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In Vitro Anthelminthic Activity of Medicinal Plants -A Review

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ABSTRACT

The present review deals with medicinal plants having anthelminthic activity widely distributed worldwide. Medicinal plants or medicinal herbs are essence of traditional practice. Anthelmisintics or antihelminthics are a group of antiparasitic drugs that expel parasitic worms and other internal parasites from the body by either stunning or killing them and without causing significant damage to the host. Several preventive and corrective methods for modern medicine are available, however, it is not safe due to serious side effects .In order to overcome these side effects, there is a need of natural anthelminthic agents with minimal side effects. In ancient and modern pharmacology period, several number of medicinal plants having anti-anthelmintic efficacy. This review article gives the list of medicinal plants having anthelminthic activity.

Keywords: Anthelmisintic, Helminthiasis, Antiparasitic Drugs, Medicinal Plants

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INTRODUCTION

The word Helminth is derived from Greek word meaning “Worm”.^[1] A macro parasitic disease of humans and other animals in which the part of the body is infected with parasitic worms known as Helminths. The Helminths are invertebrates characterize elongated, flat, or round bodies. Helminths are multicellular organisms, these organisms live in and feed on living host, receiving nourishment and protection while disrupting their nutrient absorption causing weakness and disease.

Helminthiasis:

It is an infection caused by helminths is known as Helminthiasis.^[2] It is also known as intestinal worm infestation, helminthic infestation or soil transmitted infestations. These worms gets burrowed into the organs or gastrointestinal tract of host and induces a physiological damage. The most common helminthiasis are seen in neglected tropical countries. The different types of worms includes Roundworms, Pinworms, Threadworms, Whipworm, Filaria, Guinea worm and Tapeworm.

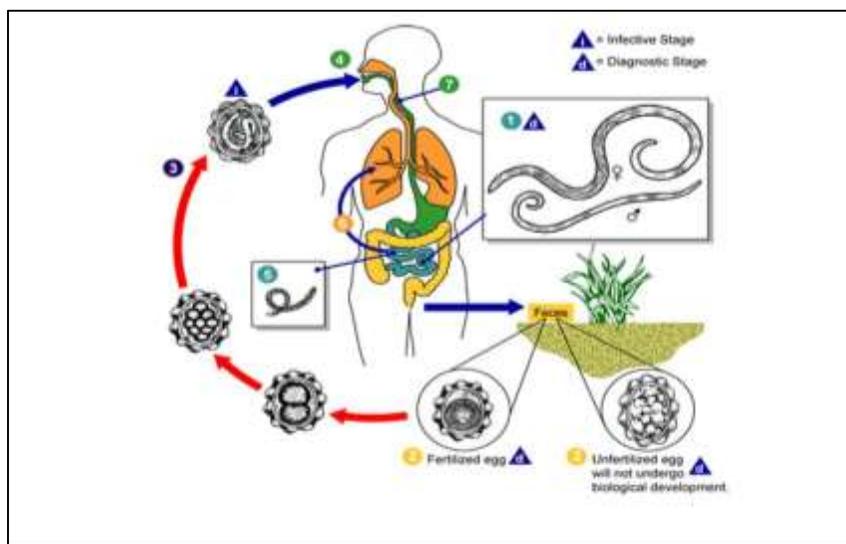


Figure 1: Life Cycle of Helminths

Life cycle of Helminths

The female produces egg (approximately 200000 per day) that are excreted with faeces. Unfertilized eggs are harmless, but fertilized once are infective after 18 days to several weeks. Infective eggs are ingested. It enters the gut. Develop into larvae in the intestine, and penetrate the blood vessels to enter lungs, where they develop further. After 10 to 14 days, penetrate the alveolar walls. Upon reaching the small intestine, they develop into adult worms. It takes 2 to 3 days for one complete cycle, adult worms can live 1 to 2 years.^[3]

Symptoms

For milder infections, no observable symptoms are seen. For long term and heavy infections, a range of health problems occurs. like

- Abdominal pain
- Protein and blood loss
- Diarrhoea
- Rectal prolapse
- Slowing down of protein and blood loss
- Slow cognitive and physical growth
- Cough
- Constipation
- Nausea
- Vomiting
- Rash
- Redness
- Skin irritation near anus
- Weight loss

TRANSMISSION

Soil transmitted helminths are transmitted by eggs that are passed in the faeces of infected people. Adult worms live in the intestine where they produce thousands of eggs each day. In areas that lack adequate sanitation, these eggs contaminate in the soil.

Several ways of transmission

Eggs that are attached to vegetables are ingested when the vegetables are not carefully cooked, washed or peeled. Eggs are ingested from contaminated water sources. Eggs are ingested by children who play in contaminated soil and the put their hand in their mouths without washing them. Hook worm egg hatch in the soil releasing larvae that mature into a form that can actively penetrate the skin. People will be infected with hook worm who walk by barefoot on the contaminated soil. There is no direct person to person transmission or infect from fresh faeces because eggs passed in faeces need about 3 weeks to mature in the soil before they become infective. Since these worms do not multiply in human host reinfection occurs only as a result of Three types of transmission.

Type 1: Direct

Eggs which are passed in stool are carried from anal margin to mouth, where they hatch and re-infected within 2 to 3 hours without reaching soil. When they reach soil the period of development is not necessary.

Example: *Enterobius vermicularis* (threadworm)^[4]

Type 2: Modified Direct

It undergoes stages of development in soil upon passing the eggs in stool. After it gets ingested, hatch and release larvae which gets penetrated into stomach wall and enters into circulation. Then reaches the lungs they get re-swallowed into respiratory tract and finally it reaches the intestine and it becomes the adult worms.

Example: *Ascaris lumbricoides* (roundworm), *Toxocara* spp^[4].

Type 3: Penetration of the Skin

Developed larvae penetrates the skin and reaches the intestine where it becomes adult worms.

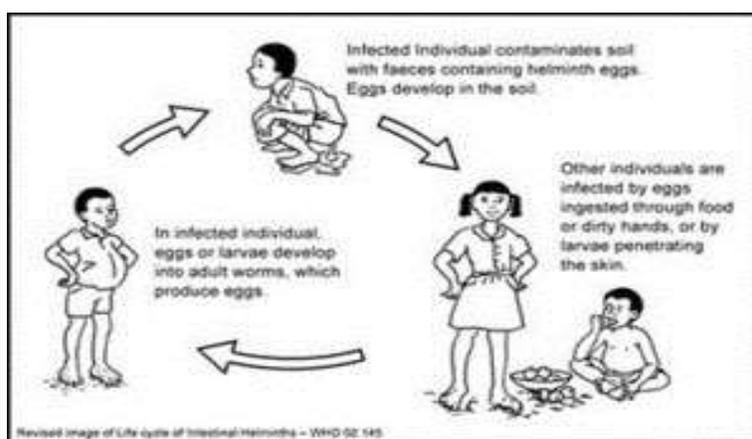


Figure 2: Transmission of Helminths

Example: *Ancylostomaduodenale* and *Necatoramericanus* (hookworms), *Strongyloidesstercoralis*^[4]

Diagnosis

Method:

Some of the diagnostic methods are

Microscopy based techniques:

A thin and smooth preparation of stool is made by using saline and iodine. Then it should be covered using cover glass and then it should be examined under microscope to identify the presence of helminthic eggs^[5]. It should be carefully examined for identifying the shape and size of parasites.

Eggs counting Kato- Katz method:

This method is used for quantification of helminth eggs. The helminthic eggs per gram of stool (EPG) as a standard infection intensity measure is calculated as Number of eggs in smear*10⁵ [5].

Serological assays : When faecal samples are not available then serological assays play a major role in diagnosis [5]. The two types of serological assays are Antigen detection assay and Antibody detection assay. It also includes ELISA test (Enzyme linked immune sorbent assay).
Endoscopy/Colonscopy: In this method the tube is inserted into mouth (Endoscopy) or rectum (Colonscopy) to examine whether there is presence of parasites [5].

X-Ray, Magnetic Resonance Imaging (MRI) Scan, Computerized Axial Tomography Scan (CAT):

These tests are used to detect the presence of lesions in the organs due to the parasitic diseases.

Prevention:

Avoid contact with earth contaminated with human waste especially faeces. Thoroughly washing hands with soap before handling food. Washing, peeling, or cooking all vegetables and fruits before consumption especially in cases where the vegetables or fruits were grown in soil fertilized with manure. Not defecating outdoors using toilets connected to effective sewage disposal systems.

Treatment

Various allopathic drugs are used in the treatment of Helminthiasis. Some of them are discussed below.

Benzimidazoles (Albendazole, Mebendazole, Thiabendazole)

These are broad spectrum anthelmintic which are used in the treatment of round worm, hook worm, pin worm, whip worm infestation (Dose of 400 mg). After some days the dead parasites get expelled out from the gut. Mebendazole and Albendazole are widely used because Mebendazole retains its Broad spectrum Anthelmintic activity and Albendazole is used as a single dose administration drug in many infestations. Thiabendazole is not used because of the availability of better tolerated Albendazole and Mebendazole.

Mechanism

It binds to β tubulin of the parasite with high affinity and inhibits the synthesis of microtubules. It also inhibits glucose uptake in the parasite and depletes glycogen storage [5].

Adverse effects

Nausea, Vomiting, Abdominal pain, Headache or temperate hair loss, dizziness, drowsiness, liver damage. At High doses, Mebendazole causes allergic reactions, loss of hair and granulocytopenia.

Piperazine Citrate

It is effective in round worm and pin worm infestation. It is available as second choice drug because of availability at more convenient and better tolerated. GABA agonist action of piperazine causes hyperpolarisation of *Ascaris* muscle.

Mechanism

It acts by competitively blocking the action of acetyl choline and causes contraction in the worms. The worms gets expelled out by peristalsis from the gut^[5].

Adverse effects

Nausea, Vomiting, abdominal discomfort and urticaria. At high doses it causes dizziness and excitement. At toxic doses it causes Convulsions.

PYRANTEL PAMOATE

It is used in the treatment of pinworm, round worm and hookworm infestation in children. They are well tolerated and single dose(10 mg/kg) yields high cure.

Mechanism

The persistent depolarisation occurs due to the activation of nicotinic cholinergic receptor which causes slow contracture and spastic paralysis^[5].

Adverse Effects

It shows symptoms such as headache, dizziness occasionally.

Levamisazole, Tetramisole

Tetramisole was developed in late 1960s. Its levo form is Levamisazole which was found to be more active and is widely used nowadays.

Mechanism

It causes interference with Carbohydrate metabolism(inhibition of fumarate reductase).It causes tonic paralysis and expulsion of live worms.^[5]

Adverse Effects

Nausea, abdominalpain, giddiness, fatigue, drowsiness or insomnia.

DIETHYLCARBAMAZINE CITRATE(DEC)

It was first developed in 1948 it was the first drug for filariasis. It is a micro filaricidal which is slow acting.

Mechanism

It acts by altering the organelle membranes of microfilariae which promotes the cell death^[5]

Adverse Effects

Nausea, loss of appetite, headache, weakness and dizziness.

IVERMECTIN

It is the drug of choice for the treatment of onchocerciasis and strong loidosis in a single dose. It is microfilaricidal. A single dose of 10-15mg (0.2 mg/kg) is used.

Mechanism

It binds glutamate gated chloride channel. It increases permeability of cell membrane to chloride ions. It causes hyperpolarisation of neuronal membrane which causes paralysis. It also potentiates GABAergic transmission in the worm.^[5]

Adverse Effects

Mild pruritus, giddiness, nausea, abdominal pain, constipation, lethargy, allergic reactions occurs due to hypersensitivity to the dying microfilarial proteins (**mazotti reaction**) and transient ECG changes.

PRAZIQUANTEL

It is effective against all schistosomes and most other trematodes and cestodes.

Mechanism

It increases cell membrane permeability to calcium resulting in contraction followed by paralysis and expels worms.^[5]

Adverse Effects

Headache, dizziness, sedation, itching, rashes, fever, bodyache.

NICLOSAMIDE

It is effective against tapeworms.

Mechanism

It acts by inhibiting oxidative phosphorylation in mitochondria and interferes with anaerobic generation of ATP by the tapeworm^[5].

Adverse Effects

Pruritis, malaise and headedness. Though Allopathic drugs produce the onset of action fastly it produces many adverse effects. So, nowadays herbal drugs are preferred mostly when compared to that of allopathic drugs because it does not produce side effects. or minimal side effects.

HERBAL DRUGS:



Figure 3: Roots of *Calotropis Gigantea*

Anthelmintic activity of *calotropis gigantea* roots

Aqueous and alcoholic extract of peeled roots of *Calotropis gigantea* belonging to the family *Asclepiadaceae* which is commonly known as crown flower was tested in *Pheretima posthuma* at the dose level of 20mg/ml, 40 mg/ml, 80mg/ml and 100 mg/ml for paralysis and death time of earthworms was recorded. The time of paralysis and death of worms at concentration of 20 mg/ml, 40mg/ml and 80mg/ml was closed to that of the standard drug Albendazole. The concentration of 100mg/ml had same effect as that of 80mg/ml Albendazole^[6]. The plant has active constituents like flavonoids, sterols, cardenolides, esters, alkaloids. The aqueous extract gives better activity than alcoholic extract.



Figure 4: Leaves of *Vitex negundo*

Anthelmintic activity of *vitex negundo* linn

Aqueous extract of leaves and flowers of *Vitex negundo linn* which is also called as Chinese chaste tree or horseshoe vitex of the family *Lamiaceae* was used to study in vitro anthelmintic activity using Indian adult earthworm. The plant contains chemical constituents like casticin, isoorientin, chrysophenol, luteolin, and p-hydroxybenzoic acid and fructose. Two different concentrations 25mg/ml and 50mg/ml of each extract was undertaken to evaluate the anthelmintic activity and results was expressed in terms of paralysis and death of the worms.^[7] Albendazole and Piperazine citrate 20 mg/ml were used as a standard drug and CMC – 0.5 % as a control group. Aqueous extract of leaves and flowers at 50 mg/ml has significant better activity when compared to control group.

Anthelmintic activity of *cleome viscosa*



Figure 5: Seeds of *cleome viscosa*

Alcohol and aqueous extract of seeds of *Cleome viscosa* commonly known as Asian spider flower, tick weed contains the chemical constituents like cleomiscosin A, B, C and D, cleosandrin, cleomeolide belonging to the family of *Capparidaceae* were investigated for the anthelmintic activity against *Pheretima posthuma* and *Ascaridia galli*. Various concentrations such as 10mg/ml-100mg/ml of each extract were tested in the bioassay which involved determination of time of paralysis and death of the worms^[8]. Both extracts exhibited considerable anthelmintic activity in dose dependent manner. The most significant activity was observed at higher concentration of 100 mg/ml against both types of worms. Piperazine citrate 10mg/ml was included as standard reference and distilled water as a control



Figure 6: Bark of *Helicteres isora*

Anthelmintic activity of *helicteres isora* bark

Methanoilc extract of *Helicteres isora* bark also called as East Indian screw tree belongs to the family *Malvaceae* contains the chemical constituents like proteins, polyphenol, tannins, flavonoids, alkaloids, saponins. Indian adult worms were collected. Earthworms were grouped and treated with extract at concentration of 10 mg/ml, 20 mg/ml, and 50mg/ml. All extracts showed concentration dependent activity that significant activity observed at 50 mg/ml.^[9] In the methanolic extract showed better activity at concentration of 50mg/ml. Albendazole 10mg/ml is used as a standard and normal saline as a control.

Anthelmintic activity of *terminalia chebula* retz

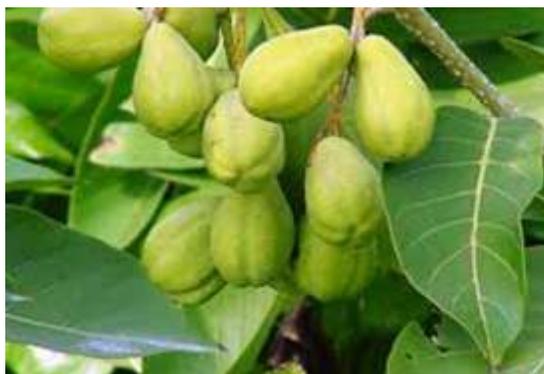


Figure 7: Fruits of *Terminalia chebula*

The alcoholic and aqueous extracts of fruits of *Terminalia chebula* also commonly called as Chebulicmyrobalan belongs to the family *Combretaceae* were screened to evaluate anthelmintic activity in Adult earth worm *Pheretimaposthuma*. The alcoholic and aqueous extract of the fruits showed significant anthelmintic activity and it was found that the alcoholic extract activity is higher than the aqueous extract and the standard drug of Albendazole^[10]. The chemical constituents

present in *Terminalia chebula* are polyphenols, terpenes, anthocyanins, alkaloids, flavonoids, and glycosides.

Anthelmintic activity of *benincasa hispida*



Figure 8: Roots of *Benincasa hispida*

Crude aqueous, petroleum ether, chloroform, and methanolic extract of *Benincasa hispida* also called as white gourd, ash gourd belonging to the family *Cucurbitaceae* contain constituents such as triterpenoids, flavonoids, saccharides, glycosides, carotenes, vitamins, β -sitosterin, uronic acid. *Pheretima posthuma* is used as test worms. Single concentration 5 % of extract were tested in bioassay^[11]. Piperazine citrate was included as standard reference and distilled water as control. The *Benincasa hispida* root extract exhibits anthelmintic activity significantly.



Figure 9: Stem bark of *Caesalpinia bonduca*

Anthelmintic activity of *caesalpinia bonduca*

The petroleum ether, chloroform and ethanol extract of stem bark of *Caesalpinia bonduca* is a scrambling woody liana commonly called as grey nicker, nicker bean or knicker nut belongs to the family *Fabaceae* contains chemical constituents such as homoisoflavanoids, hematoxylol, stereochoenol A. The extracts of stem bark were screened for anthelmintic activity using *Pheretima posthuma*. The ethanolic extract at concentration 100 mg/ml showed significant effect time of paralysis at 29.67 ± 0.88 min and death time at 60.00 ± 0.58 min, and time of paralysis and time of death of standard Piperazine citrate was 38.67 ± 0.88 min and death 59.00 ± 1.73 min

respectively [12]. At concentration of 100mg/ml of each petroleum ether and chloroform extract showed moderate activity. The ethanolic extract confirmed anthelmintic activity.



Figure 10: Bark of *Neolamarckia cadamba*

Anthelmintic activity of *neolamarckia cadamba*

Extracts of the bark of *Neolamarckiacadamba* commonly called as burflower tree, laran and leichhardt pine belonging to the family *Rubiaceae* contain chemical constituents like saponin, alkaloids and steroids are used against Indian adult earthworm *Pheretimaposthuma*. The concentration of the extracts was 10mg/ml 15mg/ml, 20mg/ml. [13] The activities were comparable with the reference drug Piperazine citrate among the tested extract, chloroform extract, and petroleum ether were found to possess promising anthelmintic activity in comparison to other extracts.

Anthelmintic activity of *curcuma caesia*



Figure 11: Rhizomes of *Curcuma caesia*

Ethanol, chloroform, and aqueous extracts of *Curcuma caesia* commonly known as black turmeric or black zedoary belonging to the family *Zingiberaceae* contains chemical constituents such as glycosides, carbohydrates, tannins, saponins, phytosterols, resins, phenols, flavonoids. The three extracts of rhizomes of *Curcuma caesia* at three concentrations 25mg/dl, 50 mg/dl, 100 mg/dl of each extract was studied for anthelmintic activity. Albendazole 20mg/dl was taken as standard. The most effective is the ethanolic extract 100mg/dl which causes death in 36.81 ± 1.13 min whereas the standard Albendazole 20mg/dl causes death in 37.20 ± 1.74 [14], this present study is

more effective than vermifugal activity in comparison with standard Albendazole in dose dependent manner.



Figure 12: Leaves of *Sophora Interrupta*

Anthelmintic activity of *sophorainterrupta*

Crude methanolic extract of leaves of *Sophorainterrupta* commonly known as adavibillu belonging to the family *Fabaceae* contains the chemical constituents like anthraquinones, terpenoids, flavonoids, saponins, tannins, alkaloids and cardiac glycosides were evaluated for in vitro anthelmintic activity on the Indian adult earthworm. At the concentration of 5mg/ml ,10mg/ml, 20mg/ml ,25mg/ml 30mg/ml.^[15]Albendazole was used as a standard drug to compare the test. The methanolic leaf extract showed significant activity.



Figure 13: Seeds of *Trachyspermum ammi*

Anthelmintic activity of *trachyspermum ammi*

The alcoholic and aqueous extract of *Trachyspermumammi* commonly called as Bishops weed contains chemical constituents volatile oil, tannins, glycosides and steroidal substances belongs to the family *Apiaceae*. The extracts of the seeds were screened for anthelmintic effects using *Pheretimaposthuma*. The various concentration of the extract such as 10 mg/ml, 20 mg/ml and 40 mg/ml were used.^[16] The standard drug used is Albendazole. The alcoholic extract showed more significant effect than the aqueous extract.



Figure 14:Leaves of coriandrum sativum

Anthelmintic activity of *coriandrum sativum*

Ethanollic and carbon tetrachloride extract of *Coriandrum sativum* plant commonly called as Chinese parsley or dhanian belongs to the family *Apiaceae* contains chemical constituents like linalool, geraniol, camphor, geranyl acetate, linalylacetate, flavonoids. The various concentrations such as 50 mg/ml, 100 mg/ml, 150 mg/ml of ethanollic and carbon tetrachloride extract were used against Indian earthworm *Pheretima posthuma*.^[17]The standard drug used is Piperazine citrate. The ethanollic extract showed more significant effect than the carbon tetrachloride extract.



Figure 15:Seeds of *Artocarpus heterophyllus*

Anthelmintic activity of *artocarpus heterophyllus*

Ethanol, aqueous and ethyl acetate extracts of *Artocarpus heterophyllus* commonly called as jackfruit belongs to the family *Moraceae* contains the chemical constituents like carbohydrates, proteins, amino acids, alkaloids, steroids, triterpenoids, tannins, glycosides, flavonoids, saponins. The various concentrations of the extracts of seeds such as 20 mg/ml, 50 mg/ml and 100 mg/ml were used against *Pheretima posthuma*^[18].The standard drugs used is Albendazole. The ethyl acetate showed more significant effect when compared to that of ethanollic and alcoholic extract.



Figure 16: Seeds of *Semecarpus anacardium*

Anthelmintic activity of *semecarpus anacardium*

Petroleum ether, chloroform, ethanolic and aqueous extracts of *Semecarpus anacardium* commonly called as marking nut belongs to the family *Anacardiaceae* containing the chemical constituents such as biflavanoids, anacardic acid, catechol, fixed oil, anacardol, semecarpol. The extracts of nuts was used against *Pheretimaposthuma*. The reference standard used are Albendazole (10 mg/ml) and Piperazine citrate (10 mg/ml).^[19] The petroleum ether and chloroform extract showed better activity than aqueous and ethanolic extract.



Figure 16: Flower of *Butea monosperma*

Anthelmintic activity of *buteamonosperma*

Ethanolic, alcoholic and aqueous extract of *Buteamonosperma* commonly called as Flame of the forest and bastard teak belongs to the family *Fabaceae* contains the chemical constituents butrin, butein, monospermoside, sulphurein, palastrin. They were tested against *Pheretimaposthuma* at a dose level of 10 mg/ml, 20 mg /ml and 50 mg /ml for paralysis and death of earth worms.^[20] The standard drug used is Albendazole. The ethanolic extract of flower shows more significant activity than the aqueous activity and alcoholic extract.

CONCLUSION:

Anthelmintic drugs are more costly and also serious side effects. Herbal drugs are very cheaper and no side effects or minimal side effects. There are many medicinal plants that are scientifically proved for anthelmintic activity. This article reviewed the list of medicinal plants having anthelmintic activity. However future study must be carried out to explore the plants having higher efficacy and no side effects for the treatment of anthelmintic activity.

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