INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Review Article

A Comprehensive Study on Natural Remedies Against Helminth Infections

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ARTICLE INFO

Published: 31 Dec. 2024
Keywords:
Helminth Infection, Medicinal herb, Worm control, Natural Treatment, Herbalism, Anti-worm treatments.
DOI:
10.5281/zenodo.14582904

ABSTRACT

Medicinal herbs have been utilised for centuries to cure a range of diseases including helminth infections, which are still a global health problem. Helminth infections create a big health problem worldwide especially in poorer countries. This review focuses on how natural remedies from plant -based sources can replace standard anti-worm treatments .The study looks at the key ingredients how they work ,and how well many medicinal plants known to fight worms perform against helminths. It also takes depth about the good things about taking herbal medicines, like fewer side effects and better nutrition uptake. By examining the clinical proof and traditions around these treatments in areas where worm infections are common, the review shows how herbal medicine could play a role in today's healthcare.

INTRODUCTION

Phytomedicine is as old as human evolution, and it began with our ancestors trial or error. phytomedicine refers to the use of herb as treatment. Herbal medicine also known as phytotherapy, Herbalism or phytomedicine1.The science of plant based medications is known as phytomedicine.[1]The history of phytomedicine stretches back to 60,000years ago, written evidence dating back to around 5000years.Pharmaceuticals from medicinal plants resulted in the discovery of wonder chemicals that directly or indirectly relived mankind's illness.[2]Due to enhanced efficacy of herbal medicine has been seen as a viable future therapy for health care management. Recently there has been a shift in the global trend from synthetic to herbal treatment which is marketed as "return to nature .[3]The US Food and Drug Administration does not categorise phytomedicine as

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Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

pharmaceuticals instead available as over -the-counter nutritional supplements.[4]Taxol one of the finest herbal drugs ,has been found to treat refractory ovarian, breastcancer . Podopyllotoxin , alteration of this chemical resulted invention of etoposide which is effective against small cell malignancies of the lungs and testes.[5]Plant sulphur compounds hep to protect against cardiovascular disease by activating nuclear factor- erythroid factor 2 and preventing cholesterol formation but terpenoids diminish atherosclerotic lesions in the aortic valve.The field of phytomedicine has a promising future as it develops along side modern medical disciplines.[6]

Anthelmintics

Medicinal plants have been utilised to treat diseases and injuries since ancient times. Medicinal herbs have been used to treat parasites and illness in humans and animals. In 2015, world health organisation reported that roughly 1.5 billion people suffered from soil-transmitted helminthiasis.[7] Plants contain a wide range of medications including antispasmodics, emetics, anticancer, antibacterial, and anthelminthics. Many plants are believed to have antibacterial qualities and are commonly used by tribal communities worldwide. Nature has given the cure for all diseases in some form. Chemical anthelmintics losing popularity due to its disadvantages. WHO has recently estimated that 80% of populations of developing countries rely on traditional drugs ,for their primary health care needs.[8] Helminth infections are among most frequent illness in humans, affecting a sizable fraction of the global population. They constitute a significant public health risk contribute to prevalence of malnutrition, eosinophilia. [9] Anthelmintics are medications that kill or expel infesting helminths, they cause harm to the host by obstructing lymphatic or intestinal flow and secreting toxins. Helminthiasis is leading source of morbidity. Anthelminthics also called as endectocides and parasiticides a new class of anthelmintic named aminoacetonitrile developed which is well tolerated and has low toxicity to mammals.[10] The main species that infect people are the roundworms(Ascaris lumbricoides), the whipworm (trichuris trichuria) and hook worms(Necator americanus and Ancylostoma duodenale).[11]To treat helminthiasis, anthelmintic medications such as albendazole ,mebendazole ,ivermectin ,praziquantel used, these medications have side effects as hepatotoxicity.The continuous use of synthetic larvicidal/anthelmintic medications also producing drug resistance problem in various parasite illnesses. Plants are free of side effects with less effectiveness.[12]Helminthic diseases are typically chronic and debilitating ,leading to increased to increased morbidity and social suffering.Parasites are known to infect the livestock and crops ,used to control infection in food producing animals.Some anthelmintic medicines have a quick selective effect on nematode neuromuscular transmission, levamisole are agonist at nicotinic acetylcholine receptors in nematode muscle causing spastic paralysis Natural killer cells play a range of roles in parasite infection by secreting cytokines, primarily interferon gamma.[13]Traditional medicinal plants are used in the treatment of anthelmintics are pineapple, citrus indica, Ficus bengalensis.

Types Of Anthelmintic Drugs

Antiparasitic agents that specifically eliminate worms belonging to the genus Ascaris are referred to as ascaricides

- **Benzimidazoles:**
  - Examples:Albendazole,Mebendazole,Febendazole,Flubendazole,Triclabendazole
  - Mechanism:Inhibits microtubule polymerisation ,affecting cell division and glucose uptake in helminths, effective against threadworms, roundworms, tapeworms.
- **Tetrahydropyrimidine**

- Examples: Pyrantel, Oxantel
- Mechanism: Effective against nematode infections residing within the intestine ,Depolarize and paralyse the helminths by acting as cholinergic agonists.

➢ **Avermectin**

- Examples: Abamectin, Ivermectin
- Mechanism**:** Increase the permeability of cell membranes to chloride ions by attaching to glutamate- gated chloride channels, which makes the parasite to die.

➢ **Salicylanilides**

- Examples: Niclosamide
- Mechanism: Disrupt energy generation in cestodes by uncoupling oxidative phosphorylation, these are mitochondrial uncouplers used only for flatworms.

➢ **Isoquinoline -pyrazines**

- Examples: Praziquantel

Mechanism: Increase the sensitivity of helminth cell membranes to calcium, resulting in muscular spasm and paralysis, Effective against tapeworms (Schistosoma).

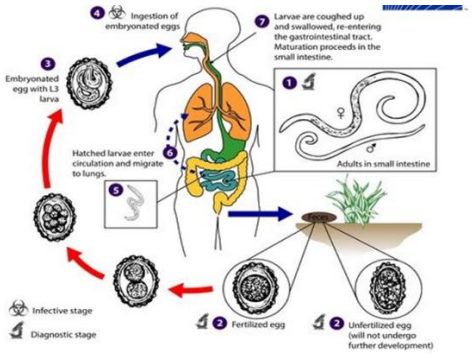
➢ **Imidazothiazoles**

- Examples: Levamisole
- Mechanism: They act as cholinergic agonists, activating nicotinic acetylcholine receptors and producing spastic paralysis in worm.

➢ **Pro-Biotics and Herbal Anthelmintics**

- Examples: Herbal extracts from Neem, Garlic, Pumpkin seeds

Mechanism: Disruption of metabolic process, paralysis and immune regulation.



Advantages Of Anthelmintic Medicinal Plants:

1. **Natural remedies** : These plants offer a safe alternative to pharmaceutical medications while minimising unwanted effects.
2. **Improved nutritional absorption** : These herbs improve gut health by removing parasites, allowing for increased nutritional absorption.
3. **Symptom relief :** They can help with symptoms of parasites infections including abdominal pain , diarrhoea, and feeling fatigued.
4. **Soil health** : They improve soil quality and can help manage pest populations naturally.
5. **Rich in compounds**: They contain bioactive compound that help eliminate parasitic infections effectively.
6. **Health maintenance**: Regular use of anthelmintic medicinal plants can play a role in maintaining overall health and preventing future infections.

Herbal Drugs Used To Treat Helminth Infection:

Botanical name	Local name	Family	Parts used	Chemical constituents	Infectious treatment	Reference
Carica papaya	Papaya	Caricaceae	Latex	Chymopapain, Papain	Earthworm	Lakshmi kanta kantal etal...[14]

Ociumum tenuiflorum	Tulsi	Lamiaceae	Leaves	Ursolic acid	Roundworm	Prakash pandey etal…[15]
Azadirachta indica	Neem	Meliaceae	Leaves and seed	Nimbin, Nimbidin	Round Worm	Kusum Lata etal...[16]
Cucurbita Pepo	Pumpkin	Cucurbitaceae	Seeds	Fatty acid, Palamitic, palamitoleic ,oleic,linnolei c acid	Nematodes	Maciej Grzybek etal…[17]
Curcuma caesia	Black haldi	Zingiberaceae	Rhizomes	Curcuminoids Volatile oils	Earth worms	Vineela chadalavada etal…[18]
Ananas comosus	Pineapple	Bromeliaceae	Fruits	Bromelain,phenolic compounds	Human whip worm	Juliana Azevedo dapaixao etal…[19]
Butea Monosperma	Palash	Fabaceae	seeds, barks	Flavonoids, quercetin kaempferol ,tannins	Round worm	Pooja saroj etal…[20]

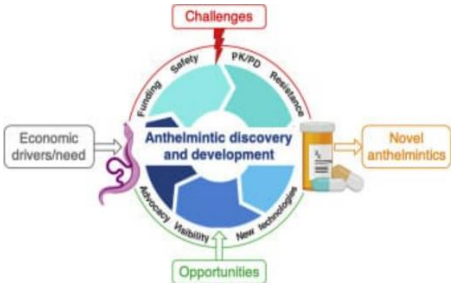
Fig 1 Carica papaya Fig 2 Ciumum tenuiflorum Fig 3 Azadirachta indica

Fig 4 Curcurbita pepo Fig 5 Curcuma caesia Fig 6 Ananas comosus

Fig 7 Butea Monosperma

Modern Drugs Used to Treat Helminths Infection:

Drug name	Mechanism of action	Worms	Route of administration	Side effects
Albendazole	The inhibitory action of tubulin polymerisation causes the loss of cytoplasmic microtubules	Roundworms Hook worms Threadworms Whipworm Pink worm Flukes	Oral route	Diarrhoea, Abdominal pain Migration
Mebandazole	The inhibitory action of tubulin polymerisation causes the loss of cytoplasmic microtubules	Nematodes	Oral route	Loss of appetite , Abdominalpain, Flatulence Diarrhea
Piperazine	Act as GABA agonist causing chloride channel opening neural hyperpolarization and flaccid paralysis of suspectable parasites	Roundworms **(**ascariasis**)** Pinworms	Oral route	Blurring of vision Clumsiness Crawling Joint pain Skin rash of itching
Ivermectin	Immobilizes infected organisms by causing tonic paralysis of parasites muscles through binding to the chloride ion channels of nerve or muscle cells	Threadworms (strongyloidiasis)	Oral parental	Irritation Headache Cellulitis Abdominal pain
Pyrantel	Nematode neuromuscular junctions are depolarized,resulting in paralysis	Roundworm Hookworm Pinworm	Oral route	vomiting Diarrohea , Loss of appetite ,stomach cramps



Anthelminthic Activity Of Various Medicinal Plants:

Carica papaya

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

The high concentration of vitamins A ,B ,and C, as well as proteolytic enzymes with antiviral, antifungal qualities like papain and chymopapain responsible for papaya's health advantages.[21]The leaves are traditionally used as a cardiotonic ,vermifuge and a therapy for dengue fever and

breast cancer.[22] Carpaine ,an alkaloid, is present in young leaves. Myrosinase, glycosides are found in seeds.[23]

Antiparasitic activity

Papaya latex was examined next to heligmosomoides polygyrus infection in mice, showed signs of antiparasitic properties.[24]

Allium Sativum

- **Common name:** Garlic
- **Active principle:**

Allicin(diallylthiosulfinate),Allin

- **Plants parts used:**Leaves,Roots

It contains 17 aminoacids, vitamins, minerals and 33 sulphur compounds. Garlic components have been identified as promising immune boosters, aids to trat neoplastic growth, rheumatism.The primary flavonoid that was separated from garlic quercetin, was found to interact with medications such as vitamin E and C .The pharmacological activities include anti-atherosclerotic,anti carcinogenic ,and antiviral. [25]

Antiparasitic Activity

Allium sativum oil has been shown to have anthelmintic properties, effectively eliminating harmful parasites from the intestine. [26] Garlic juices had antiparasitic effect invitro on the crustacean parasite. [27]

Terminal Arjuna

- **Common name:** Arjuna tree, Marudhu ,Arjan
- **Active principle:** Arjunic acid, luteolin ,Kaempferol
- **Plants parts used:** Leaves and bark

The bark powder helps as a diuretic for liver cirrhosis and relives symptoms of hypertension. It is a very good hypocholsteremic, Phytoconstituents like terpenoids mainly responsible for cardiovascular properties.The herb has shown to aid persiste smokers vasodilate their blood vessels and dissolve plaque in their arteries.[28]

Antiparasitic Activity

The effectiveness of arjuna bark against Haemonchus contortus eggs showed motility at various hours because of its efficacy, the lethal median concentration values for egg hatch was found to be 645.65ml.[29] The ethanol extract outperformed Albendazole in terms of paralytic and helmenthiatic effect due to increasing quantity of polyphenols in ethanol.[30] Against the common poultry parasite Ascaridia galli, Terminal arjuna, at concentratiomn of 100mg/ml shows the anthelmintic action.[31]

Datura Stramonium

- **Common name:**

Thorn apple, Jimsonwood, Devil' strumpet

- **Active principle**

: Hyoscyamie, Scopolamine, Apoatropine

- **Plants parts used:**

Leaves Datura is used to treat Parkinson's disease and haemorrhoids. Its leaves, when applied after roasting, can provide pain relief. The narcotic herb eases pain and aids healing.[32] Its ingestion produces distinct symptoms. The mouth gets dry, an intense thirst develops, vision blurs due to severe mydriasis and the pulse rate accelerates.This is followed by hallucinations, delirium and a lack of motor coordination, which may progess to command eventually death. Datura causes severe damage to central nervous system leading to un controlled mental state.[33]

Antiparasitic Activity

The methanolic extract of datura stomanium shows strong anthelmentic activity, achieving 100% inhibition of egg hatching and larvicidal activity at 25mg/ml, the effective dose for egg hatching inhibition shows promising results for controlling Haemonchus contortus.[34] Tropane alkaloids of datura stramonium interfere nervous system of Pheretima posthuma leading to paralysis and have saponin properties that can disrupt the cell membrane of parasites.[35]

Artimisia Absinthium

- **Common name:**Worm wood,Tethween

- **Active principle:**Caryophyllene,Artabin
- **Plants part used:**Aerial parts

It is utilised as anthelmintic and infect repellents as an additive source for ruminants, notably in stimulating the rumen fermentation .[36] Immuno-modulatory and wound-healing activities, neuroprotective and antidepressant effects, antioxidant activity, antitumer activity, hepatoprotective effects and antiprotozoal activity.[37]

Antiparasitic Activity

The ovicidal impact of wormwood and mallow aqueous extracts was evaluated using the invitro egg hatch test (EHT), which was then compared to the chemotherapeutic effect of the anthelmentic medication thiabendazole. [38] It effects angiogenesis, changing the host's immune response, creating mitocondrial malfunction, and interfering with parasite transport proteins. Arthemisinin is effective against a number parasites, including Leishmania, Trypanosoma and Haemonchus. Additionally, extracts from A.annua show test control action via changing the activities of digestive enzymes in pests.[39]

Eucalyptus

- **Common name:** Gum tree,Blue gum,Candle bark gum
- **Active principles:**Citronellal,limonene
- **Plants part used:**Bark, branchtips, fruits

Ethyl acetate extract from Eucalyptus Camaldulensis leaves has powerful antibacterial and anti-schistosomal properties, making it a potential treatment for human schistosomiasis infections.[40] Eucalyptol possesses antinoceptive characteristics,suggesting a possible calming and depressing effect on the central nervous system. It is used against periodontal disease, mouthwash applications and cough suppresants,Essential oil of eucalyptus having bio-nematicide efficacy , phytopathogen control and anthelmintic activity.[41]

Antiparasitic Activity

Essential oils at doses of 0.1and 0.2ml shows parasiticidal effects, Eucalyptus globules outperformed both anti-giardiasis and entoamoeba histolytica with mortality rates of 79.75 and 87.6% after 30 minutes.[42]Eucalyptus staigeriana essential oil invitro effects were established using the egg hatching test and suppression of larva development, shows efficacy against goat gastrointestinal nematodes was 76.57% at 15th day after the treatment.[43]

Calendula officinalis

- **Common name:** Marigold,Ruddles
- **Active principles:**Ubiquinone,Cubenol
- **Plants part used:**Flowers,Leaves,seeds

Calendula treats internal organ inflammations, gastric ulcers, menstrual abnormalities and oropharyngeal mucosal inflammations.It has a significant commercial value as a herbal remedy and has been used in cosmetics, fragrances, dyes, pharmaceutical preparations and food goods for ages. The plant has been approved for food usage and appears on the FDA's list of generally recognised as safe [GRAS] chemicals. Calendula oil is still medicinally used as an anti tumor agent. [44] An infusion of calendula officinalis may also be used to treat bee stings, herbalism, calendula solution or tincture is applied topically to treat acne, reduce inflammation, stop bleeding and soothe inflamed tissue. Calendula protects against the plague. [45]

Antiparasitic Activity

Oleanolic acid glycosides hindered the development of L3 Helignosomoides poly girus larvae, the nematode's infective stage. Furthermore, both oleanolic acid and its glycosides lowered L3 survival rates after prolonged storage, but only oleanolic acid glucuronides had an effect on nematode infection.[46]The current investigation indicated the efficacy of powdered C.officinalis and S.hortensis aerial parts against intestinal parasites in pigs when supplied at dosage of 140 mg/kg/day

and 100 mg/kg/day, respectively, during a 10-day period. The coproparasitological examination showed co-infections with protozoa and nematodes. Six species pf disgestive parasites were diagnosed: Ascaris suum, Trichuris suis, Oesophagostomum.[47]

Mentha Spicata

- **Common name:** Spearmint,Lambmint
- **Active principle:**Menthol,Menthone ,Pulegone
- **Plant parts used:**Leaves, Flowers ,Barks,Seeds

Approximately 3000EOs, 300 are utilised for perfusion, sanitory, cosmetic, food, pharmaceutical and agricultural applications.[48] Spearmint is an aromatic plant used as seasoning and flavouring herb. Spearmint and spearmint extracts are frequently employed as preservation agents to postpone the oxidative degradation that happens in food during processing or over time during storage . The menthol extract showed inhibitory activity on exocytosis in antigen-stimulated rat basophils due to sideritifladone showed the strongest activity.[49]

Antiparasitic Activity

Mentha spicata essential oils have also been studied for their antiparasitic properties in treating ectoparasites such as lies and mites are used in topical treatment in reducing infestations without severe side effects .[50] Mentha spicata extract has anthelmentic action against sheep gastrointestinal helminth eggs.At 80 mg/mL, the extract reduced egg hatching by upto 79%. Phytochemical study showed the presence of phenols . Mentha spicata essential oil has been shown to have high fumigation efficacy against a variety of pests, including mosquitos (Aedes aegypti and Anopheles stephensi) and agricultural pests (Helicoverpa aremigera, Plutella xylostella). [51]

Chicorium Intybus

- **Common name:** Chicory, Chikkari
- **Active principles:** Sesquiterpene, Lactones ,ferrulic acid
- **Plant parts used:** Roots, Buds, Leaves

Beekhe Kasni (Cichorium intybus) is a medicinal and culinary herb that has been used in traditional medicine for many year. The versatile plant is strong in protein, carbs and minerals.[52] Inulin from chicory roots is considered a functional food elements since it impacts physiology and biochemical processes, resulting in greater health and lowering the risk of numerous diseases. It has been discovered to have enormous pharmacological potential and tremendous possibility for phytochemical research. The chemical elements and their application, inulin, sesquiterpene lactones, phenolics , such as caffeic acid , chichoric acid, and coumarines as well as esculetin and cichoriin, two novel triterpenoids with good alpha glucosidase inhibitory action. The plant possesses significant hypoglycemic, hepatoprotective, antioxidant, and immunomodulatory potential. [53]

Antiparasitic Activity

When ruminants are fed diets high in chicory (> 70 of the diet consisting of chicory DM), the bioactive forage chicory has been shown to have antiparasitic effects.[54] Its bioactive components, especially sesquiterene lactones which have been shown to have strong effect against helminths and protozoa in vitro, are probably responsible for this antiparasitic activity.[55] Extracts from chicory root pulp that have low toxicity to mammalian cells and selective anthelmintic activity against C. Elegans and A.suum in vitro. Furthermore, a few of the tested forage chicory extracts demonstrated reduced toxicity in mammalian cellwhile remaining active against A. Suum. When compared to forage chicory extracts, untargeted metabolomics showed that the profile of sesquiterene lactones in chicory root pulp was significantly different. [56]

Black Walnut

- **Common name:** Juglans nigra
- **Active principles:** Ellagic acid , flavonoids , phenolic compounds, tannins
- **Plant parts used:** Wood, nots, bark, flower

Kernel extracts from various black walnut cultivars shown antimicrobial action . Green husk extracts shown considerable antifungal efficacy in female rats. The bark extract demonstrated neuroprotective effects in a rat model of cerebral ischaemia by restoring mitochondrial function.[57] Walnuts oil is considered a prominent ingredient in antiwrinkle, antiaging , and dry skin cream treatments since it has a moisturising ability.[58]

Antiparasitic Activity

Crude ethanolic extract (CEE) made from juglans regia leaves has anthekmintic properties against Ascaridia galli (A.galli), one of the most harmful nematode parasites that impact poultry. At 24 hours after exposure, CEE caused a 96.5% suppression of worm motility.[59] Juglans regia (English walnut) has proven that methanolic extracts can produce paralysis and death in worms, such as Pheretima posthuma, more quickly thand traditional therapies like piperazine citrate.[60]

Cucurbita Maxima

- **Common name:** Gaint pumpkin
- **Active principles:** Fatty acids, phenolic and flavonoids , vitamins and minerals
- **Plant parts used:** seeds, pulp and fruit stalk

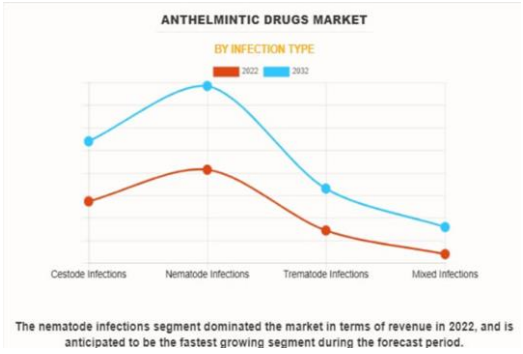
The CNS stimulant activity of crude drug extract was assessed in swiss Albino mice . The results indicated that petroleum ether extract had a good CNS stimulant effect that may be investigated for therapeutic usage.[61] The analgesic and anti-inflammatory properties of an ethanol extract of cucurbita maxima (C. maxima) and Cucumis sativus (C. sativus) seeds. These seeds are edible , have a pleasant taste, and have been utilised for a variety of therapeutic purposes.[62]

Antiparasitic activity

In rats , pumpkin seed extracts in both water and and ethanol shown strong anthelmintic activity (81 and 85% respectively) against Aspiculuris tetraptera pumpkin seeds (C. maxima lam) have an anthelmintics action and are used to treat a variety of parasite illnesses, taenia saginata.[63] When compared to the infection control group and the praziquantel group, the aqueous extract of pumpkin seeds significantly decreased the quantity and length of adult hymenolepis nana worms as well as the number and viability of eggs. It has been demonstrated that pumpkin seed aqueous extract works well as a natural anthelmintic against hymenolepis nana.[64]

Herbal Drugs Available in Market:

Herbal medicine	Treatment Condition	Plant source
Valerian	Insomnia	Valeriana officinalis
Paclitaxel	Anti-cancer Drug	Yew Tree Taxus
Cinnamon	Lowering blood pressure	Cinnamomum verum
Capsaicin	Pain relief	Capsicum annum
Metformin	Type -2 diabetes	Galega officinalis



Recent Advances In Usage Of Herbal Drugs In Anthelmintic Activity:

The increase of resistance to traditional anthelmintic medications has led to the research of alternative treatments such as herbal drugs.[65] Recent investigations have revealed many plant based substance with promising anthelmintic effects.[66]For instance, A study demonstrated clove oil has ability to treatment of parasite diseases in poultry due to the bioactive components present in it.[67]Neem oil extracts have shown promise by effectively lowering parasite infections in both human and animals.[68]Turmeric's active components ,particularly curcumin , have been examined for their ability to prevent parasite growth.[69]Field trials were also carried out to examine the efficacy of these medications in real-world conditions. Extensive clinical trials are necessary to validate the safety and efficacy of herbal drugs in human and veterinary applications.[70] These developments demonstrate how herbal medications may be used to combat the worldwide helminth infection burden and get overcome the difficulties caused by drug resistance.

CONCLUSION:

Medicinal plants have treated various illnesses for many years, including helminth infections remain a major health issue worldwide. They create a big health problem in developing nations. This review focuses on how natural remedies from plant-based sources can replace standard anti-worm treatments. The study looks at the key ingredients how they work, and how well many medicinal plants known to fight worms perform against helminths. It also talks in depth about the good things about taking herbal medicines, like fewer side effects and better nutrient uptake. By examining the clinical proof and traditions around these treatments in areas where worm infections are common, the review shows how herbal medicine could play a role in today's healthcare.

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HOW TO CITE: Jukanti Narsing Rao Srilatha*, S. Pradesha, Ancha Dheeraja, Kalal Pavan Goud, Mohammad Faiza Begum, Sonalin Sahoo, A Comprehensive Study on Natural Remedies Against Helminth Infections, Int. J. of Pharm. Sci., 2024, Vol 2, Issue 12, 3506-3520. https://doi.org/10.5281/zenodo.14582904