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An Overview of Medicinal Plants with Anthelmintic Properties

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Abstract
Helminth parasite diseases are widespread and induce a variety of clinical problems as well as long-term and irreversible morbidity in humans. Despite significant advancements in the medical sciences, the efficacy of currently available anthelmintics remains rather low. In addition to being comparatively side effect-free, modern synthetic medications are highly effective at curing illnesses. Many medicinal herbs that are used by ethnic groups all over the world are also said to have anthelmintic properties in traditional systems of medicine. Several medicinal plants have been investigated for this action using a variety of in-vitro and in-vivo techniques in response to folk claims. This review highlights some significant pharmacological and early research on medicinal plants, their products, and the principles that can be further explored to produce lead compounds in the quest for new herbal medicines.

Keywords
Terpenoids, phenolics, helminth parasitic organisms, natural products, and medicinal plants.

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INTRODUCTION:
Helminths is derived from the Greek word “worms "[4]. Helminths are parasitic worm infections that make their host sick. They pose a serious risk to human health [1]. Parasitic worms likewise taint the animals and yields in this way influencing the food creation with a resultant financial impact [5]. Parasitic worms of humans may cause chronic and occasionally fatal diseases that are regarded as neglected tropical diseases, also known as NTDs, affect approximately billion people on the planet [2]. About one-third of the nearly three billion people who survive in developing nations in Asia, the Americas, and sub-Saharan Africa have been reported to be helminth-infected.[3] parasitic worms, which are generally categorized as roundworms(also known as nematodes) include the major intestinal worms (also known as soil-transmitted helminths) and the filarial worms, whereas the flatworms(also known as platyhelminths) include the flukes (also known as trematodes), and the tapeworms (also known as the cestodes)[3].

Disease caused by helminths
Cestodes (Tapeworm)[2]
Coenurus cerebralis
- In sheep, rabbits, and rodents, - Humans become an intermediate host after ingesting food contaminated. Diphyllobothrium latum
- The fish tapeworm, infects humans who ingest raw and pickled freshwater fish.
- Compete with hosts for certain vitamins and related substances particularly for vitamin B12 and split vitamin B12 intrinsic factor complex.

Spirometra species:
- Cats and dogs (definitive host).

- Humans are accidental hosts, acquire infection by drinking contaminated water.

Nematodes [2]

Angiostrongylus cantonensis:

- Infect molluscs or fish. - In humans, it affects the upper respiratory tract, CNS

Gnathostoma spinigerum:

- Parasitizes the stomachs of cats and dogs.
- Migrate through human tissue by ingestion of cooked animal flesh, drinking contaminated water

Strongyloides stercoralis:

- Small nematodes, can parasitize the small bowel of humans.
- This female worm hatch in the intestinal duodenum and jejunum and pass into faeces.

Toxocara canis and cati:

- Infects dogs and related mammals.
- Eggs hatch into the small intestine of the host and larvae migrate into lungs, and trachea.

Most of the world's population is afflicted by bacterial and Helminthes infections, with typical causes including inadequate sanitation, inadequate family hygiene, malnutrition, and crowded living conditions. The infection sources are [5]:

Human beings: People are the most frequent cause of infection.

Animals: Numerous microorganisms can contaminate both individuals and creatures. Creatures go about as wellspring of human disease.

Insects: Insects that feed on blood can carry diseases that affect humans. Some insects may serve as hosts' reservoirs in addition to being vectors.

Soil and water: Some diseases can endure extremely lengthy lives in the soil. Because of the existence of aquatic vectors or contamination with pathogenic microorganisms, water can serve as an infection source. Food: Food that has been contaminated can spread illness.

Severity: Prematurity, low birth weight, and increased maternal morbidity and mortality are all consequences of hookworm and schistosomiasis during pregnancy. Among a few grown-up populaces living in ruined areas of non-industrial nations, onchocerciasis is a main source of visual deficiency and skin disease, while LF is a significant reason for limb and genital deformities.

Anthelmintic [4]:

Drugs known as anthelmintics are used to cure and control infections in humans and animals caused by parasitic nematodes, trematodes, and cestodes.

Significance of anthelmintic drugs:

The toxicity and chemical residues, higher expenses, in adaptability of medications, and unavailability in remote places. The usage of anthelmintics has recently caused toxicity in people. Therefore, plants, which are thought to be the best source of bio-active compounds, are being used in the research and identification of novel chemicals functioning as anthelmintics. Many herbs have been used to treat skin conditions, leucorrhoea, fever, dysentery, dysuria, wounds, swellings, abscesses, rheumatism, and lower extremity discomfort. Anthelmintics are those medications that are utilized in ousting out the worms that are parasitic in nature by either dazzling them or by killing them. They are otherwise called vermifuges or vermicides. [6]

Significance Of Medicinal Plants Over Conventional anthelmintics:

- The therapeutic benefits of plants are due to biologically active compounds possessing drug-like characteristics.[7]
- The development of novel medications and drug leads from medicinal plants is a significant source of ongoing drug research.[8]
- Several potent substances that were separated from therapeutic plants have demonstrated anthelmintic action against intestinal worms.[9]
- The active ingredients of the majority of medicinal plants that are historically used to treat intestinal worms are still unknown.
- When compared to synthetic molecules, plant-based substances usually have stronger biological activity.[10]

Secondary metabolites of plants that possess anthelmintic properties:

Secondary metabolites of certain plants shows anthelmintic properties. Every plant produces allochemicals, and primary metabolites serve as building blocks for various secondary metabolites.[11]

1. **Terpenes:** Various isoprene units combined to form terpenes (C5H8)[12]. It exhibits anthelmintic properties that harm the parasite's digestive system. Terpinen-4-ol, borneol, and β-elemene, for instance, shown efficacy against H. contortus by preventing the hatching of eggs.[13]
2. **Glycosides:** Glycosides exhibit strong anti-helminth action. Cardenolide disrupts the passage of sodium and potassium ions into helminths, which results in helminth mortality.[14]
3. **Saponins:** Saponins consist of sugar chains and contain triterpene or, less frequently, steroidal-aglycone [15]. By blocking acetylcholinesterase, saponins exhibit their anthelmintic properties and cause worm paralysis that ultimately results in death. According to reports, they exhibit inhibitory effect against worms that parasitize animals, such as *Haemonchus contortus.*[16]

4. **Flavonoids:** Flavonoids contributes to flower colors, UV protection, allelopathy, and suppression of auxin transport.[17] The phosphorylation reaction is blocked by flavonoids, which impede the parasitic worms' ability to produce energy and ultimately cause their death.46 At 10 mg/mL, quercetin had a paralysis time of 2.23 ± 4.51 minutes.[18]
5. **Tannins:** These are a water-soluble, polyphenolic group of compounds that aid in the death of nematodes by preventing the worms from absorbing nutrients from the host cell or, in the event that the larvae consume condensed tannins, by binding to the intestinal mucosa of the parasitic worms and causing autolysis.[19]
6. **Alkaloids:** By inhibiting the uptake of glucose and binding to the acetylcholine receptor, alkaloids have demonstrated anthelmintic effect. As a result, helminths perished from malnutrition.[20]
7. **Non-protein amino acids:** These are nitrogen-containing molecules with hydrogen atoms that are derivatives of ammonia. They harm the parasitic worms by interfering with their central nervous system, which results in paralysis and ultimately in death.[21]

Plants with anthelmintic properties:

It has been observed that certain plants possess anthelmintic properties. These are a few of them:

1. ***Commiphora molmol***: Several findings suggest that more than 90% of people have either fascioliasis or schistosomiasis.Half maximal effective concentration (EC50) value for *Commiphora molmol* was 0.20 mg/mL, and 56Myrrh was effective against *Trichinella spiralis* at a dosage of 0.01 mL per infective mouse (*Trichinella spiralis* infective mouse).[22]
2. ***Ocimum sanctum***: *Ocimum sanctum* was effective against *Caenorhabditis elegans* at a level of 62.15 mg/mL.58Crude hydro-alcoholic extract was evaluated against *Pheritima posthuma* at dosage concentrations of 20 and 40 mg/mL. At 6.0 ± 0.5 minutes and 13.5 ± 1.2 minutes, respectively, for 20 mg/mL paralysis and death.[23]
3. ***Melia azedarach***: a significant fatal concentration 50 (LC50) value of 572.2 µg/mL and a lethal concentration 99 (LC99) value of 1137.8 µg/mL were demonstrated by the hexane extract of *M. azedarach* fruits, which was effective against malaria.[24]
4. ***Artemisia annua***: the plant crude leaves extract was tested against *H. contortus,* showed lowest LC_{99} at 1.27 µg/mL in egg hatch test assay, and in the larval development test assay, showed LC_{99} at 23.8 µg/mL.[25]
5. ***Papaya Carica***: The plant's latex was tested at varying concentrations (20%, 50%, and 100%) against *Pheretima posthuma*. At 100% concentration, the results showed paralysis time of P = 24.5 minutes and death time of D = 56 minutes.[26]
6. ***Nigella sativa*** *:* Evaluated at 5% concentration against *Cotylophoron cotylophorum*, the ethanolic extract showed 81.02% reduction of motility after 8 hours.[27]
7. ***Flemingia vestita***: The plant's isoflavones were tested against *Rallietina echinobothrida*, and the results showed that the paralysis times for the enzymes fructose 1, 6-bisphosphatase, pyruvate carboxylase, and glucose 6-phosphate dehydrogenase were 0.98 ± 0.15, 0.880 ± 0.006, and 9.2 ± 0.2, respectively.[28]
8. ***Juglans regia:*** 10 mg/mL of crude acetone extract demonstrated anthelmintic action, resulting in paralysis in 52.00 ± 0.20 minutes and death in 114.00 ± 0.14 minutes. When crude methanolic extract was evaluated against *Eicinia feotid*, it demonstrated anthelmintic action at 10 mg/mL, with paralysis duration of 100.00 ± 0.14) min and death at (133.00 ± 0.18) min. [29]
9. ***Mimusops elengi*:** The methanolic extract demonstrated anthelmintic action at 5 mg/mL, paralyzing and killing the helminths at 163.3 and 223.2 minutes, respectively, when tested against *Pheretima posthuma*.[30]
10. ***Punica granatum****:* When tested against *Haemonchus contortus*, the crude methanolic solution resulted in hatching inhibition up to 46.33% and death at P < 0.05 at 10 mg/mL. [31]
11. ***Thymus vulgaris:*** *Thymus vulgaris essential* oil exhibited 90% inhibition against *H. contortus* at doses ranging from 50 to 0.781 mg/mL. Its half maximum inhibitory concentration (IC50) value was found to be 0.436 mg/mL. With concentrations ranging from 50 to 3.125 mg/mL and an IC50 value of 0.338 mg/mL, 97.0% larval motility inhibition was seen.[32]
12. ***Ferula foetida*:** Aqueous extracts were utilized to treat *Pheretima posthuma*, and after 6 minutes, they showed action at 100 mg/mL, paralyzing the worms. Plant extract in water at a concentration of 25 mg/mL paralyzed helminths in 24.00 ± 0.14 minutes and killed them in 56.00 ± 0.17 minutes.[33]
13. ***Embelia ribes:*** Methanolic extracts were evaluated against *Ascaridia galli,* after 48 hours of incubation, the extracts demonstrated 38.67% ± 4.10% and 38.67% ± 1.86% activity at a dosage of 60 mg/mL. [34]

14. ***Vernonia anthelmintica:*** Ethanolic extracts of the plant were tested against *Haemonchus contortus*, the survival rate was considerably reduced at a dosage concentration of 80 µg/mL.[35]
15. ***Chenopodium ambrosioides:*** After 72 hours of incubation, the ethanolic extract demonstrated a fatal effect (about 96.3%) at 40 mg/mL. *Chenopodium ambrosioides* EC50 value was 0.26 ± 0.02 mg/mL. In a test using hydro-alcoholic extract against *Schistosoma mansoni*, larvae at varying dosages perished after 180 minutes.[36]
16. ***Piliostigma thonningii:*** The ethanolic extract demonstrated anthelmintic action, causing around 60% of larval paralysis at a dosage concentration of 4.4 mg/mL within 24 hours of exposure when tested against *Ascardia galli*.[37]
17. ***Ginkgo biloba:*** 3.0% of the plant extract solution tested the plant's aqueous extract against *S. papillosus*, and in 0.75% of the plant extract solution, nematode larvae died at a rate of 92.3% ± 2.9%. When tested against *Pseudodactylogyrus*, 76 petroleum-ether extracts had median effective doses (ED50) of 2.88 and 0.72 mg/L, respectively, at 6.0 and 2.5 mg/L. [38]
18. ***Asparagus racemosus:*** a 5 mg/ml rhizome extract exhibited a 2.30 ± 0.29 h mortality time. Plant extract demonstrated mortality time (2.09 ± 0.05) h, etc., at a level of 10 mg/mL. [39]
19. ***Trifolium repens:*** An aerial shoot extract containing several chemicals, such as 1 mg/mL betulinic acid, 0.50 mg/mL ursolic acid, and 0.25 mg/mL biochanin A, was tested against the tapeworm *Hymenolepis diminuta*. The compound betulinic acid exhibited the greatest anthelmintic action among them, with a mortality time of 3.40 ± 0.66 hours. When tested against *Hymenolepis diminuta*, an aerial shoot extract at 200 and 500 mg/kg reduced the faecal egg by 47.72% and 54.59%, respectively. [40]
20. ***Ficus insipida:*** The latex was evaluated against the gills of *Colossoma macropomum*; the parasite was immobilized after 4 hours when treated with 250 µL/L of latex, and after 2 hours when treated with 500 µL/L. [41]
21. ***Cucurbita maxima:*** When the peel extract was tested at a concentration of 50 mg/mL against *Pheritima posthuma*, the earthworms became paralyzed in (90 ± 2) minutes and died in (11 ± 2) minutes. [42]
22. ***Trachyspermum ammi:*** The LC50 values for the aqueous and methanolic extracts, respectively, were determined to be 0.1698 and 0.1828 mg/mL.75In tests with GIT nematodes, the plant's seed extract shown effectiveness at a dose of 3 g/kg, which resulted in the greatest reduction in egg count. [43]
23. ***Syzygium aromaticum:*** The ethanolic extract, evaluated at 2.5 mg/mL against *Pheritma posthuma*, paralyzed the worm in 4.27 ± 0.25 minutes and killed it in 45.00 ± 2.00 minutes. At 5 mg/mL, paralysis happened in 2.43 ± 0.31 minutes and death happened in 35.05 ± 4.35 minutes.84 After 8 hours of treatment, ethanolic extract at 0.5 mg/mL demonstrated motility against *Cotylophoron cotylophorum* (86.27%). [44]
24. ***Withania somnifera:*** Crude extracted hydro-alcoholic solution was tested against Pheritima posthuma at dose concentrations of 20 and 40 mg/mL, paralysis was observed in (6.5 ± 0.5) and (2.8 ± 0.8) minutes, respectively, and death happened in (13.9 ± 1.2) and (7.1 ± 0.9) minutes. [45]
25. ***Trichilia claussenii*:** anthelmintic activity was tested against gastrointestinal nematodes; the leaves' methanol extract demonstrated a significant LC50 value of 263.8 µg/mL and LC99 value of 522.5 µg/mL. [46]

CONCLUTION:

The traditional usage of a large range of common medicinal plants is a well-known source of readily available and potent anthelmintic activity in many species. The current review of the literature shows that in order to find alternative phytochemicals that can take the place of synthetic drugs in the treatment of various parasitic infections and diseases, more molecular research on crude products, organic extracts, and various active components derived from plants is required.

Plant medicines are utilized as substitute techniques to manage livestock parasitism. Plant anthelmintics are effective in combating helminthes. Compared to chemical anthelmintics, there is less likelihood of resistance developing against phytoanthelmintics. Plant-based anthelmintics are safe, affordable, readily available, and beneficial for impoverished farmers and livestock rearers. They are also environmentally friendly and support biodiversity.

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