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REVIEW ARTICLE

EXPLORING THE ANTIPARASITIC ACTIVITY OF MEDICINAL PLANTS

Gehan Fawzy Abdel Raoof[1*], Ahmed Wael Lethy Mohamed[2]

[1]*Pharmacognosy Department, Pharmaceutical and Drug Research Industries Division, National Research Centre, Dokki, Giza 12622, Egypt.*

[2]*College of Biotechnology, Misr University for Science and Technology (MUST), 6th of October City, Egypt.*

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***Address for Correspondence:**
Dr. Gehan F. Abdel Raoof, Pharmacognosy Department, National Research Centre, Dokki, 12622, Giza, Egypt, Tel: +201223417848.
E-mail: *gehankandeel9@yahoo.com*

Abstract

Parasitic disease is one of the most important challenges impacting a large number of people. Worldwide, more than three billion cases of parasitic disease are reported yearly. Due to the resistance of parasite to the synthetic drugs, it is necessary to search for alternative sources. Plants contain different phytoconstituents with different biological activities. Many previous researches showed that many plants exerted antiparasitic activity due to its secondary metabolites. This review highlights the antiparasitic effects of different medicinal plants and mentions the mode of action of different phytochemicals against parasites. In conclusion, the medicinal plants play a vital role as antiparasitic agents, but further studies are needed to isolate and test the active constituents of the medicinal plants as antiparasitic agents targeting to enter the drug discovery area.

Keywords: Antiparasitic, medicinal plants, parasitic disease, phytoconstituents.

INTRODUCTION

Parasitic diseases are the most important public health problem impacting a large number of people worldwide. Parasites are considered to be a major problem in our life. A large variety of parasites have developed during the evolution of humans. Typically, a parasite will not destroy its host instantly. Most internal parasites are weakening our health, while think of lice and fleas are unpleasant for us. If the patients do not get appropriate therapy, some parasitic infections can be deadly, such as Chagas, trypanosomiasis or malaria[1]. The transmission of parasites is facilitated because of the bad hygienic conditions. People have often tried to mitigate the parasitic infection. Mechanically, it may minimize or eliminate external parasites. While, internal parasites are more complicated to treat[2]. A number of drugs have been synthesized from the medicinal chemists which can be used as antiparasitic drugs, but some parasites showed resistance to these drugs. So, searching for antiparasitic drugs from natural origin is necessary to be an alternative to synthetic drugs[3]. For several thousands of years, humans have used medicinal plants to treat diseases and health problems. For centuries, medicinal plants have been used as antiparasitic agents, and up till now, are still used for this purpose[4]. Many medicinal plants showed antiparasitic activity against different parasites. These medicinal plants contain different biologically active compounds that showed antiparasitic activity. For example, saponins impact on the cell membrane permeability of the parasites causing vacuolization of teguments[5]. The aim of this review is to highlight the antiparasitic effects of different medicinal plants and to know the mode of action of different phytochemicals against parasites.

Parasites

A parasite lives in or on a host; it depends on the resources of its host to maintain its life cycle. Most of parasites are invisible by the naked eye, but others can reach a length of 30 meters or more as some worm parasites. Parasites can cause spreading of different diseases[6]. Parasites cause large numbers of infections and lead to several million deaths every year[7]. There are different ways for parasitic infections as polluted vegetables, food, soil and water leading to different complications as allergies, anemia, malnutrition and gastrointestinal disorders. The parasitic infections cause many tropical diseases, such as helminthiases, leishmaniasis, onchocerciasis, malaria, lymphatic filariasis, Chagas disease, trypanosomiasis and schistosomiasis[2]. Helminth (parasitic worm) can exist

as individuals or as parasites dependent on plant or animal hosts. In human beings helminthic infections are known as one of the most common infections[8]. The lives of billions of people worldwide are affected by protozoan parasites that cause large economic impacts[9].

Table 1: Examples of some antiparasitic drugs.

Category of the drug	Examples
Anticestoda	Praziquantel, Levamisole, Niclosamide
Antirematoda	metrifonate, oxamniquine, praziquantel, bithionolsulfoxide
Antinematoda	diethyl carbamazine, ivermectin, piperazine, pyrantel, mebendazole, thiabendazole

Types of parasites

There are two main types of parasites endoparasites and ectoparasites. Human endoparasites live inside their hosts, in the alimentary canal or within cells or tissues. There are two types of endoparasites; Protozoa which include the unicellular organism called Plasmodium. The other type are helminthes (worm parasites) such as; tapeworm, fluke, pinworm, roundworm and trichina spiralis. On the other hand, ectoparasites live on, rather than in their hosts. They include fleas and lice[10].

Prevention

To avoid and prevent parasitic infections, there are several precaution should be followed such as; washing the hands regularly, drink clean water and avoid swallowing water from ponds streams or lakes, cook food to its recommended internal temperature, avoid cat feces and litter especially for pregnant woman and safe sex practicing[11].

Diagnosis

There are different ways for diagnosis of the parasitic infections such as; a blood test, a fecal exam to check the presence of parasites or their eggs in the stool sample, colonoscopy or endoscopy in which the doctor will pass a thin tube into the digestive system through the mouth or rectum of patient to examine his intestinal tract, the other ways for the diagnosis of parasitic infections by some scans to inspect the presence of any lesions or damages of organs by parasites, these scans such as; magnetic resonance imaging (MRI), computerized axial tomography (CAT), or X-ray[11].

Treatment

A number of drugs have been synthesized from the medicinal chemists that can be used as antiparasitic drugs. Some parasites showed resistance to these drugs. So, searching for antiparasitic drugs from natural origin is necessary to be used instead of synthetic drugs[3]. For the pharmaceutical industry, the production of new synthetic antiparasitic drugs is a risky affair due to a high price of the drugs and because a lot of parasitic infestations exist in developing countries where it is difficult for the people to pay. So, new drugs derived from natural products or their derivatives are necessary to be an alternative to synthetic drugs[2]. Natural products play a vital role in medicine; large numbers of new drugs were derived from natural products or their derivatives[4]. Table 1 showed examples of some anthelmintic drugs.

Table 2: Antiparasitic medcicinal plants and their secondary metabolites.

No.	Scientific name	Family	Chemical constituent
1	*Cinchona officinalis*[14]	Rubiaceae	Quinine, quinidine, cinchonine, and cinchonidine
2	*Artemisia annua*[22]	Asteraceae	sesquiterpene
3	*Streblusasper*[2]	Moraceae	Asperoside, strebloside
4	*Carica papaya*[21]	Caricaceae	Papain, Benzyl isothiocynate
5	*Cichoriumintybus*[3]	Asteraceae	sesquiterpene lactones
6	*Buteamonosperma*[16]	Fabaceae	Palasonin, and tannins
7	*Zingiberofficinale*[16]	zingiberaceae	Zingiberene, gingerols, shogaols and bisabolene
8	*Dryopterisfilix-mas*[2]	Dryopteridaceae	Vermicidal phloroglucinols
9	*Punicagranatum*[13]	Lythraceae	Alkaloid, tannins, glycosides
10	*Artemisia herba-alba*[13]	Asteraceae	Alkaloid, tannins, and phenol
11	*Ailanthus altissima*[17]	Simaroubaceae	Quassinoids, ailanthone
12	*Allium sativum*[18,20]	Amaryllidaceae	Allicin, and ajoene
13	*Dilleniasuf fruticosa*[15]	Dilleniaceae	MethylGlycolate, phenol, tridecanal
14	*Dichrostachys cinerea*[5]	Fabaceae	Cardiac glycosides, flavonoids, tannins, triterpenoids, saponins

Antiparasitic medicinal plants and their secondary metabolites

Herbal medicine plays a vital role in the management of many diseases as it has become a very safe, non-toxic, and easily available source. Owing to the existence of diverse bioactive compounds with antioxidant properties, the extracts of medicinal plants can be used as a natural treatment for the infestation of parasites. Some parasites showed resistance for many of synthetic drugs. So all the world is going to produce new drugs from natural origins and plants[13].

Cinchona officinalis

Cinchona officinalis belongs to family Rubiaceae. From *Cinchona officinalis* and related *Cinchona* species, the first medications to cure malaria were developed. Quinoline alkaloids are the main active constituents of Cinchona bark. Cinchonidine (Quinimax) was the bitter-tasting quinine that is used to cure the *Plasmodium* phases in the blood. The basic structure for synthesizing multiple antimalarial drugs is quinine. Quinine as well as its conjunction with clindamycin, doxocyclineor tetracycline are important in the treatment of severe *P. falciparum* infections[14].

***Dichrostachys cinerea* (*Fabaceae*)**

Dichloromethane extract of *Dichrostachys cinerea* stem bark exhibited a potent *in vitro* antiplasmodial effect against the chloroquine resistant strain of *Plasmodium falciparum.* In addition, it showed a potent suppression of parasite and capacity to recover disease in the animal model of *P. berghei*. Moreover, *Dichrostachys cinerea* methanol extract exhibited cytotoxicity with concentration 178.35µg/ml, indicating that *Dichrostachy scinerea* methanol extract may be defined as anti-malarial drug[5].

Cichoriumintybus

Cichoriumintybus (Chicory) belongs to family Asteraceae. It showed antiparasitic activity as it contains different bioactive compounds. Sesquiterpene lactones rich extracts from chicory exhibited a potent activity against different gastrointestinal helminths of livestock, as well as it showed antimalarial properties[3].

Dillenia suffruticosa* (*Dilleniaceae)

Different bioactive compounds are presented in the leaves of *D. suffruticosa*. The methanol extract of the leaves showed a potent effect against the deleterious leeches of hybrid groupers. It was found that *D. suffruticosa* methanol extract revealed strong antiparasitic activity against the marine leech *Zeylanicobdella arugamensis* with 100% mortality[15].

Butea monosperma

Butea monosperma belongs to family Fabaceae. The methanol extract of *B. monosperma* showed anthelmintic activity *in vitro*. The different species of *Butea* have been reported to exhibited anthelmintic activity against *Dipylidium caninum*, *Taenia*, earth worm, *A. galli* and *Ascaris lumbricoides. Butea monosperma* contains many bioactive compounds as tannins and palasonin[16].

Table 3: The mode of action of different phytochemicals.

Phytochemical	Action
Phenolic compounds[5,23]	Uncoupling the oxidative phosphorylation leads to disturbance in energy generation mechanism
Alkaloids[13, 24]	- At as an antioxidant - Steroidal alkaloid and oligoglycosides inhibit the transfer of sucrose from the stomach to the small intestine. - Cause paralysis due to its effect on central nervous system.
Tannins[5,25]	-Uncoupling the oxidative phosphorylation leads to disturbance in energy generation mechanism -Binding glycoprotein on the cuticles of the worms or the free protein of the GI tract of the host animal
Cysteine proteinases[26]	Cause digestion of nematode cuticle
Isoflavones[27]	Disturb the Ca^{+2} homeostasis in the parasites. Inhibit the enzymes of glycogenolysis and glycolysis

***Zingiber officinale* Rosc (Ginger)**

Zingiber officinale belongs to family zingiberaceae . Zingiberene, gingerols, shogaols and bisabolene are the main active compounds of *Zingiber officinale.* A monocyclic sesquiterpene (zingiberene) is the main component of ginger oil. It gives ginger its distinct flavoring and represents about 30% of the essential oils in ginger rhizomes. The alcoholic extract of rhizomes of *Z. officinale* showed the anthelmintic activity against human *A. lumbricoides*. Also it exhibited antischistosomal activity[16].

Dryopterisfilix-mas

Dryopterisfilix-mas (Dryopteridaceae) contains biologically active compounds that effective against cestodes and causing worm muscles paralysis, these compounds (vermicidal phloroglucinols) such as deaspidin, filixic acid and aspidin[2].

Punicagranatum

Punicagranatum (Lythraceae) is effective against gastrointestinal nematodes. The crude extracts of *P. granatum* showed a potential anthelmintic activity. By comparing with the negative control, the extract showed a potent nematocidal effect at the highest concentration (10 mg/ml). Moreover, plant extract showed a potent inhibitory effect against hatching of the egg within 48 hr of exposure[13].

Artemisia herba-alba

Artemisia herba-alba (Asteraceae family) is used as an anthelmintic agent. The crude extract of *A. herba-alba* showed a potential anthelmintic activity at all dose levels. *Artemisia herba-alba* flower extract showed a potent inhibitory effect against egg hatching (98.67%) at concentration 1 mg/ml comparing with the negative control, this result confirmed the nematocidal activity of *Artemisia herba-alba*[13].

Ailanthus altissima

Ailanthus altissima belongs to Simaroubaceae family. From the active extracts of *Ailanthus altissima*, 6 alpha tigloyloxy chaparrinone and ailanthone were isolated and showed a potent inhibitory effect against *Plasmodium falciparum* strains *in vitro*. Extracts of *Ailanthus altissima* (Mill.) Swingle have been tested for activity. The chloroformic extract showed a potent effecton *P. berghei* in mice and on *P. falciparum in vitro* In addition, the presence of the quassinoidail anthonein the plant plays an important role in this activity[17].

***Allium cepa* (onion) and *Allium sativum* (garlic)**

The effects of onion (*Allium cepa)*and garlic (*Allium sativum*) on adult parasite *Lernantropus kroyeri (L. kroyeri*) were studied. Results showed that onion and garlic juices exhibited the inhibitory effect on the females of *Lernantropus kroyeri* in a concentration and time dependent manner[18-20].

Carica papaya

Carica papaya belongs to family Caricaceae. Benzylisothiocynate and Papain are the main active constituents of Papya. Papain, papaya proteinase I, is a

cysteine protease enzyme present in seed, fruit and leaves of papaya. The latex containing papain showed anthelmintic properties against intestinal nematodes of poultry[21]. Papain is comprised of a polypeptide chain with three disulfide bridges and a sulfhydryl group required for the enzyme activity which is responsible for digestion of nematodes cuticle[16].

Streblus asper

Streblusasper family Moraceae exhibited a potent anti-filarial activity. The main active components of *Streblus asper* are the cardiac glycosides strebloside and asperoside[2].

Artemisia annua (Asteraceae)

Artemisia annua contains the sesquiterpene artemisinin which plays a vital role as an antimalarial agent. It showed a potent activity against *P. falciparum.* Various semi-synthetic derived products from artemisinin have been developed, and today in clinical practice[22]. Table 2 summarized the most important tantiparasitic medicinal plants and their secondary metabolites. While Table 3 showed the mode of action of different phytochemicals.

CONCLUSIONS

This review highlights the antiparasitic effects of different medicinal plants as well as the mode of action of different phytochemicals against parasites. So, the current review provides recommendations based on proof to understand the role of medicinal plants as antiparasitic agents aiming to be the first step towards the production of novel drugs for controlling the parasitic infection. Furthermore, more research is needed to run clinical trial to confirm the effect of medicinal plants as antiparasitic agents. In future, medicinal plants should be the first choice for the management of parasitic infection.

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AUTHOR'S CONTRIBUTION

Raoof GFA: writing original draft, methodology. **Mohamed AWL:** investigation, conceptualization, literature survey. Both authors revised the article and approved the final version.

CONFLICTS OF INTEREST

None to declare.

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