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A review of the effect of medicinal plant extracts on *Leishmania major* in vitro and in vivo conditions in Iran

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ABSTRACT

Background: Leishmaniasis is one of the most common parasitic diseases in tropical and subtropical regions of the world and is considered a threat to public health. Iran is also one of the most endemic areas of cutaneous leishmaniasis in the world. The causative species of cutaneous leishmaniasis is a protozoan from the *Kinetoplastida* order, which in Iran is *Leishmania major* (rural type) and *Leishmania tropica* (urban type). More than 70% of leishmaniasis in Iran is *Leishmania major*. The reservoir of the disease is humans in the urban type and field rodents in the rural type, and the vector is the female mosquito of the genus *Phlebotomus*.

Methods: This study is organized as a review, in which, by searching the keywords cutaneous leishmaniasis, *Leishmania major*, plants effective against leishmaniasis in Iran, scientific-research articles, Google Scholar search engine information, Pubmed and Science Direct databases, the available books in this field were analyzed.

Results: 5-valent antimoan compounds are used for the treatment of cutaneous leishmaniasis. Of course, not all patients need treatment because, in a large number of people, the lesion heals by itself, and due to the side effects of antimoan compounds, it is better to use fewer of these drugs. Therefore, the desire of patients and therapists to use herbal compounds has increased.

Conclusion: Although cutaneous leishmaniasis is not usually associated with high Although cutaneous leishmaniasis is not usually associated with high mortality, the rate of infection is very high and causes malformed skin lesions that remain for more than a year in some cases, and even with standard treatment, scars remain. It remains forever and causes emotional pain for the patient. Therefore, domestic researchers have provided research on herbal treatments against Leishmaniasis, considering the history of traditional treatments in Iran and the scattered vegetation in the country.

Kewwors: Leishmania major, Cutaneous leishmaniasis, Plants affecting *Leishmania*

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1. Introduction

In the past decades, it was impossible to distinguish the diseases caused by *Leishmania spp*. in humans from each other. For this reason, the species were separated based on clinical grounds, and in this way, three species of *Leishmania* were identified according to their effects. Clinically, they were divided into three types: cutaneous leishmaniasis, mucosal leishmaniasis, and visceral leishmaniasis (1). The causative agent of leishmaniasis is a protozoan called *Leishmania* from the Kintoplastida order, which was first identified by Leishman and Donovan. According to the living environment, this parasite can be seen in two forms: without flagella and free (amastigote or Leishman's body) and with flagella (promastigote), which live in the mononuclear xenophagous cells of vertebrates and multiply in the same place (2). According to reports provided by the World Health Organization (WHO), leishmaniasis is endemic in 98 countries, and more than 350 million people are at risk. Approximately 2 million people are infected with *Leishmania*, of which about 1.5 million are infected with cutaneous leishmaniasis a year (3). Oriental sore was seen in the old world and is caused by the *Leishmania L. tropica* complex. Leishmaniasis in the old world (Asia, Africa, and Europe) is divided into two types, rural and urban, which are spread by mosquitoes. A female earthworm of the genus (*Phlebotomus*) is transmitted. Cutaneous leishmaniasis in the New World (America) is caused by *Leishmania mexicana* and *Leishmania brasiliensis*. The carrier of this disease is the female mosquito of the *Lutzomyia* genus. *Leishmania tropica* causes a chronic disease that lasts for a year or more if not treated properly and produces a dry lesion that becomes scarred after a few months, which is usually isolated and occurs on the face. This disease is found in urban areas. *Leishmania major* causes an acute infection with a duration of 3 to 6 months. The lesion is moist, and after a short period of time, it becomes injured (4).

The first-line drugs for the treatment of leishmaniasis are 5-valent antimony compounds such as meglumine antimonate (Glucantim) and sodium stibogluconate (Pentostam). It should be noticed that available drugs are expensive and require multiple injections, in addition to their high resistance and drug side effects. Thus, it causes a heavy economic burden on families, especially those under financial pressure and with economic problems. The treatment of leishmaniasis may take several months to recover; of course, even with a successful treatment, there will be a possibility of scarring, which can cause psychological and emotional problems in the patient, so there is a greater need to develop effective anti-leishmanial compounds that are low-cost, have low toxicity, and also have the possibility of oral administration than in the past (5). The World Health Organization intends to use more research on the traditional use of plants to find new, better, and more effective medicinal products with less toxicity. Considering the importance of herbal treatments in Iran's traditional medicine and the mental background of people in the community in relation to traditional treatments, the distribution and diversity of vegetation in the country and the compatibility of plants with human nature for treatment caused domestic researchers to seek herbal treatment for leishmaniasis. and many efforts have been made in such a way that in this article we have tried to collect an abstract of these efforts.

2. Materials and Methods

This study is organized as a review in which scientific-research articles, information from search engines Google Scholar and SID, as well as the PubMed database and reference books in this field, have been analyzed and concluded.

3. Results

3-1. Sargassum Oligocystum

Sargassum oligocystum belongs to the Sargassaceae family and the Sargassum genus. Its original name is Sargassum oligocystum Montaga (6). Different species of the genus Sargassum contain polysaccharides with biological activity, whose basis is fucose sugar, and so far important antibacterial properties such as the effect on Bacillus subtilis, anti-herpes simplex virus, and anti-intestinal cancer are known. Algae are a rich source of useful and bioactive compounds and are economically important due to having valuable polysaccharides such as agar, carrageenan, and alginate (7).

In order to investigate the cytotoxic effects of Sargassum oligocystum extract and glucantim and the viability of Leishmania major promastigotes (MRHO/IR/75/ER), an MTT test was performed to find 50 IC. The morphological changes of promastigotes exposed to a concentration of 5 mg/ml of Sargassum oligocystum extract (50 IC) showed that after 10 hours, the changes started, and after 72 hours, all the cells became wrinkled, round, and condensed. On the other hand, the results showed that the anti-leishmanial effects (50IC) of Sargassum oligocystum extract were 87.6, 35.5, and 20 µg/ml in 24, 48, and 72 hours, respectively, and at the same time, the lethal effects of glucantim as a controlled drug in 24, 48, and 72 hours were respectively

76.96, 44.5, and 21.8. These results indicate that this extract is active against Leishmania major in different concentrations and times compared to the control drug glucantim, which indicates a better effect. The lethal dose concentration of Sargassum oligocystum, which kills almost 100% of Leishmania major cells, is 5 mg/ml (8) (61). It should be noted that this study was conducted only in extracorporeal conditions, and it is better to investigate the effect of the extract in internal conditions and even in volunteer patients.

3-2. Thymus

4 types of thyme Thymus pubesense, Thymus caucasicus, Thymus vulgaris, and Thymus kotschyan have been investigated. The results related to the analysis of the extract of the thyme plant show that 80% carvacrol, followed by linalool and thymol, have the largest share among the compounds of this plant. In a study that was conducted on 4 species of Thymus in concentrations of 50, 100, 150, 200, and 250 micg/ml and at three times of 24, 48, and 72 hours, it showed that 3 species, T. pubesense, T. kotschyanus, and T. caucasicus, had the least effect, so that at concentrations of 50, 100, 150, and 200, they were ineffective, and only at a concentration of 250 µg/ml, they were consistent with the control drug amphotrypsin B, while T. vulgaris showed the best effect, so that it was ineffective only at a concentration of 50 µg/ml. And in other concentrations, it was consistent with the control drug. This research was done only in vitro (9) (62).

3-3. Cichorium intybus

Cichorium intybus is a plant from the dark enamel flower order, starflower, and Cichorium category. There are 2 species of this plant and 6 wild species. Cichorium intybus has different types, of which 3 types are known (10). Cichorin, which is a bitter glycoside, can be mentioned among the compounds in Cichorium intybus (11). Cichorium intybus leaf juice can be mentioned as a medicine for jaundice, kidney, and liver, a poultice that removes swelling around the eyes, and it increases vision (12). The anti-leishmanial effect of this plant on the parasite has been determined, but compared to the glucantim drug, the 50IC for chicory was 1094 micrograms/ml, while in glucantim, the 50IC was equal to 616/18. Therefore, the effectiveness of the glucantim drug was greater than that of Cichorium intybus, but due to the high side effects of glucantim and, at the same time, the effectiveness of Cichorium intybus extract against Leishmania parasites in vitro, it can be replaced by Cichorium intybus by increasing research in vivo on volunteer patients. It was good for current medicines (13, 63).

3-4. Calendula officinals

Calendula is a plant of the Cassian family and has been used in the treatment of several diseases and in combination with homeopathic medicines. The history of its use goes back to the medicine of the 2nd century (14). Calendula officinals has several medicinal properties, such as antioxidant, anti-inflammatory, anti-fungal, and anti-viral. On the other hand, cytotoxic activity and tumor reduction should also be noted (15). The effective ingredients of the plant are flavonoid and hennin, which have antimicrobial properties against Staphylococcus aureus and Klebsiella pneumoniae. On the other hand, the alcoholic extract of dried marigold flowers reduces the activity of HIV-1 reverse transcription (16). However, in a study conducted on the aqueous and alcoholic extracts of marigolds on Leishmania promastigotes, the 50% inhibitory concentration (50IC) of the alcoholic extract was 170 and 215 µg/ml in the aqueous extract. A concentration of 500 µg/ml of alcoholic extract killed 100% of promastigotes in the first 24 hours, but only 75% of promastigotes were killed in aqueous extract. After 72 hours, both aqueous and alcoholic extracts at a concentration of 500 had the ability to kill promastigotes. This study was conducted only in vitro, and to ensure the anti-leishmanial performance of marigolds, the study should be conducted in vivo (64).

3-5. Crataegus aronia

Crataegus aronia can be found in the north and northwest of Iran. The fruit of Crataegus aronia has been used as a medicine for centuries, and the antioxidant and antibacterial effects of this plant have been proven in several studies (17). There are a lot of polyphenolic compounds in this plant, including the anti-bacterial and anti-inflammatory agents of the parasite. In Europe, Crataegus aronia is used to treat irregular heartbeats, angina, and arteriosclerosis (18). According to the conducted studies, Crataegus aronia extract had an almost inhibitory effect on Leishmania parasite promastigotes in concentrations of 0.5, 1, 10, 20, 40, and 60 after 24, 48, and 72 hours, and in concentrations lower than 100 µg/ml. Liter has a better effect; therefore, Crataegus aronia fruit does not have a lethal effect on Leishmania promastigotes, but to some extent, it prevents the proliferation of amastigotes inside the macrophage. These studies were performed in vitro, and more studies are needed in vivo (19, 65).

3-6. Zizyphusspina Christi

Zizyphusspina Christi, which is known as a cedar in Iran, has a wide distribution in the eastern, southern, and

northeastern regions of the country (20). In the phytochemical analysis of the plant extract, besides the presence of alkaloids, flavonoids, and tannins, saponin glycosides are present in large amounts, and the most important saponin glycosides in the plant leaf extract are besides christening A (21). Zizyphusspina christi extract has a very broad antifungal effect against Candida albicans. It also has antibacterial activity against Staphylococcus aureus, Bacillus subtilis, Klebsiella, Escherichia coli, and Proteus vulgaris (22). The methanolic extract of Zizyphusspina, which has a lower 50IC, is far more effective compared to the aqueous extract of Zizyphusspina on promastigotes. These results were less effective compared to glucantim drugs, but in general, they are valuable because the extract showed a significant effect on promastigotes in all dilutions. On the other hand, the morphological changes of Leishmania major promastigotes exposed to a concentration of 22 micrograms/ml (50 IC) of the methanolic extract of Zizyphusspina and 80 micrograms/ml (50 IC) of the aqueous Zizyphusspina extract were investigated. Parasite cells showed changes after 8 hours of being exposed to the extract, and at the end of 72 hours, all the cells started to round and condense the cytoplasm and shrink and shrink (66). Considering the positive effects of Zizyphusspina on Leishmania in aqueous and alcoholic conditions and in vitro, it is expected to be worth studying in vivo and on volunteer patients.

3-7. Berberis vulgaris

Berberis vulgaris is a plant with the scientific name Berberis vulgaris that belongs to the Berberidaceae family. Berberis vulgaris exists in different regions of the world. The history of using this plant in Chinese medicine and traditional medicine dates back to about 3000 years ago. Due to its alkaloid (berberine) properties, this plant has been noted for its effectiveness in the treatment of various diseases, especially Leishmania. Berberis vulgaris extract was used as a topical ointment in different concentrations to treat Leishmania major wounds in BALB/c mice. The results showed that of the three groups treated with concentrations of 20%, 40%, and 80%, the 20% group had a decrease in the number of parasites during the period; on the other hand, there was a complete recovery in 5 mice, and weight gain was also seen in the mice during the period. It is noteworthy that in both groups, a 40% and 80% reduction of parasites was significant compared to the control group, but due to the increase in the concentration of toxic compounds in the composition, it could be the reason for the death of the mice (67).

In another study, the effect of barberry extract on Leishmania major and Leishmania tropica was examined in vitro and in vivo. It was found that a concentration of 10 micrg/ml of berberine eliminated the parasites during a period of 3–4 days after the drug was injected into It becomes localized in C3H mice (24). The effect of barberry extract on Leishmania donovani in domestic dogs and golden hamsters was examined at the Washington Health Research Institute. Intraperitoneal injection reduced the diameter of the wound by more than 50% and reduced the number of parasites by 90% in the liver and spleen compared to the control group. Also, in dogs, intra-wound injection of berberine four times a week has been shown to be significantly effective (25).

3-8. Portulaca olerace

Portulaca olerace is one of the traditional plants of Iran known for its compounds oxalic acid, cinnamic acid, caffeic acid, malic acid, citric acid, coumarin, flavonoids, alanine, tannin, saponin, steroid, phenol, viscous substance, oil, fat. Menotropin plus the presence of antioxidants such as vitamins E, C, B2, B1, beta carotene, and other essential amino acids (25). It has been shown that the active molecules in Portulaca olerace have been used to treat parasitic infections such as trypanosomiasis (26). The alcoholic extract of Portulaca olerace aerial parts, including stems and leaves, has been used in the treatment of stomatitis (oral inflammation) in volunteer patients (27).

Recently, a flavonoid called apigenin has been extracted from this plant, which has anti-tumor properties, on the other hand, the antimicrobial effect of the ethanolic and aqueous extracts of the leaves and roots of this plant on Gram-positive and negative bacteria such as Bacillus subtilis, Bacillus cereus, Staphylococcus aureus, Klebsiella pneumoniae, Escherichia coli, Pseudomonas aerogenosa, fungi such as Aspergillus niger, Aspergillus fumicatus, and Neurospora crassa has been proven (26). The alcoholic extract of Portulaca olerace against Leishmania major promastigotes in 10 different concentrations (1600, 800, 400, 200, 100, 50, 25, 12, 6, and 3) after 24, 48, and 27 hours, 50 ICs, respectively equal to 690, 270 and 140 µg/ml and against clinically isolated promastigotes 1160, 385 and 140 µg/ml were obtained. 50IC for glucantim at three times of 24, 48, and 72 hours was 27, 12, and 8 µg/ml and 26, 19, and 11 µg/ml, respectively. There was a significant difference between the 50 IC of the extract and glucantim, and in the morphology of the cells in contact with the extract, it can be recognized that the cytoplasm is wrinkled, rounded, and condensed. Finally, the greatest change in

shape was observed in vitro under the extract with a concentration of 270 µg/ml. liter and in vivo concentration was 385 µg/ml from the alcoholic extract of Portulaca olerace stem and leaves(68).

3-9. Rumex

Rumex is a plant similar to spinach and is native to Europe. The plant grows wild in meadows, fields, along rivers, and on roads. Carbohydrates, fiber, fat, protein, vitamins B1, B2, B3, C, calcium, iron, and potassium are among the ingredients of this plant. In traditional medicine, the crushed, cooked, or boiled leaves and seeds of this plant are used for the local treatment of boils (28). It is also used to treat bruises, burns, and bites to neutralize poison, and the flavonoid compounds in the plant are known to be strong inhibitors of inflammatory cytokines. In addition to their antioxidant properties, these compounds also have effective antimicrobial effects on various microorganisms (29).

The effect of Rumex on wounds caused by Leishmania major in the tail base of BALB/c mice was studied. It was determined that the three concentrations of the alcoholic extract of Rumex seeds with concentrations of 3, 5, and 9 mg/mL were 0.8 mL. Liters were injected intraperitoneally. The control drug in this experiment was glucantim. At the end of the fifth week, the group that was treated with 9 mg/ml extract showed a greater reduction in wound size than other groups, and on the other hand, the number of parasites in the slides prepared from the wounds of mice in this group showed a significant decrease. It showed that no amastigotes were observed in one of the mice of this group, even though no amastigotes were completely removed in any group. In the comparison between the group treated with 9 mg/ml extract and glucantim, a significant reduction of the parasite and a significant difference was observed, which indicates the high effectiveness of sorrel extract on Leishmania parasite (69).

3-10. Lavendula

The essential oil of Lavendula, which is obtained from the distillation of the flowers and spray of flowers of the plant, is a yellow or greenish liquid that has a pleasant smell. Traditionally, for centuries, the decoction and extract of the plant have been used to treat various diseases (30). So far, most of the research has focused on the antibacterial and antifungal activities of Lavendula essential oil, but it should be noted that one of the main components of Lavendula essential oil is linalool, which has properties against mites, aphids, and seed beetles (31). However, its anti-protozoal properties have received less attention, as previously unreported findings claim that this essential oil has a high anti-protozoal power (32) and the positive results of studies investigating the effect of Lavendula essential oil on flagellated protozoa including Trichomonas vaginalis, Giardia duodenalis and Hexamita inflate has been proven(33). In the research conducted on the anti-leishmanial effects of Lavendula essential oil, concentrations of 5, 15, 50, 100, 150, and 200 microL/ml were used, and in the first 24 hours, the concentrations of 50, 100, 150, and 200 were reduced. compared to the control, they had significant glucantim, and in the last two concentrations, i.e. 150 and 200, the number of parasites reached zero. After 48 hours, this significant reduction increased in the concentration of 100 and the number of parasites approached zero, and after 72 hours, the effectiveness increased and in four concentrations of 50, 100, 150, 200, the amount of parasites became zero. This trend of changes shows the effectiveness of lavender essential oil over time on Leishmania major promastigotes in vitro (70).

3-11. Matricaria chamomilla

The Matricaria chamomilla plant the scientific name Matricaria chamomilla is one of the oldest medicinal plants. This plant has been introduced as a medicinal plant in all valid pharmacopeias and its therapeutic properties have been investigated. Matricaria chamomilla is one of the selected medicinal plants of the World Health Organization ("WHO") and has various uses. It is used in the treatment of digestive diseases as an anti-spasm, anti-flatulence, and anti-inflammatory agent of the small intestine, as well as in the treatment of indigestion, colitis, and stomach ulcers. The extract of the plant is used in the treatment of anxiety, inflammation, skin irritations, wounds, and superficial burns. This plant is used as an antiseptic, an antibacterial, and an antifungal. The effective ingredients of the flowers of this plant are very effective in hair and skin care and maintenance (34).

Studies have been conducted on the effects of Matricaria chamomilla on various diseases, which can be mentioned as follows: Local consumption of hydroalcoholic extract from the Matricaria chamomilla plant accelerates burn wound healing in rats and wound healing (35). The topical use of Matricaria chamomilla extract dissolved in olive oil accelerates the healing of cut wounds in rats (36). Matricaria chamomilla ointment has a positive effect on the healing of oral wounds in rats and increases the number of fibroblasts and epithelialization of wounds, as a result, Matricaria

chamomilla ointment can be considered a strong skin repair agent (37).

Matricaria chamomilla has been able to be significantly effective in preventing stomatitis caused by chemotherapy (stomatitis severity, pain intensity, survival rate of stomatitis) (38). However, the effect of Matricaria chamomilla decoction on the wound resulting from the injection of Leishmania major in the base of the tail of rats, the wounds were exposed to this decoction for 5 minutes daily for 2 weeks, so the wounds of mice with the decoction Washed and boiled Matricaria chamomilla is placed on the wound during this time. This work has been repeated every day for 14 days equal to the length of the standard treatment period with glucantim drug. Simultaneously with this treatment method, in the other group, treatment with glucantim 60 mg/kg was also done as a positive control, and in the other group, no treatment was done as a negative control. Before treatment, the wounds were measured with calipers, and after a period of 14 days, this measurement was repeated and conclusions were drawn. The status of wound healing in the studied groups was compared, and the comparison of wound healing between the Matricaria chamomilla decoction group and the untreated control showed a significant difference, on the other hand, there was a significant difference in the wound size between the control treated with glucantim and the control without treatment. But the comparison of wound healing in the group treated with Matricaria chamomilla decoction and the control treated with glucantim showed no significant difference. Therefore, based on the results of this study, the effect of decoction of Matricaria chamomilla on the healing of Salak's wound is close to the effect of glucantim in the treatment of this disease, and considering the side effects caused by glucantim, Matricaria chamomilla can be used as an alternative treatment in the future with more complete research (71 and 72).

3-12. Arnebia euchroma

Arnebia euchroma is used as a local plant as food and medicine in the mountainous regions of the country. The effective substance of this plant is alkaline. The extract of this plant is anti-scabies and anti-kidney stones. Research related to euchroma showed that the extract of this plant has anti-inflammatory effects compared to ibuprofen in rats (39). On the other hand, it has been shown that the active ingredients of this plant have anti-HIV activity (40). the suspension cultures of the A. euchroma have a specific anti-tumor effect in the in vitro and in vivo (41). In the research conducted on this plant and its effect on Leishmania major, 11 concentrations of 800, 400, 200, 100, 50, 25, 12.5, 6.25, 3.2, 1.5, and 0.78 were used. In this study, the number of Leishmania parasites increased in the control medium (without the presence of Abu Khalsa extract), while it decreased in all concentrations compared to the control medium, but in 5 concentrations, 12.5, 6.5, 3.2, and 5. This reduction was significant (0.78, 1.73).

3-13. Achillea millefolium

Achillea millefolium is belong to the Asteraceae family. In fact, this plant is one of the most famous medicinal plants that is often used in ancient medicine to treat diseases in general and wounds and burns in particular. The most important compounds in this plant include volatile oil, polyphenolic compounds, flavonoids, lactones, betaines, acetylene, resin, tannin, acetylene, etc. The study shows anticonvulsant, anti-inflammatory, anti-spasm, antibacterial, antifungal, analgesic, anti-arrhythmic, blood pressure-lowering, and blood lipid-lowering effects (42). In the investigation of the effect of different concentrations of Achillea millefolium plant extract on the Leishmania parasite, it was found that at all concentrations of this extract, there was a decrease in the number of Leishmania parasites in the in vitro environment, compared to the control environment (glucantim) concentrations of 100, 200, 400, and 800. There has been a significant decrease, but this decrease was not significant in concentrations of 1.3, 6.25, 12.5, 25, and 50 (73 and 74).

3-14. Artemisia absinthium

Artemisia absinthium, known as Artemisia absinthium, is a member of the family of sycamores, which has been used in traditional medicine since ancient times due to its properties such as insecticidal, appetizing, and eliminating intestinal worms, as well as having bitter and aromatic compounds. Today, the essential oil obtained from Artemisia absinthium is used in the flavoring of foods and drinks, in pharmaceuticals, in agriculture, and as an anti-bacterial, anti-febrile, anti-pregnancy, and anti-malarial, as well as a cardiovascular booster. There are toxic compounds in the structure of this plant that are used to prepare insecticides and acaricides (43). Artemisia absinthium has one of the most important plant compounds effective in the treatment of malaria in ancient medicine. On the one hand, it has a prophylactic effect in the treatment of Schistosoma and is also used in China and Africa to treat clonorchiasis. Moreover, it is also used to prevent the growth of Toxoplasma gondii and treat Leishmania, as well as the antifungal properties of Artemisia absinthium against Aspergillus fumigates and also

against Its microbial activity have been proven against Leptospira (44).

The most important part of the plant that has healing properties is its flower, and its important compounds include monoterpene and ketone, which have anti-inflammatory and antimicrobial properties; its bitter and toxic compounds are camagoline and thujone; and other compounds include linalool. , camphor, limonene, and... pointed out (45). In the experiment that was conducted on the effect of different concentrations of the alcoholic extract of Artemisia absinthium on Leishmania major in vitro, 9 concentrations were investigated (800, 400, 200, 100, 50, 25, 12.5, 1.6, 25/3). A decrease in the number of parasites was observed in all concentrations, but compared to the control environment that received glucantim, the concentrations of 800, 400, 200, 100, and 50 had a significant decrease, while in 4 concentrations, 25, 12.5, and 25 /6. 1/3 of this reduction was not significant. It is noteworthy that due to the good effect of this compound on the Leishmania, it is necessary to continue the research in the in vivo phase and on volunteer patients so that an alternative treatment to the current treatments can be identified (73 and 74).

3-15. Juglans

Juglans is a plant of the Juglandaceae family and the Jugland regia genus. Juglans leaf extract has germicidal and bactericidal properties. Juglans leaves are tonic and purify the blood. Because of its bitter substance and tannin, Juglans leaves are useful in the treatment of skin diseases and pigs. Juglans leaves are useful for washing wounds and healing, and the decoction of Juglans leaves cures headaches, frostbite, and skin diseases. The fresh leaves of the Juglans kill harmful insects such as willows and bedbugs. Juglans kernels are a very good source of copper, so they help the body absorb iron. Also, a decoction of Juglans leaves is prescribed to treat anemia and weakness (46).

Plant derivatives prepared from Juglans are used in the local treatment of acne, inflammatory diseases, ringworm, and fungal, bacterial, and viral infections. Antibacterial, fungal, and viral properties of this plant due to the presence of the special chemical compound 5-Hydroxy 1,4 naphthoquinone is present in it, which causes the cycle of reduction and reaction with glutathione (47). In investigating the effect of Juglans leaf extract on Leishmania, three environments were reconstructed: one group with different concentrations of Juglans leaf extract, and the other group was studied as a control group without the presence of any extract. Glucanthim was investigated. 9 concentrations were prepared from the alcoholic extract of Juglans leaves: (800, 400, 200, 100, 50, 25, 12/5, 6/25, and 3/1). In all groups with different concentrations, the number of parasites could be reduced, but compared to the control group, only the concentrations of 800, 400, and 200 had a significant reduction (74).

Moreover, the effects of yarrow, wormwood, and Juglans leaves alone and in combination were studied in vitro. The result showed that out of 4 groups (yarrow + wormwood), (yarrow + Juglans leaf), (Juglans leaf + wormwood), and (Juglans leaf + yarrow + wormwood), all 4 groups caused a decrease in the number of parasites compared to the control group, but in the yarrow + wormwood group, this decrease was significant after 48 hours; all the parasites were killed (74).

3-16. Artemisia dracunculus

The Artemisia dracunculus plant belongs to the sunflower family and dates back to 500 BC. The plant was first seen in southern Russia and Siberia. Artemisia dracunculus is a very good source of iron, calcium, and manganese, as well as potassium, magnesium, vitamins A and C. In ancient Greece, this plant was used to relieve toothaches. Also in the Middle Ages, antidote was used to treat snakebite venom. Since ancient times, Artemisia dracunculus has been used to treat abdominal pain and increase appetite. Artemisia dracunculus also regulates menstruation, increases bile production, regulates blood pressure, and treats digestive worms. The most important and effective part of Artemisia dracunculus is its volatile oil, which includes cineol, estragole, esimene, and flandrene. Artemisia dracunculus essential oils, which are prepared by steam distillation from the leaves and flowers of the plant, have different properties such as anti-rheumatism and appetite suppressant, helping to improve blood circulation, and deodorizing the body by eliminating microbes on the body surface. It stimulates the nervous system, hormonal secretions, and the immune system of the body. The important point is the very high toxicity of this oil to intestinal roundworms, tapeworms, and hookworms. It has been proven that 10% Artemisia dracunculus essential oil reduced the wound caused by Leishmania major in the area of the base of the tail of BALB/c rats, and about 2 weeks after the treatment, the small wounds were completely healed. The large lesions did not suppurate and their spread was prevented, and the slides prepared from the wounds showed a decrease in the number of parasites in the area (75).

3-17. Eucalyptus

Eucalyptus is an Australian plant and its leaves are rich in effective substances eucalyptus and thymol, which are used to prepare infusions, tinctures, drinking solutions, and capsules for the treatment of respiratory diseases, sore throat, cough, and nasal congestion. It is used to treat urinary tract infections (bladder inflammation), stomach and intestinal mucosal inflammation, deal with migraines, anti-rheumatism and antiseptic for wounds and burns and skin hives. In local areas, to keep away insects, especially mosquitoes, rub this plant on the skin is used. Also, to get rid of lice, they use hair massage with this plant, and even to rid their animals of cockroaches and other insects, rubbing the leaves of this plant on their bodies is useful. It was determined that after a 35-day treatment of wounds of rats infected with Leishmania major, and application of the ointment, the large and swollen wounds were inhibited, their size did not increase, and their parasitology test also indicated. It was from inhibiting the growth of parasites. But the size of the wound did not decrease, this was in the case that the small wounds were healed and were even on the verge of complete healing (75).

3-18. Artemisia siberi

Artemisia siberi is an example of a desert plant that grows in Iran, Palestine, Syria, Iraq, Turkey, and Afghanistan (Central Asia) (48). The anti-parasitic effects of this plant have been proven in the treatment of intestinal worm infections as well as malaria and fungal infections (49). The effect of Artemisia siberi at a concentration of 2 micrg/ml in the form of oil on L. major and L. tropica was excellent (50). The concentrations of 3, 6, 12, 24, 36, 48, and 60 micrg/ml of the essential oil of the plant were prepared, and the result of the contact of the Leishmania with the extracts was compared to 338 micrograms of glucantim. The result showed that there was a significant reduction in the number of parasites after adding herbal essential oil in the first 24 hours. Also, the reduction in the number of parasites was significant compared to the chemical drug glucantim. In addition to the decrease in the number, the decrease in parasite movement was also observed under the microscope, and this decrease continued in the following times. It was found that the lower the concentration of the essential oil, the lower its effect on reducing the number of parasites. In addition to reducing the number of parasites in effective concentrations, there was also a decrease in the mobility of parasites, and in some parasites, the loss of parts of their body structure was witnessed (76).

3-19. Pelargonium roseum

Pelargonium roseum is a medicinal plant that has been widely used in traditional medicine to treat cough, upper respiratory tract disorders, stomach and intestinal cancer. Although this plant is widely used in Europe to treat infectious diseases of the upper respiratory tract, the mechanism of its effect has not yet been precisely determined. The used part of this plant is the leaves and the aerial part of the plant, from which a substance called Pelargonium roseum Rosa is extracted, which is the main part of Geraniol. Geraniol essential oil is therapeutically anti-depressant and antiseptic. It is also a valuable astringent and hemostatic (stops bleeding). It is also a fast wound-healing agent, which makes it very useful for treating wounds. It should be remembered that the activation of macrophages by another species, Pelargonium sidoides, has been confirmed in Leishmania infections (51). In a research that was conducted on the effect of Pelargonium roseum essential oil on Leishmania major, different concentrations of 3, 6, 12, 24, 36, 48, and 60 micrg/ml were prepared and mixed with promastigotes of Leishmania major, the result showed that in the high concentrations, the lethality effect was greater and the number of parasites decreased. At high concentrations of Pelargonium roseum essential oil, movement decreased and in some cases, parts of the protozoan body were lost (76).

3-20. Medicago sativa

Medicago sativa is mostly found in mountainous and cold regions and is usually grown in the form of a wilding. According to ancient Iranian medicine, Medicago sativa is warm, has twice as much iron as spinach, and is useful for those suffering from anemia. The effects of vitamin C deficiency disappear by eating Medicago sativa. The effect of this plant on the treatment of diabetes has been shown (52).

Considering the importance of finding new drugs to speed up wound healing and considering that traditionally the fresh juice of the black Medicago sativa plant is used in wound healing, this led to research on the effect of this plant on the wound caused by Leishmania major in BALB/c rats. In studies, using a scalpel blade, a superficial wound of one centimeter was created only in their dermis area. The rats in this study were divided into five groups. Group 1: treated 5 times with fresh raw Medicago sativa extract every two days; Group 2: treated with aqueous extract once every two days; Group 3: treated with raw fresh extract only once; Group 4: treated with aqueous extract only once; and

Group 5: physiological serum was used as a control group instead of plant extract. In the case of all rats, 50 microliters of the relevant extract are poured into the wound using a sampler, and the entire length of the wound is smeared with it. The length of the wounds was measured by a caliper once every two days, and the results were recorded. So that the speed of healing improved after two days of using the raw extract of the wounds of one mouse, and after four days, the wounds of two mice improved, while the mice of the control group did not recover. In total, the number of recovered mice in 6, 8, and 10 days after the start of treatment was 3, 4, and 5 mice, respectively, while in the control group, the number of mice recovered at the same time was 2, 3, and 5 mice, respectively. This research shows that the black Medicago sativa plant has no significant effect on the healing of the superficial wound of Leishmania in an animal model (77).

3-21. Scophularia striata

The Scophularia striata belongs to the Scophulariaceae family, which is mostly a plant or shrub and rarely a tree. The five-petaled zygomorphic flowers of the goblet are usually in the form of capsules with many seeds. The branches of the plant are used as a stomach tonic. This is a perennial plant that grows in Ilam province and parts of Khuzestan province (53). The chemical composition of this plant has not been well identified, but the local people have been using this plant experimentally for many years in the form of decoction, incense, and poultice in the treatment of various diseases, including inflammation and infection of the eyes and ears, burns, infectious wounds, and colds (53). Compounds such as alkaloid, glycoside resin, eridoid, and cryptophilic acid have been identified in the flower of Scophularia striata (54).

It has been found that this plant has antibacterial properties in vitro. According to the research done by different researchers and the extraction of different materials from other scofularia species, it is possible that attention is paid to the commonality of many compounds in the species scattered all over the world, at least some of them in thirst. Therefore, it is possible that the effectiveness of this plant in healing is due to the presence of iriloid glycosidic compounds in different parts, which inhibit the production of prostaglandin 2E and various interleukins (4IL, 2IL, and a1IL), which, with TNF, reduce edema and cell infiltration and reduce the proliferation of T lymphocytes. It becomes 55. In addition, increasing the growth of fibroblasts provides the basis for more collagen secretion and, as a result, faster wound healing. At the same time, the presence of different glycoterpenoids in other scofularia species reduces edema, stops cell infiltration, and has anti-inflammatory properties. The presence of phenylpropanoid glycosides inhibits macrophage activity, thus inhibiting the production of inflammatory chemical mediators and ultimately reducing inflammation. The presence of phenolic acid with antibacterial properties in some species is another reason for the effect of the plant on healing skin wounds (56).

However, in a study that was conducted on the effect of the Scophularia striata plant on Leishmania major in vitro and on mouse peritoneal macrophage cells, three concentrations of 10, 20, and 25 mg/ml of the extract of this plant were prepared. It was observed that after 72 hours at concentrations of 25 and 10 mg/ml of Scophularia striata extract, all Leishmania major amastigotes inside the macrophage were destroyed. This was despite the fact that the reduction of parasite growth in the RPMI environment under the influence of thirst in all three concentrations was significantly reduced compared to the control group. The percentage of infected macrophages decreased significantly with increasing concentration and test time in culture media under the influence of the drug, so that no infected macrophages were observed from the second day onwards. On the other hand, Leishmania parasites in promastigote state in RPMI culture medium at a concentration of 25 mg/ml on the third day caused parasite death. This research shows that the aqueous extract of the thirsty plant has favorable anti-leishmanial activity, which, considering its cheapness and availability, is worth studying in vivo and on volunteers (78).

3-22. Curcuma longa

Curcuma longa is a plant from the ginger family and from the genus Curcumin, whose original name is often mentioned as Curcuma longa. Curcuma longa has an essential oil composed of valeric and caproic acids, especially flandrene, and an alcohol called tourmerol. In addition, it has a column called curcumin, which is a yellow resin material that can be crystallized and soluble in fatty substances called curcumin. Among its uses are topical use and treatment of some skin inflammations, and in the past, it has been used in the treatment of psoriasis (57).

To investigate the anti-leishmanial effect of Curcuma longa aqueous extract in RPMI culture medium, dilutions of 0.4, 0.5, 2.5, 5, and 10 mg/ml were prepared from the dried extract of the plant. Concentrations of 1

and 2 mg/ml quickly killed promastigotes of Leishmania major within 20 hours, and in other dilutions, the effect decreased with decreasing concentration, so that the concentration of 0.5 mg/ml after 88 hours killed all parasites. The control group, i.e., the group receiving 0.1 mg/mL amphotrypsin B, also killed all the parasites in the early hours. In the negative control group, the decrease in the number of parasites was insignificant. 50IC for Curcuma longa at 20, 42, 64, and 88 hours after adding the extract to the culture medium was 0.16, 0.12, 0.084, and 0.07, respectively. It was milligrams per milliliter. A concentration of 2 mg/mL killed all promastigotes more rapidly than the total Curcuma longa extract. A concentration of 0.2 mg/ml of total extract killed all parasites after 88 hours (79).

3-23. Glycyrrhiza glabra

Glycyrrhiza glabra is the dried root of the plant Glycyrrhiza glabra L. and belongs to the pea family, which contains 4% glycyrrhizin. Glycyrrhizin is one of the glycosidic compounds and produces two molecules of glucuronic acid and one molecule of glycyrrhizic acid as a result of acid hydrolysis. The amount of glycyrrhizin in dry roots is 6–12%. Also, from this group of compounds, we can mention triterpene acids such as glabric acid and Glycyrrhiza glabra acid. The flavonoids of Glycyrrhiza glabra are composed of a pair of isomers of chaloni (isoliquiritin) and flavanone (liquiritin). The amount of flavonoids in Glycyrrhiza glabra root is about 2-1.5% (58). Licochalcon A is the active substance extracted from Glycyrrhiza glabra root. Glycyrrhiza glabra root, also known as Glycyrrhiza glabra root, contains substances such as terpenoid saponins, which are often glycyrrhizin. Flavonoid compounds are among its other substances (57).

Among its ingredients, it is used in the treatment of ulcers and stomach inflammation, as well as as an expectorant, anti-inflammatory, flavoring, and sweetener. Anti-inflammatory effects are attributed to glycyrrhizin (58). In the traditional medicine of the past, Glycyrrhiza glabra has been used for wound healing, cough relief, pain relief, and stomach inflammation. To investigate the anti-leishmanial effect of Glycyrrhiza glabra extract in RPMI culture medium, dilutions of 0.5, 1, 2, 4, 8, and 16 mg/ml were prepared. The evidence was that low concentrations of the extract, i.e., 0.5 and 1 mg/mL, were prepared. ml had the same effect as the negative control, and with the increase in the concentration of the extract up to 16 mg/ml, the anti-parasitic effect increased and more promastigotes were killed. 50IC at 88 hours after adding Glycyrrhiza glabra extract to the culture medium was 14.8 mg/ml. It is noteworthy that Glycyrrhiza glabra did not reduce the number of parasites below 50% in the tested dilutions before 88 hours in any concentration, so the 50IC was not calculated correctly at these times (79).

3-24. Ferula assa-foetida

Ferula assa-foetida is one of the important medicinal plants of the Chetrian family, with many properties. The plant that produces Ferula assa-foetida is called Shodma, Anguzakma, or Koren Kamav in Persian. Ferula assa-foetidah resin is considered expectorant, anti-flatulent, anti-spasm, and in the form of a suppository to improve colic, as well as its suspension to drive away dogs, cats, and other wild animals. It is used in folk remedies to stop menstruation, asthma, convulsions, fever, insanity, and cancer. The main ingredients of this plant are not fully known, but the presence of essential oil, resin, and gum in this plant is certain. In the research that was conducted on the effect of the Angozah plant on Leishmania major, dilutions of 31.25, 62.5, 125, 250, and 500 were used, and compared to the control group, only 25.31 dilutions on the promastigotes of the Leishmania major parasite in vitro had a reduction. It was significant, and the rest of the concentrations did not show this difference. The 50 IC for this aqueous extract was announced as 5.9 µg/ml (80).

3-25. Gossypium hirsutum

Gossypium hirsutum is a plant from the Malvaceae family that has alternating clawed leaves that often cover the surface of the leaf with a dark web. Its flowers are bright yellow, and there is a dark spot in the center of the petals. The fruit of this plant is known as Gossypium hirsutum boll. Other names of this plant in traditional medicine are juzeq, cloze, Gossypium hirsutum, and panboq. There are different compounds in this plant, the most important of which are betaine, choline, and salicylic acid. In traditional medicine, this plant is very useful for treating malaria and other fevers, treating itching and inflammation of the anus, treating burns, and absorbing pus from deep wounds. In research conducted on Gossypium hirsutum boll extract and its effect on Leishmania major parasite, it was shown that among the concentrations of 31.25, 62.5, 125, 250, 500, and 5000 micrograms per milliliter, concentrations of 500 and 5000 micrograms per milliliter affected promastigotes. Leishmania major is effective in vitro. 50 IC for this plant was calculated as 3.6 µg/ml (80).

3-26. Artemisia aucheri Boiss

Artemisia aucheri Boiss belongs to the Compositiae family and the Radiae family. The components of this plant include 8 and 1 cineole, alpha pine, and essential oils. Cineol has a killing effect on meningococcal, Elbert bacillus, pneumococcus, staphylococcus aureus, and diphtheria bacillus. On the other hand, the compounds of this plant are used to repel worms and have anti-flatulent, antiseptic, and insecticidal effects. In research that was conducted on different concentrations of the extract of the herb on Leishmania major, it was found that the best effect was achieved at a concentration of 5000 micrograms per ml of the aqueous extract and in vitro conditions. 62)(80).

3-27. Allium sativum

Although everyone knows garlic as a spice, garlic is a medicinal plant. When we talk about the properties of garlic, we should also consider the slight smell that this plant creates, although this smell is not only annoying for lovers of this plant but may also be lovely. This medicinal plant is used to prevent and treat various types of diseases. These diseases include high blood pressure, high blood cholesterol, and heart disease. Heart attack and hardening of the heart artery are used. Some people use garlic to prevent colon cancer, stomach cancer, breast cancer, prostate cancer, and lung cancer. Garlic has sulfur compounds that give this plant antiseptic, germ-killing, and scale-killing properties. The important ingredient in this plant is helicin, which destroys typhoid and paratyphoid germs. Helicin is also a well-known anti-parasitic compound. In the reports, the therapeutic effect of blue garlic extract on Hymenolepis nana and Giardia has been proven. Allicin is also effective against Leishmania (59).

Research has shown that the immunomodulatory effects of garlic include strengthening cellular responses and increasing delayed hypersensitivity, the tendency of cytokine responses towards 1Th in the leishmaniasis model, increasing the activity of natural killer cells against tumors, increasing macrophages, and strengthening the swallowing and digestion of Leishmania major parasites. (60). Studies indicated that garlic extract has the least effect in vitro and is ineffective in concentrations of 15.5, 25.5, 40, and 75, and only at a concentration of 150 micrograms per milliliter is it compatible with the control drug, but the same extract has shown the best effect in vivo conditions and is ineffective only at a concentration of 15.5 micrograms per ml. The best concentration of garlic extract at which half of the amastigotes are destroyed is between 4.6 and 11.4 µg/ml in vitro after 48 hours. The result showed that by increasing the concentration of extracts and tartrate drugs, the inhibitory effect on Leishmania major amastigotes in vivo conditions increased compared to ex vivo conditions (81).

3- 28. Peganum harmalla

The pecan plant has alkaloid compounds such as harman, harmaline, and harmalone. The therapeutic properties of this plant can be sleep-inducing, diuretic, anti-inflammatory, eye pain treatment, appetite suppressant, insect repellent, heart and respiratory system booster, anti-fungal, anti-worm, anti-microbial, anti-viral, etc. Among the mechanisms of action of this plant, he mentioned its ability to compete with DNA, influence on membrane permeability, inhibition of topoisomerase 1 and 2, change in membrane ion channel, and formation of free radicals. According to the research conducted in vitro, the effective concentration of pecan plant extract on the Leishmania major parasite was declared to be 40 (61).

4. Discussion

Pentavalent antimoan drugs are used as the first treatment for leishmaniasis in endemic areas, along with amphoterpsin B and pentamidine. Saldanha et al. (2006) showed that common drugs for the treatment of leishmaniasis, including pentavalent compounds glucantim and pentostam, show relapse and failure in 10–25% of cases. Also, Khan et al. in 2002 showed severe toxic effects of anti-leishmaniasis on the heart, liver, and kidneys. Plant extracts or compounds derived from plants are a valuable source of anti-seeking drugs. Traditional treatments of cutaneous leishmaniasis have been carried out as a routine in different parts of Iran in endemic areas for years.

A screening program to find medicinal plants with potential anti-seeker effects based on indigenous knowledge was conducted in 2005, and several plant extracts were tested in vitro on humans and animals. With the passage of time, researchers have investigated and studied many plants relying on local treatments, and good results have been obtained in this field. Based on these studies, it can be said that the purified extracts of Nikamazor plant, Floss fruit, Shiraz thyme extract, pecan, mord, mountain tea, parsley leaf, mountain sedum, anguze, and cotton boll have anti-leishmanial

effects on promastigotes. Mountain tea, leaves Parsley, Pegalum harmala plant, Alcantinctura, and marigold have an inhibitory effect on the growth of Leishmania major promastigote, barberry extract, and cinnamon plant have reduced the size of Leishmania lesion, and thyme and yarrow extracts have been effective in healing the ulcer. In total, the presence of compounds (luteolin, quercetin), chalcone (4-dihydroxy 2,6 methoxychalcone), irodoids (amarogentin), naphthoquinone (plambagin), quinoline alkaloid (2-n-propylaquin), and chimanin B in each plant can make it a suitable option to investigate the effect of that plant extract on Leishmania major.

Conflict of interest

We declare that we have no conflict of interest.

Data availability statement

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

Table 1: Some of important medicinal plants with Effective component, Health benefits Activity and Effective concentration µg/mL

No	Name	Part of Plant	Effective component	Health benefits activity	Effective concentration µg/mL	
					In Vitro	**In Vivo**
1	Sargasum oligocystum	Whole plant	Phenol, Stigmasta, Stigmasterol	Antimicrobial, Antifungal, Antiviral, Anti-cancer	5	
2	Thymus pubesens	Whole plant	Thymol	Anti-parasite	250	
3	Thymus kotschyanus	Whole plant	Thymol	Anti-parasite	250	
4	Thymus caucasicus	Whole plant	Thymol	Anti-parasite	250	
5	Thymus vulgaris	Whole plant	Thymol	Anti-parasite	100	
6	Cichorinum intybus	Leaf	Lactucin Octane Cyanidin Cichorioside	Antimicrobial, Hepatoprotective Activity, Antidiabetic, Gastroprotective Anti-Inflammatory Antioxidant Analgesic	100	
7	Calendula officinalis	Flower	Flavonoids, Helenalin	Anti-bacterial, Antifungal, Antiviral,	500	
8	Crataegus aronia	Fruit	Polyphenol	Anti-bacterial, Antifungal, Anti-Inflammatory	100	
9	Zizyphusspina christi	Leaf	Alkaloid, Tanen, Flavonoids, Saponin	Anti-bacterial, Antifungal, Anti-malaria Anti-Schistosoma	60-80	
10	Berbris vulgaris	Fruit		Anti-amoebic Antifungal Immunomodulator y		10
11	Portulace oleracea	Leaf and stem	Alkaloid, Flavonoids,	Antifungal, Anti-bacterial, Antiparasitic	270	385
12	Rumex	Leaf and seed	Flavonoids	Antimicrobial Antiparasitic anti-venom		9
13	Lavendula officinalis	flower	Linalool	Antifungal, Antimicrobial Antiparasitic	50 100 150	

					200	
14	Matricaria chamomill	flower	Flavonoids	Anti-bacterial,		
15	Arnebia euchroma	Whole plant	Alkannin	anti scabies Antitumor Antiparasitic	3 6 12	
16	Artemisia absinthium	Flower	Absinthin Chrysanthenyl acetate	Anti-Leishmanial Anti-Schistosoma Anti-Leptospira Anti-Aspergylus Anti-toxoplasma Anti-Malaria	50-500	
17	Juglans regia	Leaf	hydroxynaphthoquinone	Anti-bacterial, Antifungal, Antiviral Anti-insect	200-800	
18	Artemisia dracunculu	Whole plant	Essential oil	Antimicrobial Antihelminth Immunomodulatory	10%	
19	Ecalyptus	Leaf	Eucalyptol Thymol	Antimicrobial Antiparasitic	10%	
20	Artemisia siberi	Whole plant	Artemisinin	Antimicrobial Antiparasitic Antimalaria	60	
21	Plargonium graveolen	Leaf	Geraniol	Anti-Inflammatory Anti-bacterial Macrophage-activating	60	
22	Scophularia straiats	Whole plant	Cryptophilic	Anti-Inflammatory Anti-bacterial Anti-parasitic	25	
23	Curcuma langoma	Rhizome	Curcumin	Anti-bacterial Anti-parasitic Anti-tumor	2	
24	chillea millefolium	Whole plant	Chamazulene	Anti-bacterial Anti-fungal Anti-parasitic Anti-oxidant	100 200 400 800	
25	Glycyrrhiza glabra	Whole plant	Licochalcone A	Wound healing Analgesic Anti cough	16	
26	Artemisia aucheri bois	Whole plant	Eucalyptol or |Cineole	Anti-fungal Anti-insect Anti-helminth Anti-microbial	5000	
27	Ferula assa-foetida	resin	Oleo-gum resin	Anti-fungal Anti-helminth Anti-microbial	500-5000	
28	Gossypium hirsutum	cotton boll	Bethanechol	Anti-helminth Anti-Inflammatory Anti-malaria		
29	Allium sativum	Rhizome	Allicin	Antibiotic Anti-bacterial Anti-parasitic Anti-Inflammatory	150	15.5-25.5
30	Lawsonia inerm is	Leaf	Lawson	Anti-fungal Anti-parasitic Anti-oxidant		
31	Cassia fistula	Fruit		anti diarrhea	50	

				Anti-constipation		
32	Peganum harmalla	Seed	Harmaline	Eugenol Anti-parasitic Anti-fungal Anti-viral	10-40	
33	Myrtus communis	Whole plant	Terpinolene	Anti-parasitic Anti-fungal Anti herpes	400	400-800
34	Cinnamonze yalnicum	wood	Eugenol	Anti-bacterial Anti-Inflammatory Anti-diabet		

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