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Phytotherapy of Brucellosis: A Pharmacological Review of Anti-Brucellosis Medicinal Plants in Iranian Flora

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ABSTRACT

Background: Brucellosis is a persistent zoonotic infection endemic in countries such as Iran. Conventional antibiotic therapies have limitations, including adverse effects and incomplete efficacy, which has led to growing interest in medicinal plants as complementary or alternative treatments.

Methods: This study reviews Iranian medicinal plants with potential anti-brucellosis activity, examining their mechanisms based on both traditional knowledge and contemporary scientific research. A comprehensive literature search was conducted using keywords including "brucellosis," "Malta fever," "traditional medicine," "medicinal plants," and "treatment" in databases such as Google Scholar, SID, Magiran, and Scopus. Relevant articles were screened, and data were systematically extracted and analyzed to provide an integrative review.

Results: The analysis identified several medicinal plants with notable therapeutic potential against brucellosis, including *Zingiber officinale* Roscoe, *Mentha piperita* L., *Cinnamomum verum* J. Presl, *Thymus vulgaris* L., *Salvia officinalis* L., *Origanum vulgare* L., *Matricaria chamomilla* L., *Aloe vera* L., *Cuminum cyminum* L., *Alcea rosea* L., *Achillea millefolium* L., *Calendula officinalis* L., *Allium cepa* L., *Anethum graveolens* L., *Apium graveolens* L., *Allium sativum* L., *Coriandrum sativum* L., *Cucurbita* spp. L., *Rosa canina* L., *Elaeagnus angustifolia* L., *Scrophularia deserti* Eig, *Berberis vulgaris* L., *Ziziphora tenuior* L., and *Alhagi maurorum* Medik. Taxonomic analysis showed that the Lamiaceae family was most represented (24%), followed by Asteraceae and Apiaceae (16% each). Mechanistic analysis indicated that antibacterial activity accounted for 32% of therapeutic effects, followed by anti-inflammatory (24%) and antioxidant (20%) activities.

Conclusion: Native Iranian medicinal plants may serve as effective complementary agents in the management of brucellosis. They show promise, but further high-quality clinical studies are required to establish their efficacy and safety.

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INTRODUCTION

Brucellosis (Malta fever) is a bacterial zoonosis caused by *Brucella* species (1). The disease also referred to as Mediterranean fever, undulant fever, or contagious abortion in animals is notable for inducing early-stage pregnancy loss and for its ability to spread across various mammalian species (2). Infected livestock, particularly during early pregnancy, produce contaminated secretions that can readily pollute pastures, farms, and the surrounding environment (3).

A primary route of transmission to humans is the consumption of unpasteurized dairy products, as well as direct contact with infected animals such as cattle, goats, sheep, and camels (4). Individuals who work closely with animals including veterinarians, farm workers, slaughterhouse staff, and microbiologists are at higher risk of infection (5). *Brucella* bacteria can enter the human body through contact with blood or other secretions from infected animals, potentially leading to chronic complications if untreated (6).

Common symptoms include fever, night sweats, arthralgia, fatigue, and weight loss, and without timely diagnosis and treatment, the disease may progress to severe complications (7, 8). Similar symptoms are observed in children, often accompanied by weakness and lymphadenopathy (9). Accurate diagnosis requires specialized laboratory tests alongside clinical evaluation, as brucellosis symptoms can resemble those of other illnesses, such as influenza (10).

The standard treatment for brucellosis relies on antibiotics; however, this approach may be limited by side effects or incomplete efficacy (11). In such cases, Iranian traditional medicine offers complementary strategies for symptom management and patient support through the use of medicinal plants (12). Bioactive medicinal plants may complement conventional therapy through their antibacterial, anti-inflammatory, and immunomodulatory effects (13).

This study aims to investigate the therapeutic potential of medicinal plants with anti-brucellosis activity in the Iranian flora, through a comprehensive analysis of their ecological, morphological, phytochemical, phenological, and pharmacological characteristics.

METHODOLOGY

This review synthesizes existing information on brucellosis, medicinal plants, and their therapeutic applications. A comprehensive search was conducted using Google Scholar, SID, Magiran, and Scopus. The searches employed keywords such as “brucellosis,” “Malta fever,” “traditional medicine,” “medicinal plants,” and “treatment.”

Initially, the retrieved articles were screened for relevance, and studies unrelated to the scope of this review were excluded. Only articles directly addressing the topic were selected for detailed analysis (14-30).

The results of the relevant studies were then systematically and comprehensively reviewed to provide evidence-based insights into the role of medicinal plants in brucellosis management.

A flowchart illustrating the search strategy, as well as the articles and sources included in this review, is presented in Figure 1.

RESULTS

The analysis revealed that numerous medicinal plants within the Iranian flora exhibit significant potential in the management of brucellosis. Notable examples include *Zingiber officinale* Roscoe, *Mentha piperita* L., *Cinnamomum verum* J. Presl, *Thymus vulgaris* L., *Salvia officinalis* L., *Origanum vulgare* L., *Matricaria chamomilla* L., *Aloe vera* L., *Cuminum cyminum* L., *Alcea rosea* L., *Achillea millefolium* L., *Calendula officinalis* L., *Allium cepa* L., *Anethum graveolens* L., *Apium graveolens* L., *Allium sativum* L., *Coriandrum sativum* L., *Cucurbita* spp. L., *Rosa canina* L., *Elaeagnus angustifolia* L., *Scrophularia deserti* Eig, *Berberis vulgaris* L., *Ziziphora tenuior* L., and *Alhagi maurorum* Medik (Table 1).

These species have demonstrated therapeutic potential in traditional medicine, largely attributed to their antibacterial, anti-inflammatory, and immunomodulatory properties, which may contribute to their effectiveness in managing brucellosis.

Table 2 summarizes essential information on the selected medicinal plants, including the plant parts utilized, principal bioactive compounds, growth habits, life cycle, and natural habitat, providing a valuable reference for investigating their pharmacological and ecological characteristics.

The analysis reveals that the Lamiaceae family, with six occurrences (24%), is the most frequently represented among the listed plant families. This prominence highlights its significance within this compilation. The Asteraceae and Apiaceae families follow, each with four occurrences (16%), while other families are mentioned sporadically, with one or two occurrences each. These findings underscore the importance of the Lamiaceae, Asteraceae, and Apiaceae families as key targets for botanical and pharmaceutical research.

Most selected medicinal plants utilize leaves and flowers as primary sources of secondary bioactive compounds, including flavonoids and essential oils. This reflects an ecological strategy focused on chemical defense and efficient light-energy capture. Underground organs, such as rhizomes, bulbs, and roots, serve both as reservoirs of bioactive compounds and as means for regeneration under adverse environmental conditions. Seeds and fruits, in contrast, contain lipid-soluble compounds and vitamins, fulfilling protective and reproductive roles. The use of different or multiple organs within a single species demonstrates a comprehensive medicinal strategy and a diverse repertoire of secondary metabolites, aligned with the plant’s ecological adaptations and life cycle requirements.

Most selected species exhibit perennial life cycles, enabling continuous regeneration and year-round production of bioactive compounds via rhizomes, bulbs, or bush-like structures an adaptation particularly suited to arid and semi-arid environments. Annual

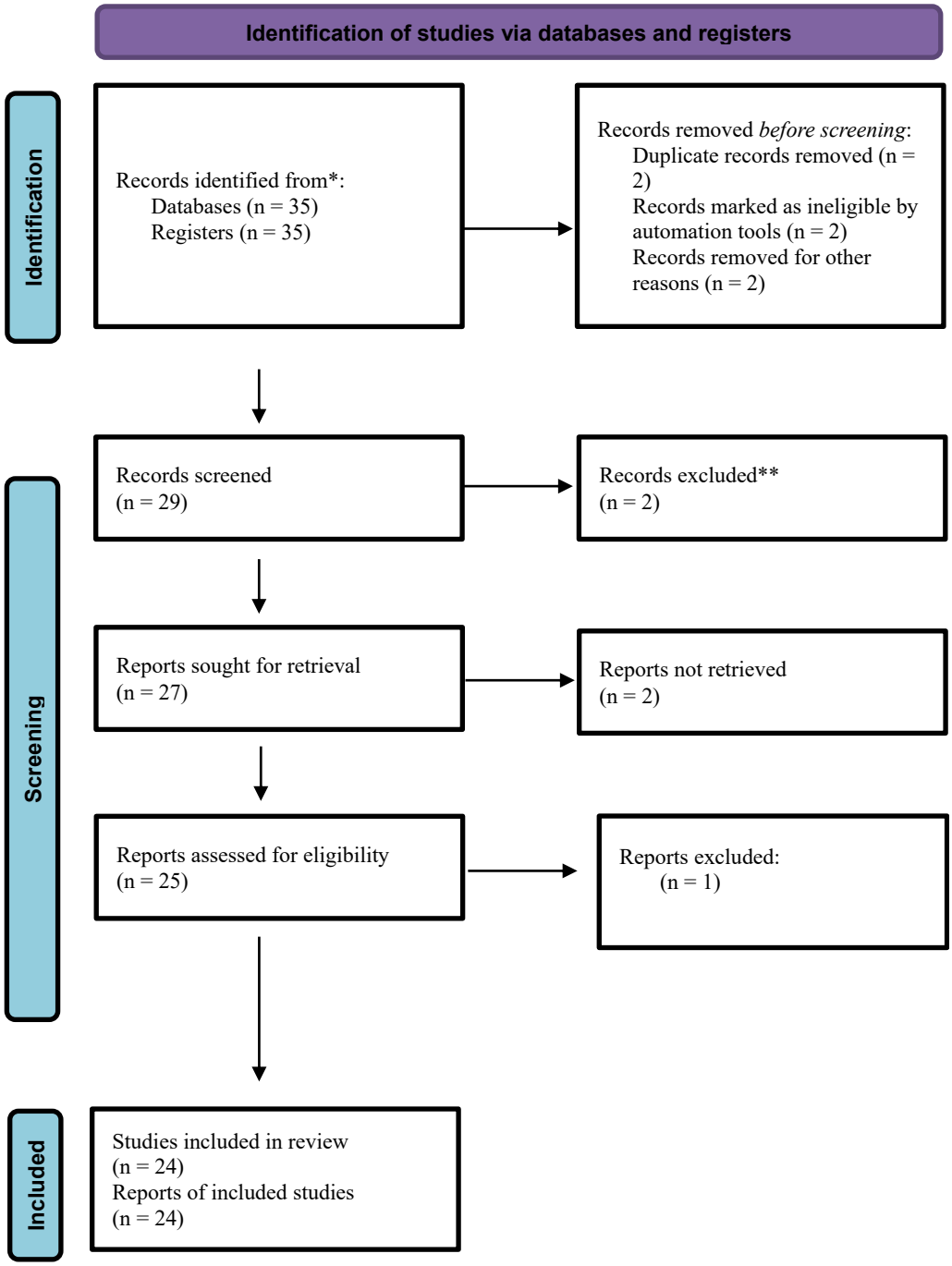

Fig 1. Flowchart of Search Strategy

plants, with their shorter life cycles, allocate energy primarily to seed production and secondary metabolite synthesis, making the timing of organ harvest critical. Evergreen and shrub species can continuously produce leaves, flowers, and fruits. This diversity of growth strategies reflects ecological adaptations and ensures optimal utilization of medicinal metabolites.

The selected medicinal plants are adapted to a wide range of habitats, from humid tropical regions to deserts and dry, calcareous soils. Habitat conditions directly influence secondary metabolite production and the medicinal potential of specific plant organs. Tropical species in moist soils predominantly produce underground organs and leaves rich in bioactive metabolites, whereas species from arid, sun-exposed environments have adapted to water scarcity through small or thick leaves, spiny stems, and storage of water and active compounds. This ecological diversity illustrates the close relationship between habitat adaptation and the synthesis and accumulation of medicinal compounds.

Functional analysis indicates that antibacterial

Table 1. Medicinal Plants Native to Iran Effective in the Treatment of Brucellosis in Traditional Medicine.

English Name	Persian Name	Scientific Name	Plant Family	Mechanism / Activity (14-30)
Ginger	Zangabil	*Zingiber officinale* Roscoe	Zingiberaceae	Anti-inflammatory, Immune-boosting
Mint	Naena	*Mentha piperita* L.	Lamiaceae	Antimicrobial, Improves digestive function
Cinnamon	Darchin	*Cinnamomum verum* J. Presl	Lauraceae	Antibacterial
Thyme	Avishan baghi	*Thymus vulgaris* L.	Lamiaceae	Contains thymol; antibacterial
Sage	Maryam goli	*Salvia officinalis* L.	Lamiaceae	Antioxidant, Immune-boosting
Oregano	Pouneh kouhi	*Origanum vulgare* L.	Lamiaceae	Contains carvacrol and thymol; antibacteria
Chamomile	Babouneh	*Matricaria chamomilla* L.	Asteraceae	Anti-inflammatory, Reduces fever and pain
Aloe vera	Aloe vera	*Aloe vera* L.	Asphodelaceae	Wound healing, Antimicrobial
Cumin	Zireh sabz	*Cuminum cyminum* L.	Apiaceae	Antioxidant, Antibacterial
Hollyhock	Khatmi	*Alcea rosea* L.	Malvaceae	Soothing, Anti-inflammatory
Yarrow	Boumadaran	*Achillea millefolium* L.	Asteraceae	Antibacterial, Immune-boosting
Calendula	Hamishe bahar	*Calendula officinalis* L.	Asteraceae	Anti-inflammatory, Antibacterial
Onion	Piaz	*Allium cepa* L.	Amaryllidaceae	Contains quercetin; antibacterial
Dill	Shevid	*Anethum graveolens* L.	Apiaceae	Antibacterial
Celery	Karafs	*Apium graveolens* L.	Apiaceae	Anti-inflammatory, Antioxidant
Garlic	Sir	*Allium sativum* L.	Amaryllidaceae	Contains allicin; strong antibacterial
Coriander	Geshniz	*Coriandrum sativum* L.	Apiaceae	Antioxidant, Antibacterial
Squash	Kadou	*Cucurbita* spp. L.	Cucurbitaceae	Immune-boosting via antioxidant activity
Rosehip	Nastaran	*Rosa canina* L.	Rosaceae	Immune-boosting; rich in vitamin C
Russian Olive	Senjed	*Elaeagnus angustifolia* L.	Elaeagnaceae	Antioxidant, Anti-inflammatory
Snapdragon	Gole meymoni biabani	*Scrophularia deserti* Eig	Plantaginaceae	Soothing properties
Barberry	Zereshk kouhi	*Berberis vulgaris* L.	Berberidaceae	Antibacterial
Ziziphora	Kakouti	*Ziziphora tenuior* L.	Lamiaceae	Antibacterial, Immune-boosting
Camelthorn	Kharshotor	*Alhagi maurorum* Medik.	Fabaceae	Antimicrobial effects

properties, with eight mentions (32%), are the most frequent therapeutic attribute among the selected plants. Anti-inflammatory properties follow with six occurrences (24%), while antioxidant and immune-boosting activities, each with five occurrences (20%), are also notable. These findings highlight the primary importance of antibacterial and anti-inflammatory effects, alongside the considerable potential of antioxidant and immunomodulatory properties. Collectively, these bioactivities are highly relevant for the development of herbal and pharmaceutical products aimed at disease prevention and treatment.

DISCUSSION

The therapeutic potential of *Zingiber officinale* is largely attributed to gingerol and shogaol, which exert antioxidant, anti-inflammatory, and immunomodulatory effects that may benefit patients with brucellosis (31). Mint (*Mentha piperita* L., Lamiaceae) exhibits antimicrobial and digestive-supportive effects. Consumption of mint may alleviate gastrointestinal symptoms commonly observed in brucellosis and also contributes to immune enhancement and relief of muscle pain associated with the disease (32). Cinnamon (*Cinnamomum verum* J. Presl, Lauraceae) contains cinnamaldehyde,

Table 2. Phytochemical Profile and Ecological Characteristics of Selected Medicinal Plants.

Medicinal Plant	Plant Part Used	Active Compounds	Growth and Life Cycle	Ecology / Habitat
***Zingiber officinale* Roscoe**	Rhizome	Gingerol, Shogaol	Perennial, rhizomatous	Tropical and subtropica regions, moist soils
***Mentha piperita* L.**	Leaves	Menthol, Menthone	Perennial, creeping stems	Moist soils, full sun
***Cinnamomum verum* J. Presl**	Bark	Cinnamaldehyde	Evergreen, small tree	Humid tropical regions
***Thymus vulgaris* L.**	Leaves, flowers	Thymol, Carvacrol	Perennial, bushy	Dry soils, full sun
***Salvia officinalis* L.**	Leaves, flowers	Salvin, Rosmarinic acid	Perennial, bushy	Dry, calcareous soils, full sun
***Origanum vulgare* L.**	Leaves, flowers	Carvacrol, Thymol	Perennial, bushy	Dry, sunny habitats
***Matricaria chamomilla* L.**	Flowers	Apigenin, Chamazulene	Annual	Sandy soils, full sun
***Aloe vera* L.**	Leaves	Aloin, Aloeic acid	Perennial, succulent	Arid and semi-arid regions
***Cuminum cyminum* L.**	Seeds	Cumin aldehyde	Annual	Light soils, full sun
***Alcea rosea* L.**	Flowers, leaves	Anthocyanins, Mucilage	Biennial or perennial	Rich soils, full sun
***Achillea millefolium* L.**	Leaves, flowers	Antol, Camphor	Perennial, bushy	Meadows, semi-moist soils
***Calendula officinalis* L.**	Flowers	Carotenoids, Flavonoids	Annual	Rich soils, full sun
***Allium cepa* L.**	Bulb	Flavonoids, Sulfur compounds	Biennial	Fertile soils, full sun
***Anethum graveolens* L.**	Leaves, seeds	Carvone, Limonene	Annual	Sandy soils, full sun
***Apium graveolens* L.**	Leaves, stems, seeds	Apiole, Limonene	Biennial	Moist soils, full sun
***Allium sativum* L.**	Bulb	Allicin	Perennial, bulbous	Fertile soils, full sun
***Coriandrum sativum* L.**	Leaves, seeds	Limonene, Linalool	Annual	Dry soils, full sun
***Cucurbita* spp. L.**	Fruit, seeds	Cucurbitin, Carotenoids	Annual	Fertile soils, full sun
***Rosa canina* L.**	Fruit, flowers	Vitamin C, Tannins	Perennial, shrub	Light soils, full sun
***Elaeagnus angustifolia* L.**	Fruit	Flavonoids, Tannins	Shrub	Dry and semi-arid soils
***Scrophularia deserti* Eig**	Leaves, flowers	Flavonoids, Saponins	Perennial	Arid and semi-arid regions
***Berberis vulgaris* L.**	Fruit, roots	Berberine, Alkaloids	Shrub	Dry soils, full sun

a compound with strong antibacterial activity, making it effective against microbes responsible for brucellosis and other bacterial infections (33). Thyme (*Thymus vulgaris* L., Lamiaceae), rich in thymol, demonstrates notable antibacterial and anti-inflammatory effects, particularly relevant for controlling infections such

as brucellosis (34). Similarly, oregano (*Origanum vulgare* L., Lamiaceae), containing carvacrol and thymol, exhibits antibacterial and anti-inflammatory properties, strengthens immune function, and aids in combating infections (35). Chamomile (*Matricaria chamomilla* L., Asteraceae) is recognized for its natural anti-inflammatory and analgesic activities. It can reduce fever and pain and is particularly useful in alleviating acute symptoms of brucellosis (36). Aloe vera (*Aloe vera* L., Asphodelaceae) possesses antimicrobial and wound-healing properties, making it effective in treating inflammation and tissue damage associated with chronic infections such as brucellosis (37). Garlic (*Allium sativum* L.) contains allicin, which provides strong antibacterial effects and enhances immune defenses against brucellosis-causing bacteria (38). Celery (*Apium graveolens* L., Apiaceae) exhibits both anti-inflammatory and antioxidant properties, supporting immune function and reducing bacterial inflammation (39). Thyme (*Thymus vulgaris* L., Lamiaceae) also demonstrates antibacterial and immunomodulatory effects, making it valuable in treating various infectious and inflammatory conditions, including brucellosis (40). Wild barberry (*Berberis vulgaris* L., Berberidaceae) possesses antibacterial activity and can aid in controlling brucellosis-related bacterial infections, improving overall disease outcomes (41). The bioactive and secondary metabolites, along with the antioxidant compounds present in plants, play a central role in mediating their antimicrobial effects (42-47).

CONCLUSION

This review has several limitations, primarily the limited availability of clinical evidence, as most published data originate from traditional medicine, in vitro studies, and animal models. Iranian medicinal plants with antibacterial, anti-inflammatory, immunomodulatory, and antioxidant activities may offer complementary benefits in brucellosis management. Nevertheless, their clinical application should be evidence-based and used alongside standard therapy under medical supervision. Well-designed clinical trials are needed to confirm their efficacy, safety, and place in future treatment strategies.

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Ethics Approval and Consent to Participate

Conflict of Interest

The authors declare that they have no conflict of interest.

Consent for Publication

Not applicable.

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