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Plant-based Therapy - How does it Work on Parasites?

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Abstract

Parasites remain one of the most important causes of morbidity and mortality in the tropical landscape. Of these, granulomatous amoebic encephalitis (GAE), leishmaniasis and malaria are 3 common parasitic diseases which can be fatal if left untreated. The available drugs seem to be ineffective as resistant strains have emerged in recent years. It is timely for medicinal plants have been given much attention as an alternative for the available chemotherapeutic drugs. This review was conducted to evaluate the anti-parasitic effects of medicinal plants from different parts of the world. It was found that large numbers of plants showed strong anti-parasitic potential; *Clerodendrum rotundifolium Oliv.* leaves water fraction, *Clerodendrum rotundifolium Oliv.* leaves methanol fraction and *Microglossa pyrifolia* showed strong anti-malarial activity with IC_{50} of 0.01, 0.02 and 0.05 µg/ml *in vitro*. *Limouni olive* is a strong amoebicidal agent with IC_{50} of 5.11 µg/ml. Ethanol extracts from *H. stignocarpa* leaves (4.69 µg/ml), *J. cuspidifolia* leaves (10.96 µg/ml) and *Jacaranda caroba* leaves (13.22 µg/ml) showed strong activity against *Leishmania* spp. with IC_{50} values lower than 25 µg/ml. In conclusion, these promising results suggest that future research on medicinal plants needs to be done to identify its active constituents, cytotoxicity, effectivity and feasibility to be utilized against infections caused by these parasites. Furthermore, phytochemical investigations should be undertaken to achieve the effectiveness of therapeutic agents particularly in limited resource settings.

Keywords: Natural products, *Acanthamoeba*, *Leishmania*, *Plasmodium*

Introduction

There are 4 categories of parasites' transmission: (i) water-borne, (ii) blood-borne, (iii) food-borne and (iv) vector-borne [1]. Such parasites remain one of the most important causes of morbidity and mortality in tropical landscapes. Of these, water- and blood-borne parasites are the main focus of attention in the present scenario. Water-borne parasites are defined as any microorganisms which can be transmitted in contaminated fresh water, sea water, tap water, contact lens solutions and air conditioning water [2]. For blood-borne parasites, as pathogenic microorganisms, are spread by either infected blood transfer or vector like insects [3]. The most well-known waterborne parasites include *Acanthamoeba* spp., whilst *Plasmodium* spp. and *Leishmania* spp. are the 2 most important killers relating to parasitic diseases in the tropics.

Acanthamoeba spp. is a free living amoeba that commonly causes keratitis and fatal granulomatous amoebic encephalitis (GAE) [4]. The clinical symptoms of keratitis involve severe eye pain and

headaches, while, fever and neurological deficits are the main common clinical symptoms found in GAE [5]. The life cycle of *Acanthamoeba* includes trophozoites and cysts. However, metabolically active trophozoites can be converted into double wall dormant, stress resistant cysts when conditions are unfavourable [6]. The difference between cysts and trophozoites are the structures. Trophozoites look thorn-like with a diameter of 14 to 40 µm and cysts look like a single nucleus with a diameter of about 10 to 30 µm subject to the species [2]. For treatment, drugs like clotrimazole [7], ketoconazole [8] and azole [9] have been reported as acting synergistically against *Acanthamoeba* keratitis and GAE. Among pathogenic *Acanthamoeba* species include *A. tringularis*, *A. castellanii*, *A. curlbertsoni* and *A. polyphaga.* Under unfavorable conditions, *Acanthamoeba* spp. acts as an aetiological agent and causes devastating waterborne outbreaks that have been reported in the USA and Puerto Rico [5].

Plasmodium spp. is a protozoan parasite that is transmitted by infected female *Anopheles* mosquitoes into human blood and 5 common species cause human malaria. The prevalence of malaria cases has been constantly reported from various parts of the world, especially from parts of Africa and Asia. In 2015, about 214 million cases of malaria worldwide were reported with 438,000 people especially young children in sub-Saharan Africa dying [10] making it the top killer disease in the world. The life cycle of *Plasmodium* spp. starts from mosquito bites into human blood and comprises a few separate stages in both mosquitoes (insects) and human blood (vertebrae hosts) development such as sporozoites, hypnozotes, merozoites and trophozoites [11]. There are 5 common *Plasmodium* species causing malaria: *P. falciparum*, *P. vivax*, *P. malariae*, *P. ovale* and *P. knowlesi*. The clinical symptoms of malaria include high fever, headaches, nausea, vomiting, diarrhea and anaemia. For therapeutic options, quinine and artemisinin have been reported as effective drugs in treating malaria caused by *Plasmodium* parasites [12].

Leishmania spp. is transmitted by the infected female *Phlebotomine* sandflies and has 2 life cycle stages: (i) Amastigote (intracellular and non-motile form) and (ii) Promastigote (extracellular and motile form). There are a few examples of *Leishmania* species: *L. chagasi*, *L. donovani*, *L. infantum*, *L. major* and *L. braziliensis* which cause leishmaniasis and can be fatal if untreated. Approximately, 900,000 to 1,300,000 leishmaniasis cases with 20,000 to 30,000 people dying annually, mostly in neglected and poor countries in Africa [13]. There are 4 types of leishmaniasis, which are visceral, mucocutaneous, cutaneous and diffuse cutaneous leishmaniasis. Of these, visceral leishmaniasis is the most severe form and causes multi-organs involvement. The clinical symptoms vary depending on the type of leishmaniasis, but are mostly cutaneous with clinical symptoms like rashes and skin sores (ulcers and skin erosion). Anti-leishmanial agents like miltefosine, amphotericin B, azoles, diamines have been reported of being effective drugs against *Leishmania* species in certain parts of South Africa, Yemen and Kenya [14].

In recent years, there have been reports on drug resistance of available mono-and combined chemotherapeutic drugs against these parasitic strains mentioned above. Therefore, it is timely to search for new antiprotozoan parasitic agents as an alternative approach for these strains not only due to resistance but also the cost effectiveness, toxicology and long term side effects. To achieve this current modality, antiparasitic agents derived from natural products are therefore the best option to offer treatment for these parasitic diseases particularly to improve the wellbeing of affected people living in marginalized conditions and in limited resource settings.

Materials and methods

The research study was done using electronic literature review methods. In this case, data bases were collected from Medline, PubMed, Science Direct, SciFinder, Google, Shibboleth and Elsevier for the natural products against these 3 selected parasitic diseases caused by *Acanthamoeba* spp., *Leishmania* spp. and *Plasmodium* spp. These published articles were then appraised for their anti-parasitic activities. Of these, 18, 24 and 22 plant extracts were found with strong anti-amoebic, anti-leishmanial and anti-plasmodial activities, respectively. All articles included in this review were based on the selection criteria; (1) type of parasites studied, (2) the effectivity, (3) cytotoxicity level and (4) the potential of its pharmacological constituents, (5) plant fractions, (6) part of the plants used and (7) parasite stages.

Results and discussion

A total of 62 literature reports met the requirements above (**Figure 1**). There were 24 active plant extracts *in vitro* against *Plasmodium falciparum* which showed different IC_{50}. The plants are *Microglossa pyrifolia*, *Clerodendrum rotundifolium Oliv.*, *Corymbia citriodora (Hook.) K.D.Hill*, *Calotropis procera (Aiton) Dryand.*, *Annona squamosa L.*, *Holarrhena pubescens Wall. ex G.Don*, *Tabernaemontana elegans Stapf.*, *Vangueria infausta Burch. subsp. Infausta*, *Stephania rotunda*, *Brucea javanica*, *Zanthoxylum chalybeum*, *Cyperus articulates*, *Cissampelos pareira*, *Erythrina caffra*, *Ochna schweinfurthiana*, *Fuerstia Africana*, *Satureja parvifolia*, *Cinchona succirubra* and *Nauclea latifolia S.M* with different fractions tested at different parts against sphorozoites stage of *Plasmodium* parasite, as shown in **Table 1**. The 3 plant fractions that have good anti-plasmodial activity recorded with the lowest IC_{50} of 0.01, 0.02 and 0.05 µg/ml were *C. rotundifolium Oliv.* leaves water fraction, *C. rotundifolium Oliv.* leaves methanol fraction and *Microglossa pyrifolia* water leaves fraction, respectively. The selection of these plants for experimental studies were based on the novelty since there was no report on anti-plasmodial activity and some of them were still not fully described. It is worthy to note that the *C. rotundifolium Oliv.* leaves water fraction and *C. rotundifolium Oliv.* leaves methanol fraction belong to the family *Lamiaceae* and the *M. pyrifolia* leaves water fraction belongs to the family *Asteracea* spp.

In this review, *M. pyrifolia* had high anti-plasmodial activity when tested against NF54 and FCR3 strains of *P. falciparum.* This finding is supported by a previous study which showed the same plant and its fractions against K39 strains [15] and 3D7 strain of this parasite [16] with high anti-plasmodial activity. This could be due to diterpene 6E-geranylgeraniol-19-oic-acid as a pure compound that has been isolated from the aqueous extract of *M. pyrifolia* [17]. It might also be due to tannins, polar compounds found in *M. pyrifolia* that play a role in high anti-plasmodial activity [18]. Interestingly, the *C. rotundifolium Oliv.* leaves methanol and water fractions demonstrated high anti-plasmodial activity on NF54 and FCR3 strains. So far, there has been no report on the anti-plasmodial activity of *C. rotundifolium*. However, *Clerodendrum myricoides* [19] and *C. phlomidis* [20] have been documented to have high anti-plasmodial activity. Supporting this, a recent study showed the efficacy of *C. rotundifolium* in water extraction against this parasite [21]. Therefore, it is strongly suggested that *Clerodendrum* spp. requires further extensive investigation as it might be a potential source for treating *P. falciparum* malaria in the future.

There were 22 active plant extracts tested *in vitro* against *Leishmania* spp. with different IC_{50}. The plants reviewed were *Solanum lycocarpum*, *Zingiber officinalis Roscoe*, *Vernonia polyanthes*, *Ocimum gratissimum*, *Anisomeles malabarica*, *Ricinus communis*, *Syzygium cumini*, *Hymenaea courbari*, *Hymenaea stignocarpa*, *Jacaranda caroba*, *Jacaranda cuspidifolia*, *Polyalthia suaveolens*, Potato tuber, *Ocimum basilicum*, *Opuntia ficus indica*, *Quercus infectoria Olivier*, *Pentalinon andrieuxii*, *Calendula officinalis*, *Datura stramonium* and *Salvia officinalis* with different fractions tested at different parts against amastigotes and promastigotes stages of *Leishmania* spp., (**Table 2**). Of these, the ethanol extracts of *H. stignocarpa* leaves (4.69 µg/ml), *J. cuspidifolia* leaves (10.96 µg/ml) and *J. caroba* leaves (13.22 µg/ml) have shown promising results on anti-leishmanial activity against promastigote stage with the lowest IC_{50} readings. Both plants in ethanol extracts of *Jacaranda: J. caroba* and *J. cuspidifolia* revealed high anti-leishmanial activities. Based on a previous study, it has been confirmed that those extracts reduce the level of parasite burden [22]. Further isolation has been done and it is found that there were tannins, flavonoids, alkaloids, steroids and saponins compounds in these extracts [22]. To date, no study has been reported on these plants, hence it deserves further investigation to validate the findings. It is still novel for the *H. stignocarpa* extract against leishmaniasis. Interestingly, the extracts which have a selective index (SI) between murine macrophages and *L. amazonensis* value range in between 0.2 and 4.0 are not considered to be anti-leishmanial agents [23]. However, it was reported to have a promising IC_{50} reading value of 4.69 µg/ml, but its selective index (SI) between murine macrophages and *L. amazonensis* value obtained in their experiment of *H. stignocarpa* was 7.4 hence it was also not considered to be an anti-leishmanial agent [22].

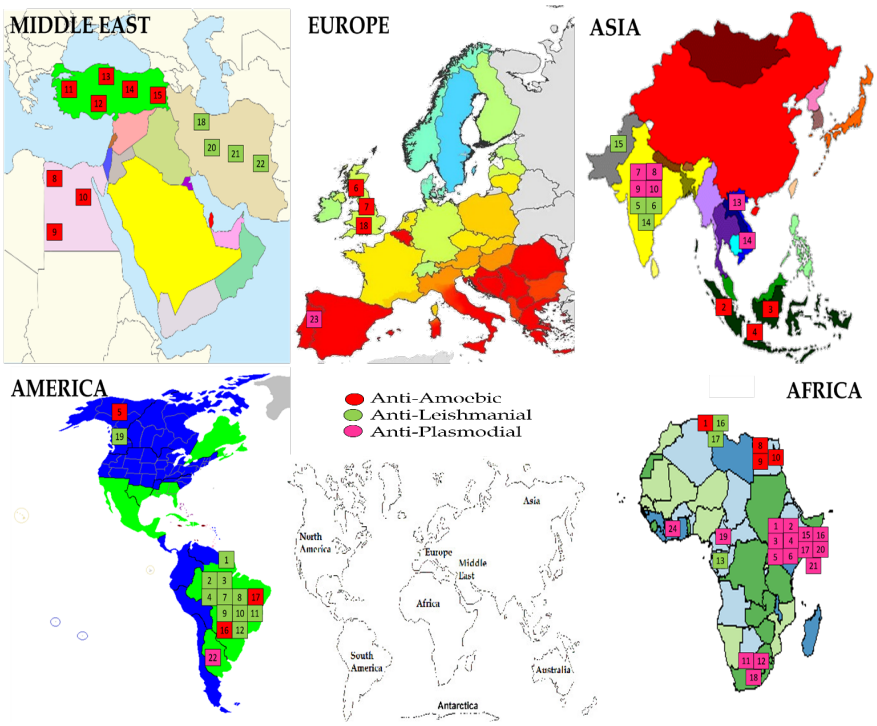

Figure 1 Global report on Natural products against *Acanthamoeba*, *Leishmania* and *Plasmodium* spp.

Table 1 Mini review of anti-plasmodial activity of plants all around the world.

No.	Country	Plant name	Plant part	Solvents	Parasite	Parasite stage	IC_{50} value	Reference
1	Uganda	*Microglossa pyrifolia*	L	EA	*P. falciparum*	Sporozoite	0.05 µg/ml	Adia *et al.* (2016)
2	Uganda	*Microglossa pyrifolia*	L	M	*P. falciparum*	Sporozoite	0.99 µg/ml	Adia *et al.* (2016)
3	Uganda	*Microglossa pyrifolia*	L	W	*P. falciparum*	Sporozoite	0.05 µg/ml	Adia *et al.* (2016)
4	Uganda	*Clerodendrum rotundifolium Oliv.*	L	EA	*P. falciparum*	Sporozoite	0.21 µg/ml	Adia *et al.* (2016)
5	Uganda	*Clerodendrum rotundifolium Oliv.*	L	M	*P. falciparum*	Sporozoite	0.02 µg/ml	Adia *et al.* (2016)
6	Uganda	*Clerodendrum rotundifolium Oliv.*	L	W	*P. falciparum*	Sporozoite	0.01 µg/ml	Adia *et al.* (2016)
7	India	*Corymbia citriodora*	L	E	*P. falciparum*	Sporozoite	≤ 5 mg/ml	Singh *et al.* (2015)
8	India	*Calotropis procera*	L	E	*P. falciparum*	Sporozoite	≤ 5 mg/ml	Singh *et al.* (2015)
9	India	*Annona squamosa L.*	L	E	*P. falciparum*	Sporozoite	≤ 5 mg/ml	Singh *et al.* (2015)
10	India	*Holarrhena pubescens*	S	E	*P. falciparum*	Sporozoite	≤ 5 mg/ml	Singh *et al.* (2015)
11	South Africa	*Tabernaemontana elegans*	S	DCM: M	*P. falciparum*	Sporozoite	0.33 µg/ml	Bapela *et al.* (2014)
12	South Africa	*Vangueria infausta*	R	DCM: M	*P. falciparum*	Sporozoite	1.84 µg/ml	Bapela *et al.* (2014)
13	Cambodia	*Stephania rotunda*	L,S	DCM	*P. falciparum*	Sporozoite	< 1 µg/ml	Hout *et al.* (2006)
14	Cambodia	*Brucea javanica*	R	DCM	*P. falciparum*	Sporozoite	< 3 µg/ml	Hout *et al.* (2006)
15	Kenya	*Zanthoxylum chalybeum*	WP	M	*P. falciparum*	Sporozoite	3.65 µg/ml	Rukunga *et al.* (2009)
16	Kenya	*Cyperus articulatus*	WP	M	*P. falciparum*	Sporozoite	4.84 µg/ml	Rukunga *et al.* (2009)
17	Kenya	*Cissampelos pareira*	WP	M	*P. falciparum*	Sporozoite	5.85µg/ml	Rukunga *et al.* (2009)
18	South Africa	*Erythrina caffra*	S	H	*P. falciparum*	Sporozoite	< 10 µg/ml	Chukwujekwu *et al.* (2016)
19	Cameroon	*Ochna schweinfurthiana*	R	EA	*P. falciparum*	Sporozoite	0.71 µg/ml	Messi *et al.* (2016)
20	Kenya	*Fuerstia africana*	R	PE	*P. falciparum*	Sporozoite	6.3 µg/ml	Kigondu *et al.* (2011)
21	Kenya	*Fuerstia africana*	R	EA	*P. falciparum*	Sporozoite	13.5 µg/ml	Kigondu *et al.* (2011)
22	Argentina	*Satureja parvifolia*	WP	M	*P. falciparum*	Sporozoite	3 µg/ml	Debenedetti *et al.* (2002)
23	Portugal	*Cinchona succirubra*	WP	M:W	*P. falciparum*	Sporozoite	< 10 µg/ml	Madureira *et al.* (2002)
24	Ivory coast	*Nauclea latifolia S.M*	S,R	W	*P. falciparum*	Sporozoite	2.5 µg/ml	Benoit-Vical *et al.* (1998)

WP-whole plants, R-roots, L-leaves, S-stembarks, EA-Ethyl acetate, E-ethanol, M- methanol, DCM-dichloromethane, H-Hexane, W-water, P-*Plasmodium*.

So far, only 16 plant extracts have been evaluated i*n vitro* against *Acanthamoeba* spp. and each showed a different IC_{50} value. The plants reviewed were *Limouni olive oil*, *Buddleja cordata*, *Origanum syriacum*, *Origanum laevigatum*, *Asbestopluma hypogaea*, *Curcuma longa*, *Pancratium maritimum*, *Satureja cuneifolia*, *Melissa officinalis*, *Peucedanum longibracteolatum*, *Thymus sipyleus subsp. sipyleus var. sipyleus*, *Allium scrodoprosum*, *Pterocaulon polystachyum*, *Piper hispidinervum* and *Teucrium chamaedrys* with different fractions tested at different parts against cyst and trophozoites of *Acanthamoeba* spp. (**Table 3**). Six plants exhibited similar IC_{50} values and had significant anti-amoebicidal activities against both cysts and trophozoites: *Satureja cuneifolia* whole plants methanol extracts, *M. officinalis* whole plants methanol extracts, *P. longibracteolatum* whole plants methanol extracts, *T. sipyleus subsp. sipyleus var. sipyleus* fruits methanol extracts, *A. scrodoprosum* whole plants methanol extracts and *P. polystachyum* aerial hexane extracts (**Table 3**). Malatyali *et al.* [24,25] claimed that the amoebicidal actions are stronger in *S. cuneifolia* methanol extracts and *P. longibracterolatum* methanol extracts compared to *M. officinalis* methanol extracts due to interactions of the active phytochemicals with the cell wall of the parasites. However, Rodio *et al.* [26] noted that fractions other than methanolic extracts of *P. polystachyum* such as hexane and dichloromethane, have higher amoebicidal activities and were active in killing trophozoites and cysts due to the lipophilic character of the sample. *T. sipyleus subsp. sipyleus var. sipyleus* fruits and *A. scrodoprosum* whole plants methanol extracts are considered to have amoebicidal and cystidal properties against both trophozoites and cysts, but no cytotoxicity activity was found in the corneal epithelium cultures [27,28].

Table 2 Mini review of anti-leishmanial plants activity all around the world.

No.	Country	Plant name	Plant part	Solvent	Parasite	Parasite stage	IC_{50} value	Reference
1	Surinamese	*Solanum lycocarpum*	L	WP	*L. guyanensis*	Promastigote	51 µg/ml	Mans *et al*. (2016)
2	Brazil	*Zingiber officinalis Roscoe*	R	W	*L. amazonensis*	Promastigote	49.8 mg/ml	Duarte *et al*. (2016)
3	Brazil	*Vernonia polyanthes*	L	M	*L. amazonensis*	Promastigote	4 g/ml	Braga *et al*. (2007)
4	Brazil	*Ocimum gratissimum*	L	M	*L. chagasi*	Promastigote	71 g/ml	Braga *et al*. (2007)
5	South India	*Anisomeles malabarica*	L	M	*L. donovani*	Promastigote	126 µg/ml	Zahir *et al.* (2012)
6	South India	*Ricinus communis*	L	M	*L. donovani*	Promastigote	184 µg/ml	Zahir *et al*. (2012)
7	Brazil	*Syzygium cumini*	L	H	*L. amazonensis*	Promastigote	31.64 µg/ml	Ribeiro *et al*. (2014)
8	Brazil	*Hymenaea courbaril*	L	E	*L. amazonensis*	Promastigote	44.10 µg/ml	Ribeiro *et al*. (2014)
9	Brazil	*Hymenaea courbaril*	L	H	*L. amazonensis*	Promastigote	35.84 µg/ml	Ribeiro *et al*. (2014)
10	Brazil	*Hymenaea stignocarpa*	L	E	*L. amazonensis*	Promastigote	4.69 µg/ml	Ribeiro *et al*. (2014)
11	Brazil	*Jacaranda caroba*	L	E	*L. amazonensis*	Promastigote	13.22 µg/ml	Ribeiro *et al.* (2014)
12	Brazil	*Jacaranda cuspidifolia*	L	E	*L. amazonensis*	Promastigote	10.96 µg/ml	Ribeiro *et al.* (2014)
13	Gabon	*Polyalthia suaveolens*	S, L	M	*L. infantum*	Promastigote	< 1 mg/ml	Lamidi *et al.* (2005)
14	India	Potato tuber	WP	SBS	*L. donovani*	Promastigote	312.5 µg/ml	Paik *et al.* (2014)
15	Pakistan	*Ocimum basilicum*	L	M	*L. tropica*	Promastigote	21.67 µg/ml	Khan *et al*. (2015)
16	Tunisia	*Opuntia ficus indica*	C, F	EA	*L. major*	Promastigote	53.9 µg/ml	Bargougui *et al.* (2014)
17	Tunisia	*Opuntia ficus indica*	C	M	*L. donovani*	Promastigote	45.2 µg/ml	Bargougui *et al.* (2014)
18	Iran	*Quercus infectoria Olivier*	WP	M	*L. major*	Promastigote	12.65 mg/ml	Kheirandish *et al.* (2016)
19	Mexico	*Pentalinon andrieuxii*	R	M	*L. mexicana*	Amastigotes	0.03 µM	Pan *et al.* (2012)
20	Iran	*Calendula officinalis*	F	M	*L. major*	Promastigote	108.19 µg/ml	Nikmehr *et al.* (2014)
21	Iran	*Datura stramonium*	F	M	*L. major*	Promastigote	155.15 µg/ml	Nikmehr *et al.* (2014)
22	Iran	*Salvia officinalis*	R	M	*L. major*	Promastigote	184.32 µg/ml	Nikmehr *et al.* (2014)

WP-whole plants, R-roots, L-leaves, S-stembarks, F-fruits, C-cladode, EA-Ethyl acetate, E-ethanol, M-methanol, H-Hexane, W-water, SBS-Sodium bisulfite, L-*Leishmania*.

Table 3 MiniReview of anti-amoebicidal plants activity all around the world.

No.	Country	Plant name	Plant part	Solvent	Parasite	Parasite stage	IC_{50} value	Reference
1	Tunisia	Limouni olive oil	L	EA	*A. castellanii*	Trophozoites	5.11 µg/ml	Sifaoui *et al*. (2014)
2	Indonesia	*Ipomoeae* sp.	L	M C, M	*A. culbertsoni, A. castellanii & A. polyphaga*	Cysts & trophozoites	N/A	Chu *et al.* (1998)
3	Indonesia	*Kaempferia. galangal*	L	M C, M	*A. culbertsoni, A. castellanii & A. polyphaga*	Cysts & trophozoites	N/A	Chu *et al*. (1998)
4	Indonesia	*Graphyllium panduratum*	L	M C, M	*A. polyphaga*	Cysts & trophozoites	N/A	Chu *et al.* (1998)
5	Mexico	*Buddleja cordata*	R, S, B, L, F	EA	*A. Castellanii & A. polyphaga*	N/A	8 mg/ml	Rodrıguez-Zaragoza *et al.* (1999)
6	UK	*Origanum syriacum*	WP	M	*A. castellanii*	Cysts&trophozoites	N/A	Degerli *et al.* (2012)
7	UK	*Origanum laevigatum.*	WP	M	*A. castellanii*	Cysts&trophozoites	N/A	Degerli *et al*. (2012)
8	Egypt	*Asbestopluma hypogaea*	WP	E	*A. castellanii*	Cysts&trophozoites	100 mg/ml	El-Sayed *et al.* (2011)
9	Egypt	*Curcuma longa*	WP	E	*A. castellanii*	Cysts&trophozoites	100 mg/ml	El-Sayed *et al*. (2011)
10	Egypt	*Pancratium maritimum*	WP	E	*A. castellanii*	Cysts&trophozoites	200 mg/ml	El-Sayed *et al*. (2011)
11	Turkey	*Satureja cuneifolia*	WP	M	*A. castellanii*	Cysts&trophozoites	32 mg/ml	Malatyali *et al*. (2012)
12	Turkey	*Melissa officinalis*	WP	M	*A. castellanii*	Cysts&trophozoites	32 mg/ml	Malatyali *et al*. (2012)
13	Turkey	*Peucedanum longibracteolatum*	WP	M	*A. castellanii*	Cysts&trophozoites	32 mg/ml	Malatyali *et al.* (2012)
14	Turkey	*Thymus sipyleus*	F	M	*A. castellanii*	Cysts& tropozoites	32 mg/ml	Polat *et al.* (2007)
15	Turkey	*Allium scrodoprosum*	WP	M	*A. castellanii*	Cysts& tropozoites	32 mg/ml	Polat *et al.* (2007)
16	Brazil	*Pterocaulon polystachyum*	Ae	H	*A. castellanii*	Trophozoites	32 mg/ml	Rodio *et al.* (2008)
17	Brazil	*Piper hispidinervum*	Ae	N/A	*A. polyphaga*	Trophozoites	0.5 mg/ml	Sauter *et al.* (2012)
18	UK	*Teucrium chamaedrys*	WP	M	*A. castellanii*	Cyst&trophozoites	16 mg/ml	Tepe *et al.* (2012)

Ae-aerial, WP-whole plants, R-roots, L-leaves, S-stembarks, F-fruits, EA-Ethyl acetate, C-chloroform, E-ethanol, M-methanol, H-Hexane, W-water, A-*Acanthamoeba*, UK-United Kingdom

Conclusions

Based on this literature review, natural products can be used as alternatives in the pharmaceutical industry, as some of the plants work effectively as antiparasitic agents. However, the novelty of their ethnobotanical, ethnopharmacological and mode of actions is not fully understood. Therefore, more additional research work and investigations on natural products are urgently needed to be done for the future therapeutic agents. Likewise the identification and isolation of the potent chemical compounds from the plant fractions are of great interest especially to study pharmacokinetics and pharmacodynamics properties.

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