves the resilience and resistance of sheep to gastro-intestinal nematodes, it also induces physiological changes in the gut of the host resulting in rapid secretion mucous and chemicals, which is harmful to the helminths (Bachaya et al., 2009).

v) Steroidal alkaloid oligoglycosides reduce the support of glucose in helminths and its antioxidant action while inhibiting the transfer of sucrose from the stomach to the small intestine. which reduce the nitrate generation (which may be used in the protein synthesis) as well as the possible inflammatory effect induced by the extract in the gastric and intestinal mucosal which interfere in local homeostasis, is essential for the development of helminths (Cruz, 2008).

vi) Ethanolic extract may lower pH, which cause the starvation effects or give rise to the osmotic abnormalities, thus leading to death of the worms (Laverack, 1963).

vii) Hydro-alcoholic extract have better activity compared to the aqueous extract on adult parasites in most cases. According to recent study, it could be happened due to easier trans-cuticular absorption of the hydroalcoholic extracts into the body of the helminth than the aqueous extracts. For enhanced anthelmintic action, hydroalcoholic plant extracts typically contain certain non-polar organic compounds with lower polarity than aqueous extracts. This makes them more lipid soluble than aqueous extracts. (Kumar et al., 2010).

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

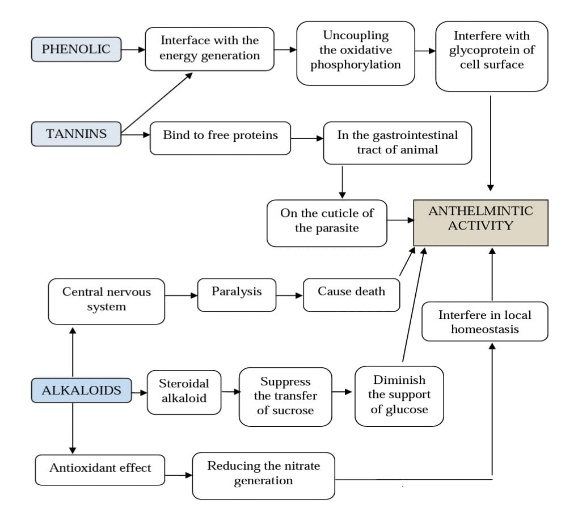


Figure 3: **Different phytochemical’s mode of action in Anthelmintic activity**

(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**

Preclinical analyses form the foundation of the majority of research studies on the use of metal-based nanoparticles in the treatment of infectious diseases. Combining metal nanoparticles with plant extract improved the anthelmintic activity in the treatment of helminth infections. The presented nanoparticles display good cell contact, improved cell uptake, and some even show good selectivity when modified with particular functions.

**1. Silver nanoparticles**

Silver nanoparticles have been coupled with plant extracts resulting in good anthelmintic activity. Rashid et al., demonstrated the anthelmintic activity of polyaniline-coated silver nanoparticles with fruit extract. The +ve charge on the Ag ion was attracted to the -ve charged cell membrane of microorganisms via electrostatic interaction while the plant extract contains phytochemicals that attach with the free proteins in the gastrointestinal tract on the helminth’s cuticle resulting in paralysis and death. (Rashid et al., 2016)

**2. Gold nanoparticles**

Apart from silver nanoparticles, gold nanoparticles are potential anthelmintic agents. Gold nanoparticles' anthelmintic activity was assessed by Kar et al. By combining gold chloride with a mycelia-free culture filtrate of the phytopathogenic fungus, gold nanoparticles were created. The gold nanoparticles directly affected the physiological function of the helminth causing paralysis and subsequent death. After being treated with gold nanoparticles, the helminth's enzyme activity significantly changed, demonstrating the potential of gold nanoparticles (Kar et al., 2014).

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

Iron oxide and zinc oxide nanoparticles, for example, have anthelmintic effects on helminth parasites. Zinc oxide nanoparticles anthelmintic effect on helminth parasite which infects Indian livestock was reported by Khan et al., 2015. Low concentrations of the nanoparticles produced oxidative stress by the production of ROS in the helminths. By raising the activity of antioxidant enzymes to scavenge the ROS, the flukes demonstrated a survival effort. The survival effort was disrupted when they were treated with high concentration of the nanoparticles. Saturation of antioxidant enzymes of the worm rendered the detoxification mechanism ineffective. The increased intracellular ROS level is thought to alter the contractile movement, disrupt the electron transport system, and make the cell membrane more permeable. of the helminth (Khan et al., 2015) Dorostkar et al., evaluated the anthelmintic activity of zinc oxide and iron oxide nanoparticles against helminth (Dorostkar et al., 2017). Due to the nature of the nanoparticles, iron oxide nanoparticles were shown to be more efficient than zinc oxide nanoparticles. Treatment with low dose of the both nanoparticles resulted in elevation of Superoxide Dismutase activity (SOD). At high concentration of the nanoparticles, a reduction of the SOD activity in helminth was significant resulting from the saturation of the enzyme. Oxidative stress generated by the nanoparticles at high concentration resulted in structural damage and overwhelms ATP synthesis. The anthelmintic activity of the metal oxides nanoparticles is via induction of oxidative stress (Dorostkar et al., 2017).

With biomolecules found inside cells and on their surfaces, metal-based nanoparticles display positive biological interactions. They can also be engineered by introducing selected biological moieties with specific binding activity to selected target cells by improving their therapeutic efficacy at the pathological field.

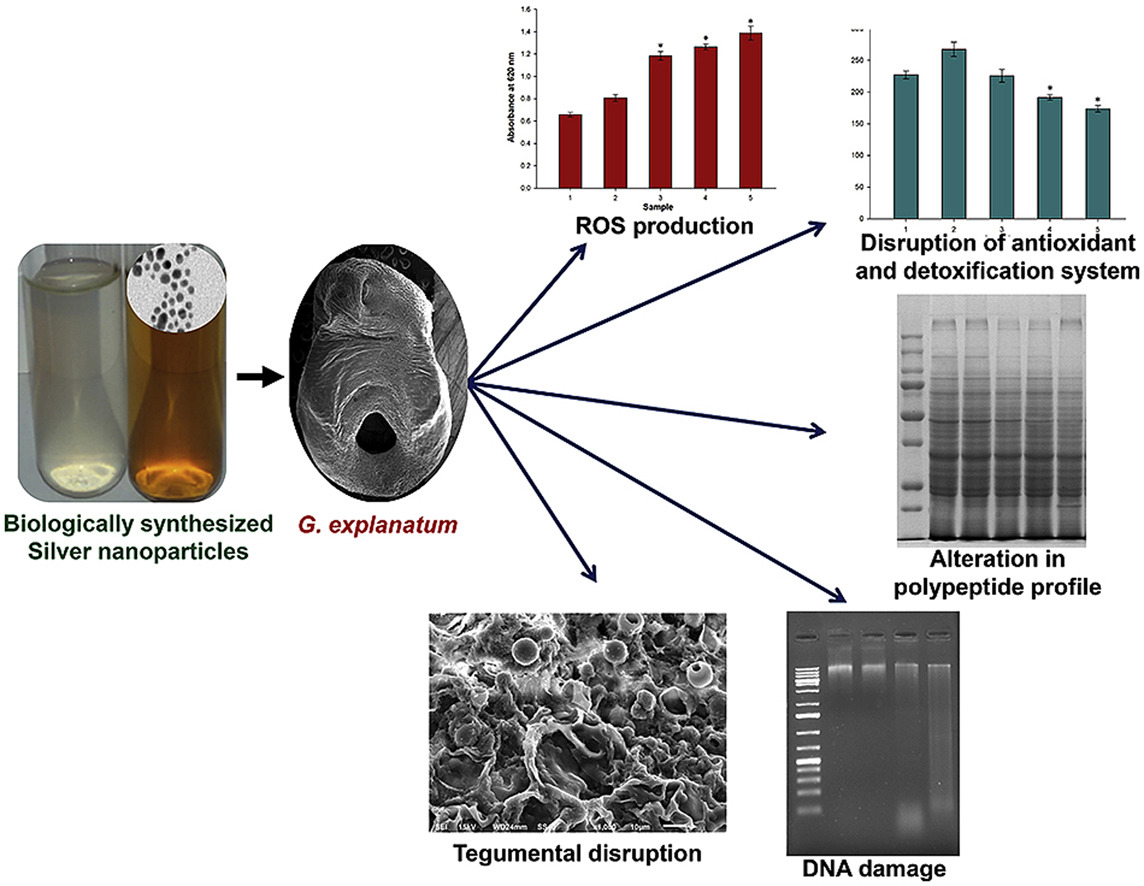


Figure 4: **Morphological alternation in *Gigantocotyle explanatum* (Trematode) due to application of biologically synthesized silver nanoparticles.**

(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, 30 mg/ml of extract caused mortality of juveniles at the initial period (0.25 ± 0.00 hrs).  In vivo, 1000 mg/kg of extract caused 79.3 % reduction in EPG counts and 70.8 % of reduction in worm counts. | Deori et al., 2016 |
| *Cynodon dactylon* | Whole plant | Methanol | Adult,  EPG in Wister rat | In vitro and in vivo | in vitro test, the 40 mg/ml conc. caused paralysis and mortality of worms in 4.12 ± 0.55 hrs and 5.16 ± 0.34 hrs, respectively. In vivo, 800 mg/kg dose for 5 days revealed up to 77.64% reduction in EPG counts and 79.00% reduction. | 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. In vivo studies revealed 61.74% reduction in the eggs per gram (EPG) counts. |
| *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 dose of rhizome extract for 5 days results into 62.30% reduction in EPG of faeces counts and 83.25% reduction in worm counts. | 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 | Crude leaf extract and N-butanol fraction at a dose of 6 mg/ml of PBS, glycogen conc. decreased by 26-51% adults. | 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 concentrations. | 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 | 50% conc. of *O.gratissimum* caused 100% mortality after 8 hrs. of exposure against each of ova. | 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 | Highest conc. of methanolic extract showed a significant reduction in the no. of eggs and helminths compared to control. | 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 cornigera,*  *Acacia* *farnesiana,*  *Artemisia absinthium,*  *Artemisia* *Mexicana,*  *Bocconia frutescens,*  *Cajanus cajan,*  *Cordia spp,*  *Hibiscus rosasinensis,*  *Lantana camara,*  *Leucaena diversifolia,*  *Melia azedarach,*  *Mentha sp,*  *Ocimum basilicum,*  *Piper auritum* and  *Teloxys ambrosioides* | Leaves | Hexane,  Ethyl acetate and  Methanol | Newly excysted flukes in ruminant | In vitro | At a dose of 500 mg/l, *C. cajan,* L. *camara* and *P. auritum* had an efficacy of 100%, while *B. frutescens* and *A. Mexicana*had a 100% efficacy at a dose 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 was less infective with 3.3% of prevalence compare to untreated with 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 decrease in total worm burden 7.00±1.00 and a significant elevation in the count of dead ova 13.11±1.68 respectively. | 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 | The maximum inhibition of motility was observed at 0.5 mg/ml conc. after 8 hrs. of exposure. | 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* | *Calotropis procera,*  *Azadirachta indica* 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 of the flesh and peel extracts were  61.73 and 41.79 mg/ml for liver fluke respectively. | Adeniran and Sonibare, 2013 |
| *Dregea volubilis* | Leaves | Methanol | Adult in cattle | In vitro | Maximum fasciocidal activity was found with conc. of 100 mg/ml at 38.83 ± 3.41 mins. | 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 | 200 μg/ml methanolic extract of the fruit showed highest efficacy. | 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 | Among all three conc. (25, 50, and 100 mg/ml), the hydroalcoholic leaf extract of *A. sativus* exhibited paralysis and death time ranged between 7.26 to 26.76 mins. and 15.40 to 35.55 mins. 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* | *Peganum harmala L.,*  *Raphanus raphanistrum L.,*  *Taxus baccata L.,*  *Sinapis arvensis L.,* and  *Ricinus communis L* | Seed,  Root and Aerial parts | Aqueous and  Ethanol | Eggs and 2nd stage Juvenile in plant root | In vitro and  In vivo | In vitro, the highest LC50of all methanolic extracts expressed by 0.75 ml/ml (extract of *R. communis*) and the lowest LC50 of all aqueous extracts by 0.51 ml/ml (extract of *T. baccata*). In vivo, reduction of the infestation rate and number of galls on the roots after the application of methanolic extracts of the 3 plants. | Zaidat et al., 2020 |
| *Abrus precatorius* Linn., *Amaranthus virdis* Linn., *Bunium persicum* Boiss., *Dioscorea deltoidea* Wall. Ex Griseb*., Teraxacum officinale* Weber., *Malva neglecta* Wall., *Podophylum hexandrum* Royle and *Robina pseudoacacia* Linn. | Seed | Chloroform and methanol (50:50, v/v) | Eggs and 2nd stage Juvenile in plant root | In vitro | The dominant mortality was observed by *T. officinale* 93.67% and *B. persicum* 89.66% seed extracts at 72 hrs. | Nengroo et al., 2021 |
| *Azadirachta indica, Arthemisia pallens, Ocimum tenuiflorum, Hibiscus rosasinensis* and *Ficus hispida* | 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% root gall development inhibition on seedlings treated with *V. colorata* methanolic extract. All 8 plant extracts showed promising nematicidal activity at 0.8 mg/ml, | 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,*  *Chenopodium album,*  *Solanum nigrum,*  *Carica papaya*and  *Euphorbia hirta* | Leaves, Stem and  Fruit | Aqueous | Eggs and Larva in root | In vitro | Maximum reduction (24.3%) in egg hatching in *C. album* stem extract at 2% conc. After 48 hrs. of exposure time and maximum larval mortality (33%) was recorded in *C. album* leaf extract at 10% conc. | Afzal et al., 2021 |
| *Tagetes erecta, Tithonia diversifolia, Chromolaena odorata* and *Occimum gratissimun* | Leaves | Aqueous extract | Second stage  of juveniles | In vitro | *T. erecta* caused 100% juvenile mortality within 24  hrs. of exposure. | 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 | The aqueous extracts of stem and flower immobilized 40·7–100% of Juveniles after 48 hrs exposure to the highest conc. (16%) in both trials. | 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 results showed an evident larvicidal effect The in vivo study, 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 induced 50% egg hatch inhibition (LD50 = 0.0255 mg/mL), larval paralysis (LD50 = 0.196 mg/mL), and adult worm mortality (LD50 = 1.0365 mg/mL) at a lower conc. (LD50). | 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 | In vitro, clove ethanolic extract (CEE) of *B. aegyptiaca* had the most significant anthelmintic activity on adult In vivo, the CEE of *B. aegyptiaca* achieved faecal egg reduction (100%) at the 7th day post-treatment. | 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 | In vitro effect (96.3%) was obtained with the E-Cham extract at 72 hrs. The highest combined effect (98.7%) was obtained after 72 hrs. at 40 mg/ml. In vivo assay, the individual administration of the E-Cato and E-Cham extracts reduced the parasitic by 27.1% and 45.8%, respectively. | Zamilpa et al., 2019 |
| *Allium sativum* and  *Tagetes erecta* | Bulb and Flower | Aqueous | Larva in ruminant | In vitro and in vitro | In vitro, larvicidal activity % at 40 mg/ml was 68% with *A. sativum* and 36.6% with *T. erecta*. The combination caused 83.3% mortality. In vivo, the oral administration of *A. sativum* and *T. erecta* extracts at 40 mg/ml, caused 68.7% and 53.9% reduction of the parasitic burden, 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 | At higher doses, *A. muricata* extract showed 84.91% and 89.08% of efficacy in egg hatch test (EHT) and larval motility test (LMT) 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 | In vitro, EC50 for EHT were 2947.0, 3347.0, 3959.6 and 4538.7 µg/ml for MWD, MW, AW and AWD, respectively. The EC50 for LEIT were 2883.4, 5927.4, 9876.3 and 9955.4 µg/ml for AWD, AW, MWD and MW, 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 | The best-fit LC50 values were significantly different (alpha < 0.0001), were 17.70 mg/ml and 56.04 mg/ml for *C. citratus* and *O. gratissimum*, respectively. | Aderibigbe  and Idowu, 2020 |
| *Toxocara canis* | *Balanites aegyptiaca* | Fruit | Methanol | Adult in dog | In vitro | Treatment with 120 μg/ml methanolic extract of BAE showed highest efficacy. | Shalaby, 2018 |
| *Toxocara vitulorum* | *Balanites aegyptiaca* | Fruit | Methanol | Eggs and  Adult in  ruminant | In vitro | The highest value reached to 100% with the conc. of 240 μg/ml. | Shalaby et al., 2012 |
| *Trichinella spiralis* | *Lasia spinosa* | Leaves | Crude | Adult,  Migrating larva and  Encysted muscle larvae in rat | In vivo | Oral administration of plant extract at 800 mg/kg dose revealed a 75.30% reduction of 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 | Six fractions of *C. citratus* had high ovicidal activity at 1000 μg/ml, and two fractions had 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 LC (50) and LC (90) 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 | Aqueous extracts of immature fruits at 100 mg/ml showed 100 % inhibition of larval development. | 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. In vivo, the average EPG decreased from 1485±386.62 to 0±0.00 during 14 days of treatment of 79 mg/ml of AAE. | Mubarokah et al., 2019 |
| *Tagetes erecta Linn*. | Leaves | Ethanolic and aqueous | Adult in  fowl | In vitro | Ethanolic extract at 100 mg/mL conc. showed more significant activity comparing the aqueous extract. | Goswami and Singh, 2018 |
| *Schleichera olesa* | Leaves | Ether  Water  Ethanol  Chloroform  Acetone | Adult in  fowl | In vitro | Inhibition of alpha-amylase by ethanolic and aqueous extracts was significant with the IC50 value of 36.63 and 73.94 μg/ml, respectively. | Goswami and Singh, 2018 |
| *Ocimum sanctum* L. | Ethanol | Ethanol | Adult in fowl | In vitro | LC50 value of ethanol extract of *O. sanctum* Linn. leaves at 6 hrs. were 14.8%, at 12 hrs. was 4.8% and at 24 hrs. was 3.0% and the LC90 at 24 hrs. was 9.1%. | Kharisma et al., 2019 |
| *Maytenus emarginata* | Stem,  Bark | Methanol,  Aqueous and Hydroalcohol | Adult in fowl | In vitro | Methanolic, aqueous, and hydroalcoholic extracts exhibited significant anthelmintic activity at a conc. of 50 mg/ml. | 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 | In vitro, The extracts' efficacy was exhibited in a conc. time-dependent manner. In vivo study of ginger and curcumin recorded lower mortality rates than the in vitro study. | 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. Aqueous and ethanolic extracts demonstrated inhibition of larval migration and the LM50 was 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. In vivo, 800 mg/kg dose revealed 93% reduction of worm load in mice. | 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 | Both crude extracts reduced worm motility by 100% in 48  h post treatment in a dose-dependent response with median  effective dose being 26.85 mg/ml, 4.60 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 exposed to 1 mg/ml of tannins dead and motility were observed in the lowest conc. of 111 µg/ml against L3 an L4 stage. | 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 | Best-fit LC50 values were 1.03 ± 0.17 and 7.90 ± 1.19 mg/ml for *G. sepium*-AC and *L. leucocephala*-AQ, 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 | In vitro, IC50 range = 9.7–20.4 μg/ml. In vivo, a single oral dosing of 100 mg/kg significantly (27.6%) better than untreated group. | Wangchuk et al., 2016 |
| *Heterakis*  *gallinarum* | *Cassia alata*  *Cassia angustifolia* and  *Cassia occidentalis* | Leaves | Crude and Ethanol | Adult in fowl | In vitro | Lost their motility at (5.71±0.10) hrs., (6.60±0.86) hrs. and (13.95±0.43) hrs with C. *angustifolia, C. alata* and C. *occidentalis* respectively at a cone, of 40 mg/ml. | 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, Aloe ferox,*  *Allium sativum,*  *Lespedeza cuneata* and *Warburgia salutaris* | 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 | After 8 hrs exposure of 50 mg/ml caused 75% mortality, being the highest value for AMA. Crude methanolic extract (LC50 =2.48 mg/ml) has higher inhibitory effects for EHA. In vivo, methanolic extract at the dose levels of 1 g/kg body wt. and 2 g/kg body wt. resulted in FECRT of 81.47% and 92.86%, 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 | The maximum mortality rate of protoscolices (100%) was observed in *N. sativa* oil at 100 mg/ml conc. after 120 min of exposure. | El-Bahy et al., 2019 |
| *Setaria cervi* | *Terminalia bellerica*  *Terminalia chebula* and  *Terminalia catappa* | Leaves | Hexane  Chloroform  Methanol Acetone | Microfilari | In vitro | In vitro, *T. Bellerica*, *T. Chebula* and *T. Catappa* showed a decline in the motility of the worms at higher doses of 5 and 10 mg/ml after 4 hrs. of incubation. | 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 highest FECR was observed for the 8 g/kg dose (IC50against 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 | At the conc. of 200 μg/ml after 135 mins of incubation highest mortality rate of microfilariae was observed in methanol and ethanol extracts. | Kausar, 2017 |
| *Haemonchus contortus* | *Curcuma longa* | Rhizome | Ethanol | Infective larva (L3) in sheep | In vitro | 78% worm mortality within 24 hrs. of exposure at the highest dose rate of 200 mg/ml. | 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 | In vitro test, according to IC50 and IC90 values, the condensed tannin-enriched extracts inhibiting EHA and LHA most potent for *R. glutinosa.* | 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 | In vitro, adult were dead at 220 mg/ml (93.33% mortality) after 8 hrs. of treatment and In vivo, the highest FECRT value of the treatment group on the 14th day after treatment was at a dose of 62 mg/ml. | Muda et al., 2021 |
| *Camellia sinensis L.* and  *Albizia lebbeck L*. | Leaves | Ethanol | Adult | In vitro  AMA | Both of ethanolic extracts exhibited 88% and 95% mortality at 6 and 8 mg/ml after 8 hrs. of treatment. | 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 highest conc. of AgNPs induced 91 ± 1.76 % egg hatch inhibition. IC50 and IC90 values for EHA were 0.007 ppm and 7.71 ppm. | 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 | Penetrating the cuticle of the larvae, causing changes in the tegument and consequently death of the nematode occurs. | 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 | AgNPs of M. oleifera seeds produced a maximum of 80.59 ± 5.65 % inhibition of egg hatching at 8 mg/ml conc. | 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 increased with an increase conc. of nanoparticles and the incubation time. | 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 | 87.5% mortality after 12 hrs. and 100% mortality after 24 and 72 hrs. of exposure. | 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**

Helminth infections are considered neglected tropical diseases. Helminth are parasitic worms which are invertebrate, elongated, round or flat bodies (Hotez et al., 2008; Headly et al., 2017). Intestinal nematodes, schistosomes, and filarial worms are the most prevalent helminths. Previously, it is worked out that, the sheep and goat or cattle industry has undergone a severe loss of Rs. 31.43 million per year (Iqbal et al., 2014). Besides livestocks, it also affects mostly children and it can compromise nutritional status resulting in stunted growth and impaired memory. Improved cleanliness, a multi-drug regimen, and health education are used to treat helminth infections. Helminthic diseases are treated using anthelmintics drugs but however, some of these infections suffer from drug resistance and causes severe side effects. In ethnomedicine, nearly, approximately 80% of the world’s population relies on our traditional medicines from phyto extracts for primary health care and health benefits (WHO, 2008). Many folklores medicinal plants are traditionally uses to cure helminthiasis in developing countries like India, China, Bangladesh. So, plant derived drugs are gaining lot of attention for treatment of parasitic infection efficiently (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). Generally, the plant’s secondary metabolites associated with the anthelmintic effect are condensed tannins, alkaloids, saponins, phenol and flavonoids, etc. (Rawani and Gope, 2021) These plant-based herbal medicines are thought to be promising sources for developing effective anthelmintic drug with minimum side effects and non-resistance to parasitic helminths. The screening for phytogenic chemical compounds like tannins, alkaloids, phenol, saponin, flavonoids etc. helps to account for the better anthelmintic activity and new herbal Anthelmintic drug. Certain metal nanoparticles, including silver, gold, and metal-based oxide nanoparticles like zinc oxide and iron oxide, have been studied for their potential to treat various illnesses. According to recent reports they act as very effective Anthelmintic (larvicides and adulticides) against different helminths species of medical and veterinary importance (Zhang et al., 2020).

**Conclusion**

From the study, it can be concluded that medicinal plants were used from the ancient period, and it is a part of traditional medicine. From the study, it is revealed that whole plant or plant parts in crude, as well as the solvent extract and synthesized green nanoparticles have potential efficacy against parasitic helminth. Metal nanoparticles have been shown to have the potential to be therapeutically effective, although some of the nanoparticles showed lower biological activity, which was related to their design, the composition of the metal, and poor selectivity towards the target cells. When the metal compounds were included into particular drug delivery methods, these restrictions were overcome in those instances. When compared to other infectious disorders, reports on the use of metal-based nanoparticles for the treatment of parasitic infections are scarce, demonstrating the urgent need for developing metal-based nanoparticles that are reasonably priced and have excellent therapeutic results. Additionally, research is required on the toxicological characteristics and pharmacokinetics of drugs based on metals. Drug resistance, which is typical with most organic compounds, may be overcome by metal-based nanoparticles. There is no doubt that metal-based nanoparticles are promising future therapeutics for the treatment of infectious diseases. Nevertheless, in the future land of the herbal products from laboratory to market, there is necessary to know the actual mode of action through in-vivo study.

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