Journal of Life and Social Sciences
eISSN: 3006-2675
www.bbasrjlifess.com
*J. Life Soc. Sci, 2024; Volume, **3**: 21*

Review *Article* ***Open Access***

ANTI-PARASITIC ACTIVITIES OF MEDICINAL PLANTS

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(Received, 19th January 2023, Revised 18th March 2024, Published 26th March 2024)

Abstract *Medicinal plants have been used locally all over the world due to their availability, accessibility, affordability, and their antiparasitic properties. Several types of medicinal plants have been used due to their activities against protozoans and helminths. Parasitic diseases are one of the major public health problems. More than three billion cases of parasitic diseases are reported yearly worldwide. This review focuses on various medicinal plants with antiparasitic properties due to their specific mode of action and their efficacy against protozoans and helminths. In most circumstances, parasites become resistant to vaccines and other therapeutics, so medicinal plants play a crucial role against parasites. These medicinal plants with antiparasitic activities due to their secondary metabolites have been studied under controlled experiments. There should be an advanced assessment of medicinal plants for their use in pharmaceutics. Further studies are needed to understand the active ingredients of medicinal plants and their antiparasitic activities.*

*[Citation: Saqlain, M., Wasif, Z., Ali, Q., Hayat, S. (2024). Anti-parasitic activities of medicinal plants. J. Life Soc. Sci, **2024**: 21]*

Keywords: *Anti-parasitic; helminths; protozoans; medicinal plants; secondary metabolites; extract; active ingredients; herbal products*

Introduction

Since the dawn of human civilization, medicinal plants have been widely identified and historically used globally. The ancient Indian mythologies, the Rig-veda and Athar-veda, had previously referenced several plants exhibiting various healing features; as a result, the origins of the usage of medicinal plants throughout India go as far as 3500–1800 B.C. These medicinal herbs have active ingredients that are extremely effective towards parasites (Bauri et al., 2015). Humans and animals are subject to significant health risks and financial losses due to parasites (Kigondu et al., 2009). Throughout history, people have relied on plants for medicinal uses. In many regions around the globe, medicinal plants continue to be applied for this objective despite being used this significance for generations to fight parasites. While most of the information about the antiparasitic properties of medicinal plants was anecdotal and lacked a rigorous scientific basis until somewhat recently, there are now a growing number of controlled laboratory investigations aiming to confirm and quantify plant activities (Wink, 2012). The dried blossom and leaf parts of the Cassia auriculata plant were utilized for medical purposes by the tribal inhabitants of in Chittor district of Andhra Pradesh, India, to cure diseases of the skin, conjunctivitis, asthma, and kidney ailments. Hexane and methanol extracts of the flowers exhibited antibacterial action, whereas the methanol extracts showed larvicidal effects towards *Culex tritaeniorhynchus* along with *Anopheles subpictus. Tinea versicolor*, ringworm, and skin conditions have all been treated using the root along with the entire plant of *Rhinacanthus nasutus*. *C. tritaeniorhynchus*, *A. gossypii* and, and A. subpictus were susceptible to larvicidal and nymphicidal effects from the leaf extracts of methanol, chloroform, and ethyl acetate. The *leaf methanol extract controlled the Aedes aegypti, Spodoptera litura, and Culex quinquefasciatus larvae well* (Bauri et al., 2015). Tropical indigenous communities in rural areas treat protozoans, and helminths, along with other parasitic disorders, with herbal medications. Most herbal remedies' effectiveness, dose, safety, and active ingredients are unknown. A wide variety of parasites can exploit us as their hosts have emerged throughout the evolution of humans. Typically, a parasite won't instantly kill its host because doing so would be an evolutionary

ending for the parasite. Most parasites still make our lives unpleasant or impair our health. But when patients aren't provided with proper treatments, some parasitic illnesses, like trypanosomiasis and malaria, might be fatal (Kamaraj et al., 2010).

The spread of parasites among humans is frequently assisted by the fact that people typically coexist in close quarters and frequently lack access to clean water and sanitation facilities. It is quite probable that parasite control has always been a priority for humans. Ectoparasites (external parasite) can be manually reduced or removed. An individual or a group may accomplish this. Internal parasites, also called end parasites, had been more challenging to cure. We know that for many thousands of years, people have been employing medicinal plants to treat diseases and other health issues. It's probable that human beings also discovered plants that had effective antiparasitic remedies (Cock et al., 2018). Nowadays, secondary metabolites extracted from plants and plant products are frequently used to treat parasitic infestations. Besides, parasite infections are frequently treated with traditional treatments, because of either economic reasons or an absence of treatments in poor nations but their presence is unreported. The seek for anti-parasitic extracts of plants or secondary metabolites produced from them can substitute synthetic medications. The use of natural substances in therapy remains significant; from 1981 until 2006, 1,184 novel medications received FDA approval, 28% of which were made from plants and derivatives of them. Most pharmacophores (functional groups with pharmacological activity) comprising 24% of the novel medications came from natural sources. The traditional medicinal plants utilized for relieving diseases, such as those from America, Africa, and Asia, could make an excellent place to start looking for antiparasitic natural products (Wink, 2012).

Activity of medicinal plants against Protozoans

Plant extracts provide exciting possibilities to create new effective chemicals against protozoans. Numerous pharmacological medications have been developed due to plants' enormous chemical diversity and variety of bioactivities (Luize et al., 2005). Numerous studies conducted in several countries, particularly Argentina, Brazil, Bolivia, Colombia and Mexico, have revealed that many plants are active against T. cruzi, Leishmania, and other protozoans. While it is false to believe that herbal medicines are completely risk-free and without side effects, phytotherapeutic substances have fewer unwanted effects than synthetic pharmaceuticals. The demand for herbal medications has grown over the past 15 years in developed and developing countries. Due to its extensive flora and cultural traditions; Brazil commonly uses plants for the treatment of common diseases using crude extracts, infusions, or plasters. The antibacterial properties of several of these medicines have not yet been confirmed by experimental scientific studies (Acevedo-Rodríguez and Strong, 2012; Luize et al., 2005)

The effects of Thai medicinal plants on *Blastocystis hominis*

The most prevalent protozoan parasite found in the human intestine is *Blastocystis hominis*. When numerous identification methods are utilized, the incidence in some parts of the world, particularly Thailand, can reach 40% or even more. *Blastocystis hominis* has been linked by numerous researchers to serious intestinal problems. People in underdeveloped nations frequently employ medicinal plants as they are secure, widely accessible, inexpensive, and simple. In this study, extracts of *Amaranthus spinosus L.* (*Amaranthaceae*) entire plant, *Brucea javanica (L.) Merr.* (*Simaroubaceae*) seed, *Piper longum L.* (*Piperaceae*) fruit, and *Quercus infectoria Oliv*, (*Fagaceae*) nut gall were examined for their impact on the proliferation in vitro of *Blastocystis hominis*. While the in vitro tests could not always be directly related to vivo studies, they are nevertheless a crucial method for activity screening that might offer the public a solid foundation for more effective basic healthcare in the community. According to this study, several extracts of Thai medicinal plants may be useful as treatments for *Blastocystis hominis*. Patients never exhibit symptoms when just a small number of *Blastocystis hominis* exist, even though some extracts minimally suppress the growth of the organisms. This indicates that they may be useful in reducing infection (Sawangjaroen and Sawangjaroen, 2005).

Anti-malarial activity

More than a third of the world's population roughly two billion people, live in places where malaria is prevalent, making it among the most significant parasite diseases in tropical regions. The methanol extracts of *Crotalaria mucronata*, *Pseudocedrela kotschyi*, and chloroform extract of *Launaea taraxacifolia* exhibited > 50% reduction in growth against the chloroquine-sensitive (D6) strain of *P. falciparum* reaching values of 52%, 60%, and 73% respectively. Extracts from those three plants have been examined yet again. At IC50 (g/mL) values of 46.5 and 21.6, respectively, the methanol extracts of *Pseudocedrela kotschyi* and *Crotalaria mucronata* showed effectiveness against a chloroquine-sensitive strain of *Plasmodium falciparum*. With IC50 (g/mL) values of 46.8 and 18.0, it exhibited efficacy against *P. falciparum* isolates that were resistant to chloroquine. Having IC50 (g/mL) values of 29.7 and 22.9 (S.I > 2.2 and > 2.6), the chloroform extract of *Launaea taraxicifolia* showed antimalarial efficacy towards chloroquine-resistant strains of *P. falciparum* as well chloroquine-sensitive strains of *P. falciparum* (Bello et al., 2017). There are numerous naturally occurring, semi-synthetic, and synthetic medications for malaria available. For instance, the antimalarial drug chloroquine acts as a synthetic version of quinine. In addition, *Artemisia annua*. is the source of the antimalarial drug artemisinin and its derivative,

artesunate, which contains a sesquiterpene lactone backbone *A. annua* has historically been used in China to cleanse the blood and reduce fever. Despite the remarkable results of the combination therapy with artemisinin against malaria, the lack of available medications calls for innovative therapies. In numerous instances, resistance to drugs is the main problem, and new treatments are being suggested to combat it. The study covers some significant genera in this domain in addition to conventional medicines, such as cryptolepis, cinchona, artemisiaand, and tabebuia, whose antimalarial actions have been thoroughly studied (Mohammadi et al., 2020).

Anti-Trypanosoma activity

Human African trypanosomiasis is a neglected tropical illness with a challenging clinical appearance, diagnosis, and therapy. The medications that are now used to treat trypanosomiasis are outdated, costly, and are not as effective. They are also linked to serious side effects and the issue of drug resistance. This circumstance highlights the urgent need to create novel, efficient, affordable, and secure medications to cure trypanosomiasis. This study uses herbal medicines as the foundation for searching for novel antitrypanosomal drugs. 36 plant extracts of ten plant species used in Nigerian ethnomedicine were tested in vitro for their ability to inhibit the growth of the bloodstream strain of *Trypanosoma brucei rhodesiense* STIB 900. It was discovered that mammalian L6 cells were cytotoxic. Antitrypanosomal and toxicity endpoints were measured using the Alamar blue assay. *Ocimum gratissimum* Linn. (*Labiatae*) leaf extracts in ethyl acetate had the best antitrypanosomal activity (IC50 of 2.08 0.01 g/ml), having a high selectivity index of 29. In addition, the ethyl acetate, methanol and hexane, extracts of, *Jatropha curcas* Linn. (*Euphorbiaceae*), *Terminalia catappa* Linn. (*Combretaceae*), *Trema orientalis* (L.) (*Ulmaceae)*, and *Vitex doniana* (*Verbenaceae*), *Pericopsis laxiflora* exhibited astounding antitrypanosomal activity (IC50 2.1-17.2 µg/ml) with a high specificity index (20-80) for the trypanosomes. For the extremely first time in Nigerian ethnomedicine, *T. catappa*, and T. orientalis, have been shown to have antitrypanosomal activity towards *T. brucei rhodesiense* (STIB 900), suggesting that they may one day serve as sources of antitrypanosomal synthetic substances (Abiodun et al., 2012).

The plant's methanol extract has been found to have antiprotozoal effectiveness in vitro against Trypanosoma, Plasmodium, and Leishmania with noticeably low IC50 values. Traditional healers in Saudi Arabia utilize *Lycium shawii*, also known as "Gul Gaider," to cure hypertension and diabetes. *In tests, lycium shawii extract has been shown to have antiplasmodial, hypoglycemic, and* antitrypanosomal action (Al Nasr et al., 2016).

Anti-leishmanial activity

The *Allium sativum*, *Achillea mille folium*, *Artemisia species*, *Thymus vulgaris*and, and *Peganum harmala* became the most often utilized Iranian plants for anti-leishmanial activities. The current systematic and meta-analysis study offers important details regarding herbal combination therapy, experimental and clinical studies, and natural substances with anti-Leishmania activities. *Allium sativum* (garlic extract) has been shown to have leishmanicidal efficacy against *L. major* illness, causing a Th1-type response, stimulating the synthesis of INF- and NO in macrophages, and inhibiting the spread of the infestation (Soosaraei et al., 2017).

The previously discussed natural compounds can be used as a foundation for developing and researching new immunity medicines or as natural immune-modulating agents in cooperation and combination with existing treatments to increase therapeutic efficacy and decrease toxicity. A possible solution to problems with the present therapies is to target anti-leishmanial medications to macrophages using drug delivery mechanisms (Soosaraei et al., 2017).

Effects of medicinal plants essential oils on *Giardia lamblia* and *E. histolytica*

The two parasitic protozoans *Giardia lamblia* and *E. histolytica* are thought to be the primary causes of diarrhoea worldwide, although infection rates differ. These types of parasites are more prevalent in tropical areas, areas with a high population, and areas with few health facilities (Azadbakht et al., 2020). Concerning that fact, numerous artificial and organic substances underwent experimental as well as clinical studies. The anti-parasitic potential of different medicinal plants has been studied in the past. To treat *G. lamblia* and E. histolytica trophozoites in vitro, methanol extract of Helianthemum glomeratum, Cuphea pinetorum, and *Rubus coriifolius* exhibited appropriate results. Kaempferol and quercetin components of *Cuphea pinetorum* were thought to be responsible for its great effectiveness. Dichloromethane/methanol extract of *Geranium mexicanum* root was efficient on *G. lamblia* at 100 µg/mL while *E. histolytica* at the amount of 79.2 µg/mL because of the flavonoid compounds, β-sitosterol 3-O-βglucopyranoside and also tyramine; whereas *Chiranthodendron pentadactylon, Punica granatum*, and *Annona cherimola* displayed appropriate effects on *E. histolytica* with an IC50. Although there have been several studies on the anti-parasitic properties of medicinal herbs, the primary issues have been a lack of the availability of some plants, attention problems, and time restrictions. Numerous studies have documented the effectiveness of natural ingredients in treating parasite illnesses. The metabolite of *A. sieberi, A. sativum, butyric aldehyde, C. botrys, E. globulus, Z. multiflora* have all been indicated to be responsible for their parasiticidal action, and a variety of research showed their antimicrobial and aseptic impacts. In the current study, *G. lamblia* cysts and *E. histolytica* trophozoites

were exposed to five different essential oils. Of these, *E. globulus* had the best inhibitory impact on both protozoa and is therefore recommended as an adjuvant treatment to be used with chemical medications (Azadbakht et al., 2020).

Anti-Toxoplasma effects

Toxoplasma gondii is a parasitic protozoan illness that causes toxoplasmosis, which affects people worldwide. When an immunocompromised person contracts, they may experience more severe symptoms that could be fatal. People employ traditional medicinal plants to treat a wide range of parasite diseases. The present study offers fresh perspectives on several medicinal plants that have historically been used to treat toxoplasmosis along with other parasitic illnesses and may be helpful as an alternate method of treating *Toxoplasma gondii* infection (Al Nasr et al., 2016). Curcuma longa alcohol extracts have been identified to have strong anti-Toxoplasma efficacy in a mouse model as displayed by 98.6% and 99.2% reductions in the growth of Toxoplasma tachyzoites with 100 and 200 mg/kg/d doses, respectively. Tachyzoites' growth was inhibited in mice with 53.5%, 50.0%, and 48.0%, respectively, when mice were given water extracts of Juniperus procera's fruits, leaves, and stems (400 mg/kg/d). At a dosage of 156 ng/mL in vitro, ethanol extracts of *Sophora flavescens* and *Torilis japonica* were reported to suppress *T. gondii* growth by 99.3% and 98.7%, respectively. With IC50 values of 1.125 g/mL and 1.375 g/mL, respectively, two active fraction of *Eurycoma longifolia* root extracts TAF355 and TAF401 are found to have considerable anti-Toxoplasma activity (Al Nasr et al., 2016).

Anti-Cryptosporidium activity

In patients with healthy immune systems, cryptosporidiosis is a self-limiting infection, however, in those with weakened immune systems, it can be fatal. There are no publicly available effective medications for full healing. Others who used azithromycin and nitrazoxamide had encouraging results, while others utilized paromomycin. Medical plants are a type of natural treatment that is becoming increasingly important globally. According to research on the impact of plant extracts on mouse oocyst shedding, mice affected with Cryptosporidium shed fewer oocysts when given 250 mg/kg body weight of various plant extracts, showing a significant change in oocyst number during pre and post-treatment (p<0.05). *Punica gramenatum* had the second-highest efficacy (66.7%), after *Prosopis farcta* (70.9%), while *Olea europea* had the lowest (34.5%).

Anti-*Trichomonas vaginalis* activity

There are 75 genera in the *Amaryllidaceae* family, mostly bulbous flowering plants. The main chemical components of this family are allyl sulphides. Anti-trichomonas efficacy has been tested on several plants in this family. *Allium sativum* (garlic) hydroalcoholic extract was found to have anti-trichomonas active qualities. *Trichomonas vaginalis* growth is inhibited by *A. hirtifolium* hydroalcoholic and dichloromethane extracts at small amounts over brief intervals. *Trichomonas vaginalis* proliferation was observed to be inhibited by dichloromethane extract, which also had a stronger minimum inhibitory concentration, or MIC, value than hydroalcoholic extract. Substantial anti-trichomonas action has been demonstrated in two separate alkaloids and the *Hippeastrum breviflorum* extract. Significant alkaloids that appear and to contribute to *H. breviflorum's* anti-trichomonas activities are lycorine and lycosinine (Mehriardestani et al., 2017).

Babesia gibsoni

The antibacterial action of brucine A, a naturally occurring quassinoid substance isolated from the dried fruit of *Brucea javanica* (L.), was examined both in vitro and in vivo. When compared to the usual antimaterial medication diminazen aceturate, brucine A suppressed the proliferation of *Babesia gibsoni* in canine erythrocytes in vitro with a lower dose and terminated the parasites in 24 hours at a dose of 25 nM. A dog with adequate haematological and biochemical blood values showed no clinical signs after receiving brucine A orally at a dose of 6.4 mg/kg/day for five days. Three dogs got infected by *B. gibsoni*, while two of them received brucine A treatment for six days starting on the fifth post-infection day with a dose of 6.4 mg/kg/day. The classic acute babesiosis symptoms, such as severe anaemia, a high temperature, and a total loss of appetite and activity, manifested among untreated dogs. Despite there was not a full removal of parasites to the peripheral blood while there were decreases in packed cell volume, erythrocyte and platelet counts, the two bruceine A-treated dogs continued to be healthy throughout the 4-week experiment. The above findings imply that bruceine A or other comparable compounds are possible options to consider in the treatment of canine babesiosis because natural quassinoid chemicals have been utilized as traditional remedies for a variety of illnesses, including cancer as well as malaria (Ryo et al., 2009).

Anti-Coccidial activity

Seven different types of protozoa from the *Eimeria* produce the disease that has an enormous financial effect on the chicken business. The search for new and alternative means of control has been sparked by the detrimental impact of coccidiosis on the health and productivity of poultry and the growing issues linked to drug resistance. The current study assesses the anticoccidial action of curcumin (*diferuloylmethane*). This naturally occurring polyphenolic chemical is present in high concentrations in the rhizome of the perennial herb turmeric (*Curcuma longa*), which can be utilized as a spicy and food colourant in sauces and as medicine. On *Eimeria tenella* sporozoites, the impacts were assessed in terms of morphological changes, sporozoite vitality, and infectivity to Madin-Darby bovine kidney (MDBK) cells (Khalafalla et al.,

2011). The sporozoites' morphological changes were noted as distortion brought on by swelling and ridges in the cell membrane. Lesser curcumin doses (6.25 and 12.5 M) were ineffective. Still, higher concentrations (25, 50, 100, 200, and 400 M) had a significant impact on sporozoite shape along with survival in a dose-dependent way following incubating over 3, 6, 18, and 24 h. At curcumin doses of 100 and 200 M, sporozoite infectiousness anddecreased to 41.6% and 72.8%, respectively, in contrast to the control group without treatment. Curcumin did not have any adverse impacts on MDBK cells at such doses, but it was lethal to the cells at 1,800, 600, and 400 M, which impacted cell growth. Curcumin caused morphological alterations, decreased sporozoite vitality, and decreased infectivity on *E. tenella* sporozoites in vitro, showing a clear inhibitory impact (Khalafalla et al., 2011).

Anti- *Theileria lestoquardi* activity

Wild and domesticated animals have been affected by Theileria species in tropical and subtropical areas of the globe. While little information is available about ovine theileriosis, bovine theileriosis in cattle has been thoroughly examined. Theileria spp. infected sheep have attracted attention lately. Chemotherapeutic medicines are used to treat theileriosis but are exceedingly expensive and frequently unavailable in developing nations. Therefore, this study aims to find new medicinal plants for treating the condition (Farah et al., 2012). *Theileria lestoquardi* was the target of the current research's in vitro testing of *Gardenia ternifolia* fruit aqueous extract. Using Ficoll-paque, *T. lestoquardi* infected lymphocyte cells were recovered to heparinized blood. Such cells were constantly subcultured and cultured in minimal essential medium until phase 8, which was employed for the test. It was done to screen the plant extract with a 6-well plate. Through the use of an indirect fluorescent antibody test, a parasite was located. The research revealed that the plant extract's vitro activity towards *T. lestoquardi* macroschizonts was 0% at a concentration of 250 ppm, but significantly (p<0.05) rose at concentrations of 500, 5000, and 10000 ppm, where it was 13, 40, and 60%, respectively. The 50% as well 99% lethal doses (LC50 and LC99), respectively, consisted of 6745.28 and 177010.90 ppm. The extract substantially (p<0.05) lowered the mean number of functional cells at 500, 5000, and 10,000 ppm, the mean number of macroschizonts per cell, and the mean number of cells dividing. The maximum concentration of lymphoblast cells having vacuolated cytoplasm appeared visible under a microscope. It has been determined the plant extracts exhibit significant anti-*T. lestoquardi* action. It is advised that more in vivo research be done to determine the effectiveness of plant extracts in treating malignant ovine theileriosis (Farah et al., 2012).

Anti-parasitic activity of turmeric

Babesia and Theileria are parasites spread by ticks that cause significant financial losses for the livestock sector and international trade in animals. Present anti-piroplasm medications have a history of parasite resistance along with host harm. Novel medications could come from plants. To discover new anti-piroplasm therapies that are both efficient and secure, a fresh approach should be adopted. In the current study, we assessed the impact of methanolic turmeric (Curcuma longa) extract in the in vitro development of *B. caballi*, *B. divergens*, *Babesia (B.) bovis*, and *Theileria (T.) equi*. A fluorescent test was used to evaluate turmeric's in vitro suppressive potency. Utilizing in vitro cultures of various piroplasm parasites, researchers looked into the improvement in turmeric's in vitro inhibitory activity when administered together with diminazene aceturate (DA). Having IC50 values of 0.830 0.078, 0.375 0.055, 1.405 0.575, and 0.720 0.090 mg/mL, correspondingly, turmeric inhibited the in vitro proliferation of *B. caballi*, *B. bovis*, *T. equi*, and *B. divergens*. Turmeric at concentrations of 1 mg/mL for *B. bovis*, 0.5 mg/mL for *B. divergens*, 1 mg/mL for *T. equi*, and 0.5 mg/mL for *B. caballi* each inhibited parasite development by 73.43%, 80.065%, 73.47%, and 47.375%, respectively. Turmeric's in vitro inhibiting effect on cattle Babesia and horse Babesia/Theileria parasites was enhanced when coupled with DA. These results suggest that turmeric in a methanolic extract can be an attractive medicinal plant to use in the treatment of babesiosis, particularly when combined with DA (Rizk et al., 2021).

Effect of medicinal plants against different microorganisms

Balantidium coli

The typical host can transmit zoonotic infection balantidiosis to humans through the fecal-oral pathway. For centuries, herbal medicines have been used to treat human parasite infections and may be useful in reducing the emergence of resistance (Al-Hilfi et al., 2021). Lemon and mint are therapeutic herbs that contain a variety of powerful chemicals, including oils which are helpful against a variety of infections, like the *Balantidium coliparasite*. For the goal of the separation and purification of lemon and mint oils via thin-layer chromatography (TLC), a crude hexane extract of lemon peels and the leaves of mint was made in the current work, and the flow coefficient was calculated for each oil individually. In a water agar medium, the efficiency of pure oils against parasitic *Balantidium coli* was evaluated. Page solutions were put into the medium to activate the oils' effects. Results indicated that lemon oil was significantly more efficient towards the parasite after four days than peppermint oil and the drug albendazole. Because of the financial and health problems associated with parasite infection, and the quantity of chemical drugs used to treat these parasites, plant-based drugs have not received the same level of research and focus as synthetic drugs.

To determine the extent of lemon along with mint extracts' efficiency against the parasite, this research tested their anti-parasitic efficacy in vivo (Al-Hilfi et al., 2021).

helminths

Infection with helminths is primarily a health issue connected to the human-animal food system. Human faeces contain parasite eggs that pollute the soil in which they develop and are then ingested by humans through contaminated food and water. This builds up a vicious cycle of repeated infections, which is frequently challenging to stop or break. Helminthiases can appear clinically either intestinal (hookworms, intestinal roundworms, and whipworms,) or tissue (tissue roundworms, hydatid tapeworms and trematodes,) parasites depending on where the adult parasite is located in the body (Jato et al., 2022).

lungworm

The entire numbers of abomasal helminths were discovered considerably lower in the sheep grazing on this kind of plant, suggesting that animals feeding on chicory have a lower risk of intestinal nematode infections. The plant's anthelmintic properties are linked to the presence of sesquiterpene lactones and condensed tannins. The larval migration inhibition (LMI) assay was applied to examine the impact of the condensed tannins (CT) and an extract of chicory (*Cichorium intybus*) upon the first- (L1) or third-stage (L3) larvae of the deer lungworm *Dictyocaulus viviparus* along with the L3 larvae of nematodes of the gastrointestinal tract. The CT and CSL significantly reduced larval motility as evidenced by their capacity to prevent larvae from passing via nylon mesh sieves. Lungworm L1 larvae incubated within rumen fluid containing 100, 400, and 1000 microns CT/ml were unable to move via the sieves 12, 28, and 41% of the time, respectively. In contrast, lungworm L3 larvae incubated in rumen fluid (pH 6.6) with similar amounts could not pass through the sieves 26, 37, and 67% of the time, respectively. Particularly at greater dosages, intestinal larvae are more vulnerable to CT than lungworm larvae. At concentrations of 100, 400, and 1000 microg/ml, CT prevented 27, 56, and 73% of gastrointestinal larvae from getting utilizing sieves, respectively (Katiki et al., 2011). Lungworm L1 and L3 larvae's motility was decreased by CT more successfully when introduced to rumen fluid as opposed to abomasa fluid (pH 3.0). The effect of CT was confirmed to be caused by the addition of the 2-micron polyethylene glycol/micro-CT, which completely removed the inhibitory action of CT towards L1 & L3 larvae, particularly when incubated in rumen fluid. The CSL extract also exhibited comparable inhibitory action in both fluids towards L1 and L3 lungworm larvae and L3 gastrointestinal larvae, showing the fact that this extract was unaffected by the fluid's pH and proved far more efficient than L1 lungworm larvae towards L3 lungworm larvae. When it came to inactivating L1 and L3 lungworm larvae and L3 intestinal larvae in rumen fluid, condensed tannins (CSL) proved to be more successful than the others. However, CSL were more efficient against the L3 lungworm larvae in abomasal fluids (Katiki et al., 2011).

***Strongyloides stercoralis* third-stage infective larvae**

Strongyloides stercoralis is a prominent parasitic nematode that is found all over the world. This parasite can live for decades in a human hosts before spreading and leading to a deadly infection, especially in immunocompromised people with allergic disorders or those who need steroid therapy. Antihelmintics must be used effectively and when necessary. *Strongyloides stercoralis* third-stage infectious larvae have been proven to be susceptible towards the fruit hexane extract (PHE) of Piper retrofractum. The efficacy of *Cardiospermum halicacabum* extracts towards *Strongyloides stercoralis* third-stage larvae was examined in vitro. Agar plate culture was used to separate *S. stercoralis* third-stage larvae from the culture of dog faeces. The larvae were subjected to aqueous and alcohol extracts of *C. halicacabum* (2,000 lg/ml) at 37C having 5% CO2 while suspended in a phosphate-buffered saline solution (pH 7.4) with a 1,000 larvae per millilitre. Based on its motility, the ability to persist of Strongyloides larvae was assessed every day for seven days. Strongyloides larvae were still alive after being into exposure to ivermectin, piperazine, and *C. halicacabum* (aqueous and alcohol) solutions, yet many of them became immobile after being exposed to the extracts of *C. halicacabum* on aqueous and alcohol within 72 and 48 hours, accordingly. Ivermectin took between 72 and 144 hours, while piperazine took over seven days to cause the same level of immobility. It is obvious that exposure to extracts of *C. halicacabum* severely decreased the survival rate of *S. stercoralis* larvae (Sangkhantree et al., 2018).

***Trichinella spiralis* muscular larvae**

Trichinellosis is a zoonotic illness spread through contaminated food that can harm both humans and animals. Due to the quick development of drug resistance, especially against encapsulated larvae, treatments through commercially available medications have not succeeded. The demand to find alternative anthelmintics from plants with medicinal properties is growing. The goal of the current study was to compare the in vitro antiparasitic effects of myrrh volatile oil and myrrh crude extract on *T. spiralis* larvae with albendazole to determine the effect of myrrh sublethal doses on the infectiousness of *T. spiralis* larvae within mice. While measuring the death rate and analyzing ultrastructural alterations in the larval cuticle with scanning electron microscopy, the in vitro effects of these drugs were assessed. Albendazole and crude myrrh extract caused more drastic changes to the surface of the skin than myrrh volatile oil did. Each reaction to the drugs was time-dependent, dose-dependent, and significantly distinct

from those in the control group (p<0.001). The 4th day of being exposed to 3, 5, and 7 mg/ml of myrrh crude extract and the 7th day to volatile oil resulted in a 100% mortality rate of larvae. Still, the first day of being exposed to 5, 10, 15, and 20 mg/ml of albendazole resulted in total larval death. In vitro treatment to sub-lethal doses of volatile oil extract, crude myrrh extract, and albendazole reduced infections in the intestinal phase from 100%, 98%, and 88%, respectively, along with the muscular phase by 100%, 98%, and 59%, respectively (Abd-Elrahman et al., 2020).

Hymenolepis nana

For ages, ginger has been widely utilized in traditional medicines such as shokyo (fresh rhizomes), kankyo (dry, steamed rhizomes), or kanshokyo (dried rhizomes). These pharmaceutical treatments are and useful for conditions like the common cold, asthma, neurological disorders, stroke, gastrointestinal bloating, oxidative stress, inflammation, hypercholesterolemia, schistosomiasis, and helminthiasis. It has been determined that ginger contains the essential oils zingiberol, zingiberone, zingiberene, pungent substances including [6]-gingerol and [6]-shogaol, and pharmacological characteristics. In that research, the anti-helminthic properties of gingerenone A, [6]-dehydrogingerdione, [4]-shogaol, 5-hydroxy-[6]-gingerol, [6]-shogaol, [6]-gingerol, [10]-shogaol, [10]-gingerol, hexahydrocurcumin, and others were examined. For the parasite *Hymenolepis nana*, researchers isolated the constituents 3R,5S-[6]-gingerdiol and 3S,5S-[6]-gingerdiol to the ginger roots. The cytocidal activity and ability of the ingredients above to stop the spontaneous movement of the parasite in *H. nana* was attained from 24 to 72 h in a time- and dose-related manner, respectively. At 24-72 hours, the deadly efficacy of the [10]-shogaol and [10]-gingero1 reaches its maximum and they lose their ability to move spontaneously (Lin et al., 2014). We performed an in vivo assessment on mice infected with H. nana to assess the cytocidal activity and cytokine production brought on by ginger's extract R0. We gave 500 eggs orally to BALB/c mice as an inoculation. By producing cytokines in vitro, the R0 demonstrated cytocidal action in vivo, resulting in a marked decrease in worms. INF- and IL-2 were found to be considerably elevated by R0 in Con A-stimulated Spleen Cells. Murine KC and IL-12 weren't significantly altered by R0, however, IL-4, IL-5, IL-6, IL-10, and IL-13 significantly observed declines. Together, our findings demonstrate the possibility of using these components of ginger to treat *H. nana* by using them as cytocidal agents (Lin et al., 2014).

Gastrointestinal nematodes

Helminth infections in animals cause the most substantial losses to the world's food output. One of the major obstacles to the breeding of small ruminants in southern Italy has become gastrointestinal nematode (GIN) illness, which is brought on by various worm genera (such as *Teladorsagia*, *Haemonchus*, *Trichostrongylus*, and *Oesophagostomum*). The three produced fractions were tested for anthelmintic effectiveness in vitro (egg hatch test) using the egg hatch method. Faecal samples from sheep that were infected naturally with GINs were obtained for this study. At and1.00, 0.5, 0.25, 0.125, 0.05, and 0.005 mg/mL, fractions were mixed in H2O/DMSO 0.5%. Deionized water and thiabendazole (0.25 and 0.5 mg/mL) were utilized as negative and positive controls, respectively. The findings of the egg hatch test showed that all fractions significantly (p <0.05) inhibited egg hatching within 48 hours of exposure, demonstrating a high activity (>82%) in vitro at all test dosages. The insoluble residues and even gallic acid came in second and third place, respectively, with 94.7%, 85.3%, 94.0%, and 82.7% at 1 and 0.005 mg/mL dosages. The methanol fraction demonstrated the greatest egg-hatching suppression impact (99.3% and 89.3% at 1 and 0.005 mg/mL dosages). The results of the current investigation confirmed the anthelmintic activity of conventional *P. granatum* macerate towards GIN infection in sheep, showing the importance of gallic acid as a primary component and supporting the necessity for additional in vivo research on these conventional veterinary treatments (Castagna et al., 2020).

Anti-macrofilaricidal activity

A tropical disease spread by a vector called lymphatic filariasis can cause clitoris, breasts, and limbs to swell excessively. Against *Litomosoides carinii* as well *Brugia malayi* in rats, a crude extract from the stembark of *Streblus asper*, a commonly utilized medicinal plant of India, showed considerable macrofilaricidal action. According to the study, the extract's K029 (asperoside) and K030 (strebloside) cardiac glycosides also have antifilarial efficacy. Glycosides were also effective in vitro towards all three filarial species. Glycon and aglycon parts of their parent glycosides (K029 and K030) showed noticeably low activity. Different cardiac glycosides from different sources did not exhibit equivalent antifilarial efficacy. However, only 44.5% of the extract's aglycosidic component had adulticidal action towards *L. carinii* at 1 g/kg. Thus, the current discovery creates an opportunity to discover new possibilities in the creation of innovative macrofilaricides (Chamariya et al., 2022).

Anti-schistosomiasis activity

A serious parasite disease called schistosomiasis, commonly known as snail fever and bilharzia, is brought on by blood-dwelling flatworm trematodes belonging to the genus Schistosoma. The physiologically active alkaloid/amide pipeplartine, commonly called piperlongumine, is derived from peppers and is found in significant concentrations in the roots of *Piper tuberculatum*. It has been demonstrated that it has performed in vitro

schistosomicidal actions. Its anthelmintic effect on an animal host hasn't yet been documented. A mice model of schistosomiasis infested with either the adult (patent infection) or juvenile (pre-patent infection) stages of the *Schistosoma mansoni* was used in the current study to assess the in vivo antischistosomal characteristics of extracted piplartine. Mice infested with schistosomes were given either a single dosage of piplartine (100, 200, or 400 mg/kg) and a daily dose for five days (100 mg/kg/day), which both reduced the burden of worms and the production of eggs. In mice containing adult parasites, medication with the maximum dose of piplartine (400 mg/kg) substantially decreased the total worm load by 60.4%. Piplartine also greatly reduced the pathology-causing process in schistosomiasis, *S. mansoni* egg formation. Significant tegumental changes have been observed during scanning electron microscopy experiments in parasite isolated from mice. Results show that piplartine, a bioactive chemical generated from medicinal plants, possesses well-characterized mechanism of toxicity, is accessible, and is reasonably priced. These factors make piplartine a promising lead compound for innovative antischistosomal agents (Mengarda et al., 2020).

Haemonchus contortus

In experimentally infected lambs with *Haemonchus contortus*, the anthelmintic ability of *Cymbopogon schoenanthus* essential oils was assessed. Experimental transmission of a multi-drug-resistant *Haemonchus contortus* strain occurred in two-month-old lambs with a mean body weight (BW) of 22.5 kg. Essential oil of *Cymbopogon schoenanthus* was administered orally to infected animals (Katiki et al., 2011). Three kinds of treatment were given for each of the three groups of six animals: Group 1 acquired a control (10 ml of water); Group 2 acquired *Cymbopogon schoenanthus* essential oil as a treatment (180 mg/kg bw); and Group 3 acquired *Cymbopogon schoenanthus* essential oils (360 mg/kg bw). There were 18 animals in total. The oil was given to the animals at once per day for three days in a row. Blood biochemistry was clinically assessed in lambs and before 1, 5, 10, 15, and 20 days after therapy. During 1, 5, 10, and 15 days after administering the essential oil, treated animals' faeces were used for the larval development assay (LDA) and egg hatch assay (EHA). Larvae collected from the faeces of animals subjected to 360 mg/kg essential oil showed a reduction in LDA 1 day following the 3-day treatment. With sheep infected naturally with 95% *Haemonchus contortus* along with 5% *Trichostrogylus spp*., *Cymbopogon schoenanthus* essential oils were tested using the egg hatch assay (EHA), larval development assay (LDA), larval feeding inhibition assay (LFIA), and larval exsheathment assay (LEA). The essential oil of *Cymbopogon schoenanthus* has shown good action against ovine *trichostrongylids*. 0.009 mg/ml in LFIA, 0.045 mg/ml in EHA, 0.063 mg/ml in LDA, and 24.66 mg/ml in LEA were its LC50 values (Katiki et al., 2011).

Ancylostoma caninum

Millions of individuals worldwide suffer serious health effects from gastrointestinal nematode infections, resulting in significant financial losses for cattle farmers. The most efficient method of preventing parasite infections has been thought to be synthetic drugs. Anthelmintics provide a straightforward, affordable, and cost-effective technique of managing parasites without causing any side effects because these medications are expensive, occasionally inaccessible to people, and display adverse effects. This study examined the anthelmintic properties of *Carica papaya* extract towards mouse infections with *Ancylostoma caninum*. For this investigation, two experiments have been set up. In experiment number 1, mice were collected from two distinct groups (A and B) and three groups (A, B, and C) of mice for measuring mast cells along with eosinophil count and with larval recovery, respectively. On days 14 and 7 before the first infection, group A mouse received 0.2 ml/mouse of a plant extract (*Carica papaya*) treatment (Bi and Goyal, 2012). On day 0, mice were challenged with 500 *A. caninum* larvae. The only challenge given to group B mice was a dosage of 500 *Ancylostoma caninum* larvae. Group C was used as a control group without treatment. Findings of mice subjected to plant extracts showed a clear decrease in larvae in group (A) as compared to group (B) of mice. On day 16, a significant number of mucosal mast cells were seen in all groups. In each group, eosinophil levels significantly decreased 24 days following the challenge infections. The findings point to a potential use of *Carica papaya* extract as an anthelmintic agent for treating intestinal worms. The presence of a variety of proteolytic enzymes including papain, chymopapain, and lysozymes in papaya's resins along with leaves may be the reason for the fruit's effectiveness as an anthelmintic (Bi and Goyal, 2012).

Meloidogyne spp

Fruit, seed, and pulp methanolic extracts were tested for nematicidal efficacy towards *Meloidogyne spp*. Following 72 hours of treatment, seed extracts demonstrated 100% nematode mortality at the maximum dosage, whereas fruit and pulp extracts showed sixty percent and eighty percent mortality, respectively. Two methods were used to assess different creeper extracts in nematicidal efficacy towards *Meloidogyne* species. The less polar component was screened for nematicidal activity using route 1. After 72 hours of being subjected to the extract, the nematode died 60% of the time when exposed to ethyl acetate extract at its greatest concentration (1.0), compared to 40% for the ethyl acetate and water fraction. Hexane sub-fraction (HH-CC) in route 2 demonstrated 100% nematode mortality after 72 hours, but HE-CC and HW-CC

demonstrated 100% mortality only at some high concentrations (Rizvi and Shahina, 2014).

Caenorhabditis elegans

The stable and cyclic mini-proteins known as cyclotides are only present in plants and contain nematicidal and anthelmintic properties. They are found in the plant groups *Cucurbitaceae*, *Violaceae*, *Solanaceae*, *Rubiaceae*, and *Fabaceae*, which are thought to operate as pest deterrents. In this study, the free-living model worm *Caenorhabditis elegans* was used to investigate the nematicidal abilities of extract of four important cyclotide-producing plants: *Hybanthus enneaspermus*, *Viola odorata*, *Oldenlandia affinis* and *Clitoria ternatea*. We tested the cycloviolacin O2, hyen D and cyclotides kalata B1 identified in the extracts for their nematicidal action and discovered that they were effective towards *C. elegans* larvae. The toxicity from isolated cyclotides and plant extracts upon *C. elegans* first-stage larvae was dose-dependent. When isolated cyclotides came into contact with the worms' mouth, pharynx, midgut, or membrane, it killed them or caused them harm. Blebs, or bubble-like structures generated by hyen D as well cycloviolacin O2 adjacent to the *C. elegans* membrane, indicate that disruption of the membrane is cause of death of C. *elegans*. Although the hydrophobic patches on the tested cyclotides were damaged through single-point mutations, all of them regained their toxic properties. The current findings offer a simple test design to assess and investigate the nematicidal effects of pure cyclotides and plant extracts on *C. elegans* (Bajpai et al., 2023).

Ascaridia galli

The parasitic roundworm *Ascaridia galli* (*A. galli*), which can cause financial loss, occurs most often in birds. There are numerous ways to treat preventing worm infection, including employing plants that contain antiparasitic compounds. The purpose of the research was to examine the ovicidal and larvicidal effects of *Areca catechu* crude aqueous extract (AAE) in both eggs and larvae (L2) in vitro, and any alterations to the ultrastructure. While incubating eggs, eggs containing embryos, and larvae (L2) for 48 hours at 10%, 12.5%, 15%, 17.5%, 20%, 22.5%, and 25% AAE, the ovicidal along with larvicidal effects were examined. 0.62% saline water served as the negative control while 5% pyrantel pamoate served as the positive control. The eggs along with L2 larvae were next analyzed with scanning electron microscopy (SEM), separating the dead and live eggs, the eggs carrying embryos, and the eggs were identified. When compared to the control, the ovicidal as well larvicidal activities of the 12.5-25% AAE were significantly distinct ($p< 0.05$). However, they didn't significantly differ with the ovicidal, larvicidal, and vermicidal effects of the positive control (pyrantel pamoate; $p > 0.05$). The strongest ovicidal and larvicidal activity was observed at 25% AAE. The egg outer walls had shrinkages, and ruptures, along with other general defects, according to the SEM findings. With 25% AAE, the cuticle layers of the L2 larvae burst as the anterior teguments shrunk. Results showed that AAE could be utilized as an anthelmintic because it exerts ovicidal and larvicidal effects on *A. galli* (Mubarokah et al., 2021).

Nippostrongylus brasiliensis

East African *Xylopia aethiopica* is frequently used throughout Nigeria among traditional herbal practitioners and pastoralists to manage gastrointestinal helminth infections. The crude methanol extract's efficacy as an anthelmintic was examined in rats that had been infected artificially with the parasitic rat hookworm Nippostrongylus brasiliensis. A total of 35 rats were randomly divided into seven distinct groups after receiving subcutaneous infections of 200 infective third-stage parasite larvae. Rats in each group were given a different dose of extract five days after infection, depending on the group. Propylene glycol was given to every rat in the seven (control) group. Anthelmintic activity was determined when evaluating the number of worms retrieved from treated to untreated infected control rats. In comparison to untreated control rats, the extract at doses of 0.8 g/kg, 1.0 g/kg, 1.2 g/kg, 1.4 g/kg, 1.7 g/kg, and 2.0 g/kg resulted in deparasitization rates of 21%, 47%, 51%, 50%, 63%, and 76% that were significant ($p>0.05$) (Suleiman et al., 2005).

Conclusion

This review discusses the activity of medicinal plants and their mode of action against parasites. Parasites are part of our environment causes variety of diseases different medicinal plants have been used for centuries, but some lack experimental evidence. Variety of medicinal plants their extracts, and oils are being used against parasites, and even some drugs have been developed from natural sources with good activity against protozoans and helminths. Isolation and identification of new medicinal plants against parasites will be helpful in the future to develop more new drugs and overcome parasite resistance.

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Declarations

Author contribution

MS wrote up initial draft. ZW, QA and SH make final editing in the manuscript. All authors approved final version to publish.

Data Availability statement

All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Funding

Not applicable

Conflict of Interest

Regarding conflicts of interest, the authors state that their research was carried out independently without any affiliations or financial ties that could raise concerns about biases.