

# Exploring the Antiparasitic Activity of Medicinal Plants

## ABSTRACT

Parasitic disease is one of the major public health problems affecting hundreds of millions of people. Worldwide, more than three billion cases of parasitic disease are reported yearly. The parasites have sometimes become resistant to the available synthetic therapeutics, so it is important to search for alternative sources of anti-parasitic drugs. 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 to know the mode of action of different phytochemicals against parasites.

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

## INTRODUCTION

Parasitic diseases are the major public health problem affecting hundreds of millions of people. Parasites are considered to be a major problem in our life. A broad set of parasites have evolved during the evolution of humans that use the human as a host organism. Usually a parasite will not kill its host (at least not immediately). Most internal parasites are weakening our health, while think of lice and fleas are unpleasant for us. If the patients are not treated with adequate therapeutics, some parasitic infections can be deadly, such as Chagas, trypanosomiasis or malaria<sup>1</sup>.

The transmission of parasites is facilitated because of the badhygienic conditions. Humans have always tried to minimize the parasitic infection. Mechanically, external parasites could be reduced or eliminated. While, internal parasites are more complicated to treat<sup>2</sup>.

A number of drugs have been synthesized from the medicinal chemists which can be used as antiparasitic drugs. Some parasitic strains have become resistant to these drugs. To overcome this problem, the search for anti-parasitic plant extracts or secondary metabolites derived from them is necessary to be an alternative to synthetic drugs<sup>3</sup>.

For several thousands of years, humans have used medicinal plants to treat illness and health disorders. For centuries, medicinal plants have been used as antiparasitic agents, and up till now, are still used for this purpose<sup>4</sup>.

Many medicinal plants showed antiparasitic activity against different parasites. These medicinal plants contain different biologically active compounds that showed antiparasitic activity. For example, saponins affect the permeability of the parasites cell membrane causing vacuolization of teguments<sup>5</sup>.

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 is an organism that lives in or on another organism (a host). The parasite uses the host's resources to maintain its life cycle. Most of parasites are invisible by the naked eye, , but others as some worm parasites can reach over 30 meters in length. Parasites can cause spreading of different diseases<sup>6</sup>. Parasites cause large numbers of infections and lead to several million deaths every year<sup>7</sup>. 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 helminthiasis, leishmaniasis, onchocerciasis, malaria, lymphatic filariasis, Chagas disease, trypanosomiasis and schistosomiasis<sup>2</sup>. 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<sup>8</sup>. The lives of billions of people worldwide are affected by protozoan parasites that cause large economic impacts<sup>9</sup>.

### 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 main types of endoparasites; Protozoa which include the single-celled organism known as Plasmodium. The other type are helminths (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<sup>10</sup>.

### PREVENTION

To avoid and prevent parasitic infections, there are several precautions 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<sup>11</sup>.

### 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 that are used to check the presence of signs of lesions or injury to organs caused by parasites, these scans include; computerized axial tomography (CAT), magnetic resonance imaging (MRI) or X-ray<sup>11</sup>.

### TREATMENT

A number of drugs have been synthesized from the medicinal chemists which can be used as antiparasitic drugs. Some parasitic strains have become resistant to these drugs. To overcome this problem, the search for anti-parasitic plant extracts or secondary metabolites derived from them is necessary to be an alternative to synthetic drugs<sup>3</sup>. For the pharmaceutical industry, the development of new synthetic antiparasitic drugs is a risky affair due to a high price of the drugs and because many of the parasitic diseases occur in poor countries where the populations cannot afford to pay. So, new drugs derived from natural products or their derivatives is necessary to be an alternative to synthetic drugs<sup>2</sup>. Natural products play a vital role in medicine, large number of new drugs were derived from natural products or their derivatives<sup>4</sup>. Table (1) showed examples of some antiparasitic drugs.

**Table (1) Examples of some Antiparasitic drugs<sup>12</sup>**

Category of the drug	Examples
Anticestoda	Praziquantel, Levamisole, Niclosamide
Antirematoda	metrifonate, oxamniquine, praziquantel, bithionol sulfoxide
Antinematoda	diethyl carbamazepine, ivermectin, piperazine, pyrantel, mebendazole,

## ANTIPARASITIC MEDICINAL PLANTS AND THEIR SECONDARY METABOLITES

Herbal medicine plays an important role in the treatment of many diseases as it has become a very safe, non-toxic, and easily available source. The medicinal plant extracts can be used as a bio-safe and natural remedy for the parasite infestations due to the presence of various bioactive compounds with antioxidant properties. Some parasitic strains have become resistant to many of synthetic drugs. So all the world is going to produce new drugs from natural origins and plants<sup>13</sup>.

### *Cinchona officinalis*

*Cinchona officinalis* belongs to family Rubiaceae. From *Cinchona officinalis* and related *Cinchona* species, the first drugs to treat malaria were developed. Quinoline alkaloids, as quinine, quinidine, cinchonine, and cinchonidine are the main active constituents of *Cinchona* bark. cinchonidine (Quinimax) was the bitter-tasting quinine that is used to treat the blood stages of *Plasmodium*. served The lead structure for the synthesis of several antimalarial drugs is Quinine. Quinine alone or in combination with clindamycin, tetracycline or doxocycline are used in the treatment of severe *P. falciparum* infections<sup>14</sup>.

### *Dichrostachyscinerea* (Family Fabaceae)

Dichloromethane extract of *Dichrostachyscinerea* stem bark showed good in vitro antiplasmodial activity against the *Plasmodium falciparum* chloroquine resistant strain. Also there was a significant parasite suppression and disease recovery ability in *P. berghei* animal model. Moreover, *Dichrostachyscinerea* methanol extract possessed a cytotoxic concentration (CC50) of 178.35 µg/mL, indicating that *Dichrostachyscinerea* methanol extract can be used as anti-malarial drug<sup>5</sup>.

### *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<sup>3</sup>.

### *Dillenia suffruticosa* (Dilleniaceae)

Different bioactive compounds are presented in the leaves of *D. suffruticosa*. *D. suffruticosa* the methanol extract showed a potent antiparasitic activity against the harmful 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<sup>15</sup>.

### *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 exhibit anthelmintic activity against *Dipylidium caninum*, *Taenia*, earth worm, *A. galli* and *Ascaris lumbricoides*. *Butea monosperma* contains many bioactive compounds as tannins and palasonin<sup>16</sup>.

### *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<sup>16</sup>.

### ***Dryopteris filix-mas***

*Dryopteris filix-mas* (Dryopteridaceae) contains biologically active compounds that are active against intestinal cestodes and probably paralyze the worm's muscles, these compounds (vermicidal phloroglucinols) such as deaspidin, filixic acid and aspudin<sup>2</sup>.

### ***Punicagranatum***

From the Lythraceae family, *Punicagranatum* (Roman) is used against GI nematodes. The crude extracts of *P. granatum* showed a potential anthelmintic activity. By comparing with the negative control, the extract showed a significantly ( $p < 0.05$ ) nematocidal activity at the highest concentration (10 mg/mL). Moreover, plant extract showed a significant egg hatching inhibition effect. So, the plant caused a significantly ( $p < 0.05$ ) greater egg hatch inhibition within 48 hr of exposure<sup>13</sup>.

### ***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 in a concentration- and time-dependent fashion at all dose levels. The flower extract of *A. herba-alba* showed the highest (98.67%) egg hatching inhibition effect at concentration 1 mg/mL. By comparing with the negative control, the highest concentration (10 mg/mL) of the extract exhibited a significantly ( $p < 0.05$ ) superior nematocidal activity<sup>13</sup>.

### ***Ailanthus altissima***

*Ailanthus altissima* belongs to Simaroubaceae family. From the active extracts of *Ailanthus altissima*, 6 alpha tigloyloxychaparrinone and ailanthone were isolated and showed activity against both chloroquine-sensitive and chloroquine-resistant strains of *Plasmodium falciparum* *in vitro*. Extracts of *Ailanthus altissima* (Mill.) Swingle have been tested for activity. The chloroformic extract showed a potent activity against *Plasmodium falciparum* *in vitro* and against *P. berghei* infections in mice. In addition, the presence of the quassinoid ailanthone in the plant plays an important role in this activity<sup>17</sup>.

### ***Allium cepa* (onion) & *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 possess a killing effect on *L. kroyeri* females in a time and concentration-dependent manner<sup>18-20</sup>.

### ***Carica papaya***

*Carica papaya* belongs to family Caricaceae. Benzylisothiocyanate and Papain are the main active constituents of Papaya. 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<sup>21</sup>. Papain consists of a single polypeptide chain with 3 disulfide bridges and a sulfhydryl group necessary for the activity of the enzyme which is responsible for digestion of nematodes cuticle<sup>16</sup>.

### ***Streblus asper***

*Streblus asper* family Moraceae exhibited a potent anti-filarial activity. The main active components of *Streblus asper* are the cardiac glycosides strebloside and asperoside<sup>2</sup>.

### ***Artemisia annua* (Asteraceae)**

*Artemisia annua* contains the sesquiterpene artemisinin which plays a vital role as an antimalarial agent. It showed a potent activity against resistant strains of *P. falciparum*. Several semisynthetic derivatives of artemisinin have been developed, and today in clinical practice<sup>22</sup>.

Table 2 summarized the antiparasitic medicinal plants and their secondary metabolites. While table 3 showed the mode of action of different phytochemicals.

**Table(2). Antiparasitic Medicinal Plants and their Secondary Metabolites**

No.	Scientific name	Family	Chemical constituent	Reference
1	<i>Cinchona officinalis</i>	Rubiaceae	Quinine, quinidine, cinchonine, and cinchonidine	(Willcox, 2011)
2	<i>Artemisia annua</i>	Asteraceae	sesquiterpene	(Efferth et al., 2011)
3	<i>Streblus asper</i>	Moraceae	Asperoside, strebloside	(Wink, 2012)
4	<i>Carica papaya</i>	Caricaceae	Papain, Benzyl isothiocyanate	(Adu et al., 2009)
5	<i>Cichorium intybus</i>	Asteraceae	sesquiterpene lactones	(Peña-Espinoza et al., 2018)
6	<i>Butea monosperma</i>	Fabaceae	Palasonin and tannins	(Bauriet al., 2015)
7	<i>Zingiber officinale</i>	zingiberaceae	Zingiberene, gingerols, shogaols and bisabolene	(Bauri et al., 2015)
8	<i>Dryopteris filix-mas</i>	Dryopteridaceae	Vermicidal phloroglucinols	(Wink, 2012)
9	<i>Punica granatum</i>	Lythraceae	Alkaloid, tannins, glycosides	(Ahmed et al., 2020)
10	<i>Artemisia herba-alba</i>	Asteraceae	Alkaloid, tannins and phenol	(Ahmed et al., 2020)
11	<i>Ailanthus altissima</i>	Simaroubaceae	Quassinoids, ailanthone	(Al-Snafi, 2015)
12	<i>Allium sativum</i>	Amaryllidaceae	Allicin and ajoene	(Krstinet al., 2018; ; Yildiz et al., 2019)
13	<i>Dillenia suffruticosa</i>	Dilleniaceae	Methylglycolate, phenol, tridecanal	(Shah et al., 2019)
14	<i>Dichrostachys cinerea</i>	Fabaceae	Cardiac glycosides, flavonoids, tannins, triterpenoids and saponins	(Kweyamba et al., 2019)

**Table (3). The Mode of Action of Different Phytochemicals**

<b>Phytochemical</b>	<b>Action</b>	<b>Reference</b>
Phenolic compounds	Uncoupling the oxidative phosphorylation leads to disturbance in energy generation mechanism	23,5
Alkaloids	<ul style="list-style-type: none"><li>- Act as an antioxidant</li><li>- Steroidal alkaloid and oligoglycosides inhibit the transfer of sucrose from the stomach to the small intestine.</li><li>- Cause paralysis due to its effect on central nervous system.</li></ul>	24,13
Tannins	<ul style="list-style-type: none"><li>-Uncoupling the oxidative phosphorylation leads to disturbance in energy generation mechanism</li><li>-Binding glycoprotein on the cuticles of the worms or the free protein of the GI tract of the host animal</li></ul>	25,5
Cysteine proteinases	Cause digestion of nematode cuticle	26
Isoflavones	Disturb the Ca <sup>+2</sup> homeostasis in the parasites. Inhibit the enzymes of glycogenolysis and glycolysis	27

## CONCLUSION

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 an evidence-based contribution to understand the role of medicinal plants as antiparasitic agents aiming to be the first step towards the novel drugs development for the management of parasitic infection. Moreover, further research is required 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 treatment of parasitic infection.

## CONFLICTS OF INTEREST

No conflict of interest associated with this work.

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