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Phytotherapy for Healing of Invasive Infectious Lesions of Cutaneous Leishmaniasis: Effective Medicinal Plants and Analysis of Their Mechanisms of Action

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A B S T R A C T

Objective: Cutaneous leishmaniasis is a skin disease caused by the Leishmania parasite, prevalent in many tropical and subtropical regions. Current treatment options include various chemical drugs that often come with side effects and limited effectiveness. Recently, there has been growing interest in medicinal plants as alternative treatments for this disease. Due to their natural compounds, medicinal plants may offer effective solutions with minimal side effects. This study aims to review and assess the medicinal plants effective against cutaneous leishmaniasis, providing a comprehensive overview of the identified plants and their active compounds that could be beneficial in treating this condition.

Methods: In this review study, keywords such as Leishmania, leishmaniasis, traditional medicine, medicinal plants, and treatment were searched in databases like Google Scholar, SID, Magiran, and Scopus. Irrelevant articles were excluded, and relevant articles were selected for literature review.

Results: Based on the findings, several medicinal plants such as Urtica dioica, Ferula assa-foetida, Artemisia absinthium, Allium sativum, Eucalyptus globulus, Achillea millefolium, Lavandula angustifolia, Myrtus communis, Satureja Khuzestanica, Onosma dichroanthum, Rosmarinus officinalis, Quercus spp., Cassia spp., Capparis spinosa, Linum usitatissimum, Ricinus communis, Juglans regia, Thymus vulgaris, Lawsonia inermis, Mimosa pudica, Aloe vera, Vigna mungo, Berberis vulgaris, Matricaria chamomilla, and Curcuma longa are identified as effective for treating cutaneous leishmaniasis. The families Asteraceae and Lamiaceae, with a frequency of 16%, have the highest representation among the samples, indicating their significance. Other families account for smaller percentages of the overall data. The natural compounds in medicinal plants play a vital role in boosting the immune system, reducing inflammation, and inhibiting parasite growth. These compounds, with antioxidant properties, apoptosis induction in parasites, and anti-inflammatory effects, help cleanse the digestive system and improve general body health.

Conclusion: This study indicates that various medicinal plants, particularly from the Asteraceae and Lamiaceae families, could serve as effective treatments for cutaneous leishmaniasis. The natural compounds in these plants significantly enhance immune function, reduce inflammation, and inhibit parasite growth, leading to notable improvements in general health and disease control. Hence, further research is necessary to identify and utilize these plants in the treatment of cutaneous leishmaniasis.

Keywords: Parasite, Leishmania, Leishmaniasis, Medicinal plants, Lesion, Treatment

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Introduction

Cutaneous leishmaniasis is a parasitic disease caused by the *Leishmania* parasite, transmitted to humans through the bite of infected female phlebotomine sandflies [1]. The disease primarily affects the skin and, if left untreated, can lead to persistent and significant ulcerations [2]. Transmission occurs when an infected sandfly bites a human [3]. These sandflies become carriers after feeding on the blood of a person infected with the *Leishmania* parasite. Risk factors for leishmaniasis include geographic location (tropical and subtropical areas), environmental conditions (such as poor housing and sanitation), and occupations

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involving outdoor work, such as agriculture and construction [4]. The early signs of cutaneous leishmaniasis typically appear a few weeks to months after the bite of an infected sandfly [5]. Initial symptoms often include red bumps and itching at the bite site. If untreated, these lesions can develop into deeper ulcers, leaving permanent scars. Diagnosis of the disease involves a combination of clinical evaluations and specialized tests [6]. Healthcare providers examine skin lesions and take the patient's medical history, with a particular focus on recent travel to endemic areas. Confirmation of the diagnosis is achieved through methods like microscopic examination, parasite cultures, and molecular techniques such as PCR (Polymerase Chain Reaction) [7]. Treatment of cutaneous leishmaniasis depends on the severity of the disease and the specific *Leishmania* species involved [8]. Medications such as sodium stibogluconate and amphotericin B are commonly used. For milder cases, topical treatments and cryotherapy may be employed [9].

Prevention mainly involves protecting against sandfly bites through the use of insect repellents, wearing protective clothing, and sleeping under bed nets [10]. Environmental measures, such as improving sanitation and controlling sandfly populations, are also effective strategies [11]. In traditional medicine, herbal treatments are sometimes used to manage and alleviate the symptoms of cutaneous leishmaniasis [12-14]. However, these methods should be considered as complementary to conventional medical therapies and should be used under the guidance of healthcare professionals for proper management.

In Iran, a variety of medicinal plants have been traditionally used therapies for leishmaniasis. These plants, due to their anti-inflammatory and healing properties, aid in regions and alleviating symptoms. Additionally, certain native Iranian plants with immune-boosting properties are believed to help mitigate the effects of the disease. Nevertheless, while these plants may offer beneficial effects alongside standard treaties are necessary to verify their efficacy and safety as definitive treatments for leishmaniasis. The aim of this review study is to identify medicinal plants effective against cutaneous leishmaniasis t complementary treatments alongside conventional therapies. This comprehensive review seeks to report on these plants' potential role in the control and management of this skin disease.

Methodology

In this review study, a comprehensive search was conducted to gather and evaluate scientific evidence regarding medicinal plants effective in treating cutaneous leishmaniasis. The search was performed across reputable databases including Google Scholar, the Scientific Information Database (SID), Magiran, and Scopus. The search process employed specific keywords such as *Leishmania*, *leishmaniasis*, *traditional medicine*, *medicinal plants*, and *treatment*, using Boolean operators (AND, OR) to identify all relevant articles. Initially, all retrieved articles were screened based on their titles and abstracts. Those that were not directly related to the primary topic were excluded. In the subsequent step, the remaining articles were evaluated according to specific inclusion and exclusion criteria. Studies that focused on traditional treatments for cutaneous leishmaniasis were included in the analysis. The data from various studies were then systematically categorized and analyzed to derive a comprehensive conclusion on the effectiveness of medicinal plants in the treatment of this disease. This structured approach aimed to provide a clear overview of the potential therapeutic roles of these plants in managing cutaneous leishmaniasis.

Results

The findings of the study indicate that several medicinal plants have shown significant therapeutic properties in controlling and alleviating the symptoms of cutaneous leishmaniasis. These plants include:

nettle (Urtica dioica), asafoetida (Ferula assa-foetida), wormwood (Artemisia absinthium), garlic (Allium sativum), eucalyptus (Eucalyptus globulus), yarrow (Achillea millefolium), lavender (Lavandula angustifolia), myrtle (Myrtus communis), Satureja Khuzestanica, mountain jewel (Onosma dichroanthum), rosemary (Rosmarinus officinalis), oak (Quercus spp.), Cassia (Cassia spp.), caper (Capparis spinosa), flax (Linum usitatissimum), castor oil plant (Ricinus communis), walnut (Juglans regia), thyme (Thymus vulgaris), henna (Lawsonia inermis), mimosa (Mimosa pudica), aloe vera (Aloe vera), black bean (Vigna mungo), barberry (Berberis vulgaris), chamomile (Matricaria chamomilla), and turmeric (Curcuma longa).

These medicinal plants have been identified as effective in traditional medicine for treating cutaneous leishmaniasis. Their therapeutic effects are attributed to their anti-inflammatory, wound-healing, and antiparasitic properties. Table 1 presents a detailed list of these medicinal plants

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used in traditional medicine for the treatment of cutaneous leishmaniasis.

Table 1: Medicinal Plants Used in Traditional Medicine for the Treatment of Cutaneous Leishmaniasis

Persian Name	English name	Scientific name	Herbal family	Mechanism [15-29]
Gazaneh	Nettle	*Urtica dioica*	Urticaceae	The enhancement of the immune system and the reduction of inflammation.
Anghouzeh	Asafoetida	*Ferula assa-foetida*	Apiaceae	Anti-inflammatory and antiparasitic effects.
Dermaneh	Wormwood	*Artemisia spp.*	Asteraceae	Inhibition of parasitic growth with artemisinin compounds.
Sir	Garlic	*Allium sativum*	Amaryllidaceae	Induction of apoptosis in parasites and inhibition of growth.
Okaliptus	Eucalyptus	*Eucalyptus spp.*	Myrtaceae	Anti-inflammatory effect and inhibition of parasitic growth.
Boumadaran	Yarrow	*Achillea millefolium*	Asteraceae	Antioxidant and antiparasitic properties.
Ostokhodos	Lavender	*Lavandula spp.*	Lamiaceae	Anti-inflammatory and soothing properties.
Mourd	Myrtle	*Myrtus communis*	Myrtaceae	Inhibition of parasitic growth with antioxidant effects.
Marzeh khozestani	Satureja	*Satureja khuzistanica*	Lamiaceae	Anti-inflammatory and antiparasitic effects.
Laele kouhestan	Mountain Cornflower	*Centaurea montana*	Asteraceae	Antioxidant and anti-inflammatory properties.
Rozmary	Rosemary	*Salvia rosmarinus*	Lamiaceae	Immune-boosting and antiparasitic effects.
Balout	Oak	*Quercus spp.*	Fagaceae	Anti-inflammatory and inhibition of parasitic growth.
Flous	Senna	*Cassia fistula*	Fabaceae	Cleansing of the digestive system and reduction of inflammation.

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Kebr	Caper	*Capparis spinosa*	Capparaceae	Anti-inflammatory and antioxidant properties.
Katan	Flaxseed	*Linum usitatissimum*	Linaceae	Immune boosting and inhibition of parasitic growth.
Karchak	Castor	*Ricinus communis*	Euphorbiaceae	Antioxidant and antiparasitic effects.
Gerdou	Walnut	*Juglans regia*	Juglandaceae	Anti-inflammatory and antioxidant effects.
Avi9shan	Thyme	*Thymus vulgaris*	Lamiaceae	Inhibition of parasitic growth and immune enhancement.
Hanna	Henna	*Lawsonia inermis*	Lythraceae	Anti-inflammatory and antiparasitic properties.
Mimosa	Mimosa	*Mimosa pudica*	Fabaceae	Anti-inflammatory effects and inhibition of parasitic growth.
Aloevera	Aloe	*Aloe vera*	Asphodelaceae	Soothing and anti-inflammatory.
Lobiaye siah	Black Bean	*Phaseolus vulgaris*	Fabaceae	Immune system enhancement.
Zereshk	Barberry	*Berberis vulgaris*	Berberidaceae	Inhibition of parasitic growth with berberine compounds.
Babouneh	Chamomile	*Matricaria chamomilla*	Asteraceae	Soothing and anti-inflammatory effects.
Zardchoubeh	Turmeric	*Curcuma longa*	Zingiberaceae	Inhibition of parasitic growth with anti-inflammatory effects.

The plant families studied exhibit a considerable diversity in both their number and percentage representation. The Asteraceae and Lamiaceae families, each with four occurrences, account for 16% of the total data, making them the most abundant. Following them, the Fabaceae family, with three occurrences and a 12% share, ranks next. Myrtaceae, with two occurrences, represents 8% of the data. Other families, such as Urticaceae, Apiaceae, Amaryllidaceae, Fagaceae, Capparaceae, Linaceae, Euphorbiaceae, Juglandaceae, Lythraceae, Asphodelaceae, Berberidaceae, and Zingiberaceae, each with a single occurrence, contribute only 4% of the total data. Based on these results, it can be concluded that the Asteraceae and Lamiaceae families, due to their higher frequency, hold greater significance among the samples under study.

Table 1 presents the diverse effects of medicinal plants and natural compounds on enhancing the immune system and combating inflammation and parasitism. These effects can be categorized into several key areas. First, the strengthening of the immune system and reduction of inflammation, which help improve the body's defense and alleviate inflammatory symptoms. Compounds with anti-inflammatory and antiparasitic properties can play a crucial role in preventing the progression of inflammation and combating parasites. The inhibition of parasitic growth, with specific compounds like artemisinin and berberine, demonstrates the targeted properties of certain plants in eliminating parasites. Additionally, traits such as the induction of apoptosis in parasites and the inhibition of their growth reflect the effective mechanisms of

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these compounds in destroying parasitic cells. Other beneficial properties include antioxidant and antiparasitic effects, which help reduce oxidative stress and strengthen the body's defenses against parasites. Soothing and calming effects, which aid in reducing inflammation while providing relief and relaxation to the body, are also noteworthy. In summary, these compounds, through cleansing the digestive system, inhibiting parasitic growth, boosting immunity, and offering antioxidant properties, provide a range of benefits for maintaining general health and combating inflammation and parasitic infections.

Discussion

The results of this study indicate that plants such as nettle, Asafoetida, Artemisia, and garlic, due to their active compounds and unique physiological properties, can play a significant role in inhibiting parasitic growth and reducing inflammation [30]. Artemisia, with its artemisinin compounds, widely used in the treatment of parasitic diseases, directly inhibits the growth of Leishmania parasites responsible for leishmaniasisnd Asafoetida, through the induction of apoptosis in parasitic cells, prevent parasite proliferation and help reduce the severity of infection [31,32]. Other tus and yarrow, with their strong antioxidant properties, counteract the destructive effects of free radicals caused by infection, thus being effective in reducing inflammation and improving the overall condition of the patient [33,34]. Plants from the Asteraceaes, due to their phenolic and flavonoid compounds, exhibit antioxidant and anti-inflammatory effects, which can serve as complementary treatments to reduce the symptoms and severity of cutaneous leishmaniasis [35,36]. These antioxidant and immune-boosting properties have been observed in plants like nettle and rosemary, which help strengthen the body's defense mechanisms and accelerate wound healing [35,36]. Some plants such as barberry and turmeric, witcurcumin compounds, act specifically in inhibiting parasitic growth and improving skin symptoms associated with cutaneous leishmaniasis [37,38]. These compounds have the ability to reduce inflammation, soothe sywound healing, potentially serving as alternatives or complements to conventional treatments. Plants like henna, flax, and walnut, with their antioxidant and anti-inflammatory effects, contribute to boosting the immune system and preventing the progression of infection [39,40]. Overall, the findings of this study emphasize that medicinal plants can be used as effes for cutaneous leishmaniasis.

Conclusion

Given their efficacy and low side effects, further research is necessary to identify optimal dosages, extraction methods, and the use of their active compounds. The integration of these plants in the treatment of cutaneous leishmaniasis can provide a complementary solution with high effectiveness and lower costs, promoting the general health of patients.

Statements and Declarations

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Competing interests

The authors have no competing interests to declare that are relevant to the content of this article.

Ethics approval

This study was performed in line with the principles of the Declaration of Helsinki.

Consent to participate

Informed consent was obtained from all individual participants included in the study.

Author contributions

MA: Conceptualization, the original draft writing, investigation, writing including reviewing and editing and investigation and formal analysis; MHA: Conceptualization, supervision, and project administration; MHA and MA: Conceptualization, the original draft writing, investigation, writing including reviewing and editing

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