

A review of the most important native medicinal plants of Iran effective on cutaneous Leishmaniasis in mouse model

Leishmaniasis is a zoonotic parasitic disease that is caused by different *Leishmania* species. Most cases of Leishmaniasis are reported from Afghanistan, Saudi Arabia, Algeria, Brazil, Iraq, and Iran. Antimony compounds have long been used as standard treatment and first line drugs for Leishmaniasis, but *Leishmania* species have recently acquired drug resistance. Nowadays, medicinal plants are being increasingly used to treat parasitic diseases especially Leishmaniasis. In this review, the search terms *Leishmania*, Leishmaniasis, mouse, Iran, and medicinal plants were used to retrieve publications from databases such as Scopus, Islamic World Science Citation Center, Scientific Information Database, and Magiran. According to the results of this review, nine medicinal plants, *Eucalyptus camaldulensis*, *Matricaria chamomilla*, *Cathartus roseus*, *Echinacea purpurea*, *Lawsonia inermis*, *Artemisia sieberi*, *Berberis vulgaris*, *Allium sativum L.*, and *Lavandula spica L.* have been reported to be effective on Leishmaniasis wound in mouse model. Lawson, berberine, jatrorrhizine, colombamine, palmatine, oxyacanthine, berbamine, berulicin, magnoflorine, allicin, eucalyptol, paracymene, alpha-pinene, caffeic acids, alkylamides, echinacosides, glycoproteins, polysaccharide, chamazulene, pigenin, trihydroxyflavone, and patholiterin, berberrubine, flavonoid compounds, santonin, and coumarin are the active compounds of the native medicinal plants of Iran that are effective on Leishmaniasis wound.

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Introduction

Leishmaniasis is a zoonotic parasitic disease that is caused by different *Leishmania* species [1]. The most common form of Leishmaniasis is cutaneous that is widely known as Salak in Iran [2]. Each year, around two million cases of Leishmaniasis are reported [3]. In Iran, about 15000 cases of cutaneous Leishmaniasis occur each year [4]. Depending on the type of *Leishmania* species, Leishmaniasis causes a wide spectrum of clinical manifestations [5]. Most cases of Leishmaniasis are reported from Afghanistan, Saudi Arabia, Algeria, Brazil, Iraq, and Iran [6].

Antimony compounds have long been used as standard treatment and first line drugs for Leishmaniasis. These drugs require repeated injections and therefore are not well tolerated by the patients, which is a reason for low efficiency of such drugs [7]. In the recent years, *Leishmania* species have acquired drug resistance [8,9]. Although the cause of Leishmaniasis has long

been detected, there has not yet been any definite treatment for cutaneous Leishmaniasis [5].

Complementary and alternative medicine refers to those medical interventions that are not widely taught in medical schools and are not commonly accessible in hospitals [10]. Complementary and alternative medicine includes several disciplines, namely phytotherapy, message therapy, and acupuncture, most of which were derived from nations' cultures and histories [11]. Herbal medicine and phytotherapy have long attracted public attention [12-15]. Medicinal plants represent the most important constituent of phytotherapy. Medicinal plants are those plants whose one or more organs contain active compounds [16-21].

Medicinal plants are closely linked with the history of human life. Man in all historical periods has needed medicinal plants to relieve his physical suffering, and using these plants has always been one of the effective methods of treatment [22]. Nowadays, medicinal plants are

being increasingly used to treat parasitic diseases especially Leishmaniasis [23-26].

Materials and methods

In this review, the search terms *Leishmania*, Leishmaniasis, mouse, Iran, and medicinal plants were used to retrieve publications from databases such as Scopus, Islamic World Science Citation Center, Scientific Information Database, and Magiran. Then, the relevant articles were reviewed.

Results

According to the results of this review, nine medicinal plants, *Eucalyptus camaldulensis*, *Matricaria chamomilla*, *Cathrantus roseus*, *Echinacea purpurea*, *Lawsonia inermis*, *Artemisia sieberi*, *Berberis vulgaris*, *Allium sativum* L.,

and *Lavandula spica* L., have been reported to be effective on Leishmaniasis wound in mouse model (TABLE 1).

Discussion

According to the evidence on medicinal plants in Iran, *E. camaldulensis*, *M. chamomilla*, *C. roseus*, *E. purpurea*, *L. inermis*, *A. sieberi*, *B. vulgaris*, *A. sativum*, and *L. spica* are effective on Leishmaniasis wound. *L. inermis* has antimicrobial effect and its active compound is lawson [27-36]. *B. vulgaris* has hypotensive effect [37,38]. This plant contains berberine, jatrorrhizine, colombamine, palmatine, oxyacanthine, berbamine and magnoflorine [39,40]. *A. sativum* has antibacterial, antiviral, and antifungal effects [41-45]. Allicin is the main compound of *A. sativum* [46,47]. In

Table 1. The native medicinal plants of Iran effective on leishmaniasis wound in mouse model.

Row	Scientific name	Family name	Persian name	Effect/Description	Ref.
1	<i>Eucalyptus camaldulensis</i>	Myrtaceae	Eucalyptus	An interventional-experimental study on BALB/c mice demonstrated that 40 µg/ml of methanolic <i>E. camaldulensis</i> extract exerted anti-leishmaniasis effect on cutaneous leishmaniasis due to an Iranian strain <i>Leishmania major</i> .	[26]
2	<i>Matricaria chamomilla</i>	Asteraceae	Chamomile	An interventional-experimental study on BALB/c mice demonstrated that leishmaniasis wound improved in 58.3% of group treated with <i>M. chamomilla</i> tea.	[27]
3	<i>Cathrantus roseus</i>	Apocynaceae	Vinca	An interventional-experimental study on BALB/c mice demonstrated that 30 µg/ml of purified <i>C. roseus</i> extract caused improvement of leishmaniasis wound due to <i>L. major</i> .	[28]
4	<i>Echinacea purpurea</i>	Asteraceae	purple coneflower	An interventional-experimental study on laboratory mice demonstrated that 200 µg/ml of purified <i>E. purpurea</i> extract caused improvement of leishmaniasis wound due to <i>L. major</i> .	[29]
5	<i>Lawsonia inermis</i>	Lythraceae	Henna	An interventional-experimental study on BALB/c mice demonstrated that ethanolic <i>L. inermis</i> extract 80% ointment caused decrease in the diameter of leishmaniasis wound due to <i>L. major</i> .	[30]
6	<i>Artemisia sieberi</i>	Asteraceae	Sagebrush	An interventional-experimental study on BALB/c mice demonstrated that hydroalcoholic <i>A. sieberi</i> extract 5% ointment caused decrease in the diameter of leishmaniasis wound due to <i>L. major</i> .	[31]
7	<i>Berberis vulgaris</i>	Berberidaceae	Barberry	An interventional-experimental study on BALB/c mice demonstrated that alcoholic <i>B. vulgaris</i> extract 80% ointment caused decrease in the diameter of leishmaniasis wound due to <i>L. major</i> .	[32]
8	<i>Allium sativum</i> L	Amaryllidaceae	Garlic	An interventional-experimental study on BALB/c mice demonstrated that aqueous <i>A. sativum</i> extract ointment caused decrease in the diameter of leishmaniasis wound due to <i>L. major</i> .	[33]
9	<i>Lavandula spica</i> L.	Lamiaceae	Lavender	An interventional-experimental study on BALB/c mice demonstrated that <i>L. spica</i> extract 80% ointment caused decrease in the diameter of leishmaniasis wound due to <i>L. major</i> .	[34]

traditional medicine, *E. camaldulensis* is used to treat infection and common cold [48].

Eucalyptol, paracymentene, and alpha-pinene are some of the compounds of *E. camaldulensis* [49]. *E. purpurea* exerts antioxidant effect [50,51]. This plant contains caffeic acids, alkylamides, echinacosides, glycoproteins, and polysaccharide [52]. Phytochemical investigations demonstrated that *M. chamomilla* contains chamazulene, pigenin, trihydroxyflavone and patholiterin [53]. *B. vulgaris* is rich in antioxidant compounds such as berbamine, berberine, and berberrubine [54,55]. *B. vulgaris* is used to treat diabetes and hypertension [56]. *A. sieberi* contains flavonoid compounds, santonin, and coumarin [57].

The evidence indicates that in addition to anti-worm activity, *A. sieberi* has many biological activities such as microbicidal, antifungal, virucidal, and antiparasitic. Besides that, the analgesic, antioxidant, and vasodilatory effects of this plant were confirmed [58-64].

Lawson, berberine, jatrorrhizine, colombamine, palmatine, oxyacanthine, berbamine, magnoflorine, allicin, eucalyptol, paracymentene, alpha-pinene, caffeic acids, alkylamides, echinacosides, glycoproteins, polysaccharide, chamazulene, pigenin, trihydroxyflavone, sarranoside and patholiterin, berberrubine, flavonoid compounds, santonin, and coumarin are the active compounds of the native medicinal plants of Iran that are effective on Leishmaniasis wound.

The mechanism actions of the presented plants are not clearly established. Plants contain multiple compounds having antimicrobial activities for protection against microorganisms. The mechanisms actions of plant compounds in general have been attributed to various factors including disintegration in cytoplasmic membranes, electron flow, active transport and coagulation of the cell content and destabilization of proton motive force [65,66]. The most important factors responsible for antimicrobial actions are hydrophobic properties that allow lipids penetration from the bacterial cell membranes, disturbing cell structures which in turn imposes more penetration [67]. They also may act on the proteins of cytoplasmic membranes or ATPase enzymes located on cytoplasmic membranes which are surrounded by lipid molecules, or cause distortion of lipid-protein interaction, or interact with hydrophobic parts of the proteins or act on the enzymes which are involved in the synthesis of microbial structural sections [68-70]. In some

plants, terpenes, for example, obtained from essences have high level of antibacterial activities [65]. Phenolic compounds have been shown to mostly have antibacterial and anti-Leishmania activities. These compounds are available in a lot of plants. Hence, these herbs may also possess anti-Leishmania activities. In sum, plants have been used since ancient times by various communities for treatment various of diseases, including Leishmaniasis. Medicinal plants have the potential for the production of new drugs to be used as alternative or complementary with conventional drugs. They may decrease the costs and improve the quality of treatment.

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