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 IC50 of 0.01, 0.02 and 0.05 µg/ml in vitro. Limouni olive is a strong amoebicidal agent with IC50 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 IC50 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, amphoterin C, 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 parasite 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* Brucke 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 spherorozites 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 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 Asteraceae 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 stigmocarpa*, *Jacaranda caroba*, *Jacaranda cuspidifolia*, *Polyalthia suaveolens*, *Potato tuber*, *Ocimum basilicum*, *Opuntia ficus indica*, *Quercus infectoria* Olivier, *Pentalinon andrietzii*, *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].
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Table 1 Mini review of anti-plasmodial activity of plants all around the world.

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

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

Figure 1 Global report on Natural products against Acanthamoeba, Leishmania and Plasmodium spp.
So far, only 16 plant extracts have been evaluated in 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 sipyileus* subsp. *sipyileus* var. *sipyileus*, *Allium scrodoprosom*, *Pierocaulon polyschachyum*, *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. *sipyileus* var. *sipyileus* fruits methanol extracts, *A. scrodoprosom* whole plants methanol extracts and *P. polyschachyum* aerial hexane extracts (Table 3). Malayali et al. [24,25] claimed that the amoebicidal actions are stronger in *S. cuneifolia* methanol extracts and *P. longibracteolatum* 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. polyschachyum* 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. *sipyileus* var. *sipyileus* fruits and *A. scrodoprosom* 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.

<table>
<thead>
<tr>
<th>No.</th>
<th>Country</th>
<th>Plant name</th>
<th>Plant part</th>
<th>Solvent</th>
<th>Parasite stage</th>
<th>IC_{50} value</th>
<th>Reference</th>
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<tbody>
<tr>
<td>1</td>
<td>Suriname</td>
<td>Solanum lycocarpum</td>
<td>L</td>
<td>WP</td>
<td>Promastigote</td>
<td>51 µg/ml</td>
<td>Mans et al. (2016)</td>
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<tr>
<td>2</td>
<td>Brazil</td>
<td>Zingiber officinalis Roscoe</td>
<td>R</td>
<td>W</td>
<td>Promastigote</td>
<td>49.8 mg/ml</td>
<td>Duarte et al. (2016)</td>
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<tr>
<td>3</td>
<td>Brazil</td>
<td>Vernonia poytanthes</td>
<td>L</td>
<td>M</td>
<td>Promastigote</td>
<td>4 mg/ml</td>
<td>Braga et al. (2007)</td>
</tr>
<tr>
<td>4</td>
<td>Brazil</td>
<td>Ocimum gratissimum</td>
<td>L</td>
<td>M</td>
<td>Chagasi</td>
<td>71 mg/ml</td>
<td>Braga et al. (2007)</td>
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<tr>
<td>5</td>
<td>South India</td>
<td>Anisomeles malabarica</td>
<td>L</td>
<td>M</td>
<td>Donovani</td>
<td>126 µg/ml</td>
<td>Zahir et al. (2012)</td>
</tr>
<tr>
<td>6</td>
<td>South India</td>
<td>Ricinus communis</td>
<td>L</td>
<td>M</td>
<td>Donovani</td>
<td>184 µg/ml</td>
<td>Zahir et al. (2012)</td>
</tr>
<tr>
<td>7</td>
<td>Brazil</td>
<td>Syzygium cumini</td>
<td>L</td>
<td>H</td>
<td>Promastigote</td>
<td>31.64 µg/ml</td>
<td>Ribeiro et al. (2014)</td>
</tr>
<tr>
<td>8</td>
<td>Brazil</td>
<td>Hymenea courtarit</td>
<td>L</td>
<td>E</td>
<td>Promastigote</td>
<td>44.10 µg/ml</td>
<td>Ribeiro et al. (2014)</td>
</tr>
<tr>
<td>9</td>
<td>Brazil</td>
<td>Hymenea courtarit</td>
<td>L</td>
<td>H</td>
<td>Promastigote</td>
<td>35.84 µg/ml</td>
<td>Ribeiro et al. (2014)</td>
</tr>
<tr>
<td>10</td>
<td>Brazil</td>
<td>Hymenea stignocarpura</td>
<td>L</td>
<td>E</td>
<td>Promastigote</td>
<td>4.69 µg/ml</td>
<td>Ribeiro et al. (2014)</td>
</tr>
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<td>Brazil</td>
<td>Jacaranda caroba</td>
<td>L</td>
<td>E</td>
<td>Promastigote</td>
<td>13.22 µg/ml</td>
<td>Ribeiro et al. (2014)</td>
</tr>
<tr>
<td>12</td>
<td>Brazil</td>
<td>Jacaranda cuspidifolia</td>
<td>L</td>
<td>E</td>
<td>Promastigote</td>
<td>10.96 µg/ml</td>
<td>Ribeiro et al. (2014)</td>
</tr>
<tr>
<td>13</td>
<td>Gabon</td>
<td>Polyalthia suaveolens</td>
<td>S, L</td>
<td>M</td>
<td>Infantum</td>
<td>&lt; 1 mg/ml</td>
<td>Lamidi et al. (2005)</td>
</tr>
<tr>
<td>14</td>
<td>India</td>
<td>Potato tuber</td>
<td>WP</td>
<td>SBS</td>
<td>Promastigote</td>
<td>312.5 µg/ml</td>
<td>Paik et al. (2014)</td>
</tr>
<tr>
<td>15</td>
<td>Pakistan</td>
<td>Ocimum basilicum</td>
<td>L</td>
<td>M</td>
<td>Tropica</td>
<td>21.67 µg/ml</td>
<td>Khan et al. (2015)</td>
</tr>
<tr>
<td>16</td>
<td>Tunisia</td>
<td>Opuntia ficus indica</td>
<td>C, F</td>
<td>EA</td>
<td>Promastigote</td>
<td>53.9 µg/ml</td>
<td>Bargougui et al. (2014)</td>
</tr>
<tr>
<td>17</td>
<td>Tunisia</td>
<td>Opuntia ficus indica</td>
<td>C</td>
<td>M</td>
<td>Donovani</td>
<td>45.2 µg/ml</td>
<td>Bargougui et al. (2014)</td>
</tr>
<tr>
<td>18</td>
<td>Iran</td>
<td>Quercus infectoria Oliver</td>
<td>WP</td>
<td>M</td>
<td>Major</td>
<td>12.65 mg/ml</td>
<td>Kheirandish et al. (2016)</td>
</tr>
<tr>
<td>19</td>
<td>Mexico</td>
<td>Pentalinon andristi</td>
<td>R</td>
<td>M</td>
<td>Mexicanana</td>
<td>0.03 µM</td>
<td>Pan et al. (2012)</td>
</tr>
<tr>
<td>20</td>
<td>Iran</td>
<td>Calendula officinalis</td>
<td>R</td>
<td>M</td>
<td>Major</td>
<td>108.19 µg/ml</td>
<td>Nikmeht et al. (2014)</td>
</tr>
<tr>
<td>21</td>
<td>Iran</td>
<td>Datura stramonium</td>
<td>F</td>
<td>M</td>
<td>Major</td>
<td>155.15 µg/ml</td>
<td>Nikmeht et al. (2014)</td>
</tr>
<tr>
<td>22</td>
<td>Iran</td>
<td>Salvia officinalis</td>
<td>R</td>
<td>M</td>
<td>Major</td>
<td>184.32 µg/ml</td>
<td>Nikmeht et al. (2014)</td>
</tr>
</tbody>
</table>

WP-whole plants, R-roots, L-leaves, S-stem bark, 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.

<table>
<thead>
<tr>
<th>No.</th>
<th>Country</th>
<th>Plant name</th>
<th>Plant part</th>
<th>Solvent</th>
<th>Parasite</th>
<th>Parasite stage</th>
<th>IC50 value</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Tunisia</td>
<td>Limoumi olive oil</td>
<td>L</td>
<td>EA</td>
<td>A. castellanii</td>
<td>Trophozoites</td>
<td>5.11 µg/ml</td>
<td>Sifaioui et al. (2014)</td>
</tr>
<tr>
<td>2</td>
<td>Indonesia</td>
<td>Ipomoeae sp.</td>
<td>L</td>
<td>M</td>
<td>A. culbertsonii, C, A. castellanii &amp; M</td>
<td>Cysts &amp; trophozoites</td>
<td>N/A</td>
<td>Chu et al. (1998)</td>
</tr>
<tr>
<td>3</td>
<td>Indonesia</td>
<td>Kaempferia. galangal</td>
<td>L</td>
<td>M</td>
<td>A. culbertsonii, C, A. castellanii &amp; M</td>
<td>Cysts &amp; trophozoites</td>
<td>N/A</td>
<td>Chu et al. (1998)</td>
</tr>
<tr>
<td>4</td>
<td>Indonesia</td>
<td>Graphyllium panduratum</td>
<td>L</td>
<td>M</td>
<td>A. polyphaga</td>
<td>Cysts &amp; trophozoites</td>
<td>N/A</td>
<td>Chu et al. (1998)</td>
</tr>
<tr>
<td>5</td>
<td>Mexico</td>
<td>Buddleja cordata</td>
<td>R, S, B, L, F</td>
<td>EA</td>
<td>A. Castellanii &amp; A. polyphaga</td>
<td>N/A</td>
<td>8 mg/ml</td>
<td>Rodriguez-Zaragoza et al. (1999)</td>
</tr>
<tr>
<td>6</td>
<td>UK</td>
<td>Origanum syriacum</td>
<td>WP</td>
<td>M</td>
<td>A. castellanii</td>
<td>Cysts&amp;trophozoites</td>
<td>N/A</td>
<td>Degerli et al. (2012)</td>
</tr>
<tr>
<td>7</td>
<td>UK</td>
<td>Origanum laevigatum</td>
<td>WP</td>
<td>M</td>
<td>A. castellanii</td>
<td>Cysts&amp;trophozoites</td>
<td>N/A</td>
<td>Degerli et al. (2012)</td>
</tr>
<tr>
<td>8</td>
<td>Egypt</td>
<td>Asbestopluma hypogaea</td>
<td>WP</td>
<td>E</td>
<td>A. castellanii</td>
<td>Cysts&amp;trophozoites</td>
<td>100 mg/ml</td>
<td>El-Sayed et al. (2011)</td>
</tr>
<tr>
<td>9</td>
<td>Egypt</td>
<td>Curcuma longa</td>
<td>WP</td>
<td>E</td>
<td>A. castellanii</td>
<td>Cysts&amp;trophozoites</td>
<td>100 mg/ml</td>
<td>El-Sayed et al. (2011)</td>
</tr>
<tr>
<td>10</td>
<td>Egypt</td>
<td>Pancratium maritimum</td>
<td>WP</td>
<td>E</td>
<td>A. castellanii</td>
<td>Cysts&amp;trophozoites</td>
<td>200 mg/ml</td>
<td>El-Sayed et al. (2011)</td>
</tr>
<tr>
<td>11</td>
<td>Turkey</td>
<td>Satureja cuneifolia</td>
<td>WP</td>
<td>M</td>
<td>A. castellanii</td>
<td>Cysts&amp;trophozoites</td>
<td>32 mg/ml</td>
<td>Malatyali et al. (2012)</td>
</tr>
<tr>
<td>12</td>
<td>Turkey</td>
<td>Melissa officinalis</td>
<td>WP</td>
<td>M</td>
<td>A. castellanii</td>
<td>Cysts&amp;trophozoites</td>
<td>32 mg/ml</td>
<td>Malatyali et al. (2012)</td>
</tr>
<tr>
<td>13</td>
<td>Turkey</td>
<td>Peucedanum longibracteolatum</td>
<td>WP</td>
<td>M</td>
<td>A. castellanii</td>
<td>Cysts&amp;trophozoites</td>
<td>32 mg/ml</td>
<td>Malatyali et al. (2012)</td>
</tr>
<tr>
<td>14</td>
<td>Turkey</td>
<td>Thymus sylveus</td>
<td>F</td>
<td>M</td>
<td>A. castellanii</td>
<td>Cysts&amp;trophozoites</td>
<td>32 mg/ml</td>
<td>Polat et al. (2007)</td>
</tr>
<tr>
<td>15</td>
<td>Turkey</td>
<td>Alium scrodoprossum</td>
<td>WP</td>
<td>M</td>
<td>A. castellanii</td>
<td>Cysts&amp;trophozoites</td>
<td>32 mg/ml</td>
<td>Polat et al. (2007)</td>
</tr>
<tr>
<td>16</td>
<td>Brazil</td>
<td>Pterocaulon polystachyum</td>
<td>Ae</td>
<td>H</td>
<td>A. castellanii</td>
<td>Trophozoites</td>
<td>32 mg/ml</td>
<td>Rodio et al. (2008)</td>
</tr>
<tr>
<td>17</td>
<td>Brazil</td>
<td>Piper hispidinervum</td>
<td>Ae</td>
<td>N/A</td>
<td>A. polyphaga</td>
<td>Trophozoites</td>
<td>0.5 mg/ml</td>
<td>Sauter et al. (2012)</td>
</tr>
<tr>
<td>18</td>
<td>UK</td>
<td>Teucrium chamaedrys</td>
<td>WP</td>
<td>M</td>
<td>A. castellanii</td>
<td>Cysts&amp;trophozoites</td>
<td>16 mg/ml</td>
<td>Tepe et al. (2012)</td>
</tr>
</tbody>
</table>

Ae-aerial, WP-whole plants, R-roots, L-leaves, S-stem bark, 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.

Acknowledgements

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http://wjst.wu.ac.th


