Journal of Medical Microbiology and Infectious Diseases

JoMMID
ISSN: 2345-5349
eISSN: 2345-5330

Iranian Medicinal Plants with Antimicrobial Properties: A Narrative Review

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ARTICLE INFO

Narrative Review

Keywords: Medicinal plants, Antibacterial, Antifungal, Antiviral, Antiparasitic, Nanotechnology, Iran

Received: 29 Sep. 2025
Received in revised form: 26 Oct. 2025
Accepted: 17 Dec. 2025
DOI: 10.61882/JoMMID.14.1.1

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ABSTRACT

Medicinal plants have played a significant role in traditional Iranian medicine due to their antimicrobial properties, making them valuable resources for the development of alternative therapies. With the increasing threat of antimicrobial resistance (AMR) and limitations in new antibiotic development, interest has intensified in traditional medicine and natural products as sources of antimicrobial agents. Given this context, Iran's climatic and geographical diversity has fostered a rich flora containing numerous plants with potent antimicrobial activity against a wide range of pathogens. This review aims to consolidate and critically discuss the literature on the antimicrobial properties of Iranian medicinal plants. Relevant studies were identified by searching PubMed, Scopus, Google Scholar, ScienceDirect, and Civilica databases using relevant keywords. The findings are organized into sections addressing antibacterial, antiviral, antifungal, and antiparasitic properties. The role of biotechnology in advancing medicinal plant research is also discussed. This review highlights that numerous Iranian medicinal plants, including *Zataria multiflora*, *Thymus daenensis* Celak., *Myrtus communis*, and *Nigella sativa*, exhibit potent, broad-spectrum antimicrobial activity against bacterial, fungal, viral, and parasitic pathogens. Furthermore, biotechnological applications, such as green-synthesized nanoparticles (NPs) derived from plant extracts, have been shown to enhance antimicrobial efficacy and formulation stability. In conclusion, Iranian medicinal plants constitute a rich repository of antimicrobial agents with significant potential for combating bacteria, viruses, fungi, and parasites. However, realizing their therapeutic potential requires rigorous scientific validation, including the standardization of extraction methods, comprehensive chemical characterization, and in-depth investigations into their mechanisms of action and clinical efficacy.

INTRODUCTION

The rise of multidrug-resistant (MDR) microorganisms is a significant global threat, creating an urgent demand for new antimicrobial agents, particularly those derived from natural sources and traditional medicine [1]. It has been reported that more than 80% of the world's population uses herbal medicines for primary health care, and approximately 50% of modern medicines are derived from natural sources [2, 3]. Within this framework, Iran is notable for its rich biodiversity and long history of traditional herbal medicine. The country's flora encompasses over 8,000 plant species, including nearly 1,900 endemic species, which are traditionally used to treat a range of ailments, particularly infectious conditions such as skin disorders, wound infections, and sepsis [1]. Plants such as *Zataria multiflora*, *Thymus daenensis* Celak., *Ferula gummosa* Boiss., and *Nigella sativa* exhibit well-documented antimicrobial activity against antibiotic-resistant bacteria and fungi [4, 5]. Modern phytochemical and microbiological studies have validated the antimicrobial properties of many of these plants, attributing this activity to their constituent bioactive compounds. For example, thymol and carvacrol in *Zataria multiflora* potently inhibit Gram-positive and Gram-negative bacteria by disrupting bacterial cell membranes and metabolic pathways [6]. Phenolic compounds are key contributors to this antimicrobial activity, and their concentration often correlates with antimicrobial potency [1]. Consequently, variations in chemical composition-influenced by factors such as plant species, genotype, and geographical origin-can lead to

[DOI: 10.61882/JoMMID.14.1.1]

significant differences in antimicrobial activity among different species and even within the same species grown in various regions [1, 7-9].

Previous research has often adopted a narrow focus, investigating the antimicrobial activity of medicinal plants against single pathogens, such as human immunodeficiency virus (HIV) [10], severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [11-19], dengue virus [20], and *Candida albicans* [21]. Other studies have taken a plant-centric approach, focusing on the diverse antimicrobial properties of a single plant, such as *Artemisia scoparia* [22] and *Ziziphus jujuba* Mill. [23]. A third approach has focused on individual compounds, assessing the antimicrobial activity of specific phytochemicals, such as coumarins and alkaloids [24, 25]. However, few studies have comprehensively investigated the antibacterial, antifungal, antiviral, and antiparasitic properties across a wide range of Iranian medicinal plants. Therefore, this review aims to consolidate the literature on the antimicrobial activities of Iranian medicinal plants and associated biotechnological advancements, thus evaluating their potential as natural alternatives to synthetic antimicrobial agents.

Antibacterial activity of medicinal plants

Pathogenic bacteria cause numerous significant infections in both humans and animals. The emergence and spread of MDR bacterial strains necessitate the exploration of alternative infection control strategies [26]. Among these alternatives, medicinal plants represent a promising resource. A diverse array of bioactive constituents, including flavonoids, alkaloids, tannins, and terpenoids, underlies the antibacterial activity of these plants [27].

Hamidi *et al*. [1] evaluated the antibacterial and anti-biofilm properties of various Iranian plant extracts against several pathogenic bacterial species. The results demonstrated that *Hypericum scabrum* L. and *Hymenocrater calycinus* exhibited potent antibacterial activity against *Bacillus cereus* (*B. cereus*). Additionally, *Hypericum scabrum* L. inhibited biofilm formation by *Staphylococcus aureus* (*S. aureus*), *Streptococcus mutans* (*S. mutans*), and *Staphylococcus epidermidis* (*S. epidermidis*), highlighting its potential for controlling drug-resistant infections [1]. Zomorodian *et al*. [6] investigated essential oils from three distinct chemotypes of *Zataria multiflora*, characterized by high concentrations of carvacrol, thymol, or linalool, and evaluated their antimicrobial activity against both Gram-positive and Gram-negative bacteria, including *S. aureus*, *Enterococcus faecalis* (*E. faecalis*), *Enterococcus faecium* (*E. faecium*), *Escherichia coli* (*E. coli*), *Pseudomonas aeruginosa* (*P. aeruginosa*), *Shigella flexneri* (*S. flexneri*), *Klebsiella pneumoniae* (*K. pneumoniae*), and *Salmonella enterica* (*S. enterica*) [6, 28]. The essential oil, particularly from the carvacrol-rich ecotype, exhibited potent inhibitory activity, with the proposed mechanism of action involving disruption of the bacterial cell membrane [6, 28]. Similarly, the essential oil extracted from *Dracocephalum kotschyi* demonstrated bactericidal activity against *Bacillus subtilis* (*B. subtilis*) [29]. Numerous studies have reported that diverse Iranian medicinal plants—notably *Gundelia tournefortii* L., *Satureja laxiflora* C. Koch, *Myrtus communis* L., and *Hymenocrater longiflorus* Benth.— exhibit potent bactericidal activity against *S. aureus*, *P. aeruginosa*, *E. coli*, and *B. subtilis* [30-43]. This broad-spectrum activity is largely attributed to various bioactive compounds, including primarily phenolic monoterpenoids (*e.g*., carvacrol, thymol) and other terpenoids (*e.g*., pulegone, menthol, 1,8-cineole, α-pinene, β-pinene, limonene, and linalool), as well as flavonoids, alkaloids, and tannins [30-43]. Extracts obtained using organic solvents (methanol, ethanol, ethyl acetate, dichloromethane) from several plants, particularly *Zataria multiflora*, *Eremostachys macrophylla*, *Thymus vulgaris*, and *Satureja hortensis*, have exhibited potent antimicrobial activity against pathogens including *S. aureus*, *E. coli*, and *P. aeruginosa* [44, 45]. Additionally, the essential oil of *Pycnocycla bashagardiana* Mozaff. has demonstrated antibacterial activity against the same pathogens, an effect attributed to its high content of secondary metabolites, including the monoterpenes α-pinene and limonene, as well as the sesquiterpene β-caryophyllene [46]. Extracts from *Eucalyptus camaldulensis*, *Datura stramonium*, and *Prosopis farcta* have demonstrated both antibacterial and anti-biofilm activity against *S. aureus*, *E. coli*, and *P. aeruginosa* [47, 48]. The *Datura stramonium* extract was particularly active against Gram-positive bacteria, while the *Prosopis farcta* extract was moderately effective against Gram-negative bacteria. Moreover, extracts from both *D. stramonium* and *P. farcta* inhibited biofilm formation, indicating their potential to combat drug-resistant infections [47]. These activities are attributed to various secondary metabolites, including terpenoids, flavonoids, and phenols, which exert antimicrobial effects through membrane disruption, enzyme inhibition, and interference with cellular metabolism [47-50]. *Myrtus communis*, *Thymus daenensis* Celak., *Nepeta* spp., *Iris germanica*, *Parietaria officinalis*, *Berberis integerrima* Bunge, *and Marrubium vulgare* L. (horehound) have demonstrated notable antibacterial activity against *S. aureus* and *E. coli* [50-56]. This activity is broadly attributed to various phytochemicals, such as the phenolic compounds carvacrol, thymol, and *p*-cymene, as well as isoflavones and various other essential oil components, which are proposed to act by disrupting microbial cell membrane integrity and inducing oxidative stress [42, 51]. Furthermore, aqueous and alcoholic extracts as well as essential oils of *Eucalyptus camaldulensis*, *Allium sativum*, *Matricaria chamomilla*, *Satureja khuzestanica*, and *Thymus daenensis* exhibit potent inhibitory activity against *P. aeruginosa*, largely attributable to key bioactive compounds such as allicin, carvacrol, and thymol [57].

[DOI: 10.61882/JoMMID.14.1.1]

Soheili *et al*. demonstrated that root extracts of *Hypericum scabrum* L. inhibited *B. cereus*, *B. subtilis*, *E. faecalis*, and *Salmonella enterica* serovar Typhimurium (*S*. Typhimurium) [58]. Similarly, Javadian *et al*. [59] reported that extracts of *Hyssopus officinalis* and *Solanum nigrum* (black nightshade) inhibited *E. faecalis*, *P. aeruginosa*, and *E. coli*. Furthermore, methanolic, ethanolic, and ethyl acetate extracts of *Potentilla recta* were effective against *S. aureus*, *Listeria monocytogenes* (*L. monocytogenes*), and *E. coli* [60]. In another study, Rostami *et al*. (2012) analyzed essential oils from *Lavandula angustifolia* (lavender) and *Melissa officinalis* and identified their main compounds as α-pinene, camphor, menthol, 1,8-cineole, β-pinene, linalool, thymol, and carvacrol [61]. These essential oils were active against numerous Gram-positive and Gram-negative bacterial species, including *S. aureus*, *B. cereus*, *B. subtilis*, *Bacillus megaterium* (*B. megaterium*), *Micrococcus luteus*, β-hemolytic *Streptococcus* spp., *S.* Typhimurium, *Shigella* spp., including *S. dysenteriae*, *S. flexneri*, *S. sonnei*, and *S. boydii*, *E. coli*, *P. aeruginosa*, *Klebsiella* spp., and *Proteus* spp. Among the components, thymol, carvacrol, and menthol exhibited the strongest antibacterial activity, whereas β-pinene and linalool showed the weakest activity compared to streptomycin (positive control) [61]. Furthermore, notable antimicrobial activity against antibiotic-resistant strains of *P. aeruginosa* has been reported for a range of Iranian plants, including *Juglans regia*, *Urtica dioica*, *Myrtus communis*, and species from the *Salvia*, *Thymus*, and *Nepeta* genera [55, 62, 63]. This activity is primarily attributed to key bioactive compounds such as thymol, carvacrol, cineole, and tannins, which act via several mechanisms, including the inhibition of biofilm formation, disruption of quorum-sensing systems and cell membrane integrity, and the inhibition of virulence enzymes [55, 62, 63]. Aghaee *et al*. evaluated the phytochemical composition and antimicrobial activity of aerial extracts from *Salvia sharifii* against Gram-positive and Gram-negative bacteria, demonstrating that the essential oil potently inhibited *S. aureus* [64]. Similarly, both the methanolic extract and essential oil of *Echinophora platyloba* were active against *S. aureus*, *L. monocytogenes*, *S.* Typhimurium, and *E. coli* [65]. Chemical analysis identified the key constituents of the methanolic extract as *o*-cymene, α-pinene, and γ-decalactone, while the essential oil contained *o*-cymene, 2,3-dimethylcyclohexa-1,3-diene, α-pinene, and γ-dodecanolactone [65]. Of the tested pathogens, *L. monocytogenes* and *S. aureus* were the most susceptible to both the essential oil and the extract [65]. In another study, the essential oil from the aerial flowering parts of *Tanacetum fisherae*, with 1,8-cineole as its predominant compound, exhibited broad-spectrum antimicrobial activity against *B. subtilis*, *E. faecalis*, *S. aureus*, *S. epidermidis*, *E. coli*, *K. pneumoniae*, and *P. aeruginosa* [66]. Additionally, the extract and essential oil of *Gontscharovia popovii* were evaluated for their activity against several bacterial species, including *S. aureus*, *B. subtilis*, *E. coli*, and *K. pneumoniae* [67]. The antimicrobial activity of the *G. popovii* extracts was reportedly comparable to or superior to that of conventional antibiotics, including penicillin, gentamicin, and ciprofloxacin [67]. Razavi *et al*. isolated two pyranocoumarin compounds, aegelinol and agasyllin, from the roots of *Zosima absinthifolia*. These compounds exhibited weak-to-moderate antimicrobial activity against *B. subtilis*, *S. aureus*, *E. coli*, and *S.* Typhimurium [68]. Similarly, methanolic extracts from the flowers and leaves of *Malva sylvestris* L. demonstrated potent antibacterial activity against both the plant pathogen *Pectobacterium carotovorum* (formerly *Erwinia carotovora*) and human pathogens, such as *S. aureus*, *Streptococcus agalactiae* (*S. agalactiae*), and *E. faecalis* [69]. Leaf extracts of *Olea europaea* (olive) are valued for their broad biological activities, which are primarily attributed to a high concentration of phenolic compounds, most notably oleuropein and hydroxytyrosol [70]. Behbahani *et al*. evaluated an ethanolic olive leaf extract for its antimicrobial activity against *E. coli*, *Enterobacter aerogenes* (*E. aerogenes*), *B. cereus*, and *Listeria innocua* (*L. innocua*). The antimicrobial activity was both concentration-dependent and species-specific; the Gram-positive bacteria (*B. cereus* and *L. innocua*) were more susceptible to the ethanolic extract than the Gram-negative bacteria (*E. aerogenes* and *E. coli*) [70]. Overall, *B. cereus* was the most susceptible, and *E. aerogenes* was the most resistant strain [70]. In another study, Karbandeh *et al*. reported that an extract from *Ferula assafoetida* exhibited potent inhibitory activity against *L. monocytogenes*, with minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) values of 7.25 and 12.5 mg/mL, respectively. This extract also produced a wide zone of inhibition, with a diameter comparable to, though slightly smaller than, that of the positive control, ampicillin [71]. In a separate study, Fani *et al*. demonstrated that the essential oil of *Myrtus communis* inhibited key oral pathogens, including *S. mutans* and *Porphyromonas gingivalis* (*P. gingivalis*) [72]. This activity was attributed to the oil's primary components—1,8-cineole, α-pinene, and myrtenyl acetate—which are proposed to act by disrupting bacterial cell membranes and inhibiting biofilm formation [72]. Ghavam reported that *Rosa* × *damascena* Herrm. exhibited antimicrobial activity against *Proteus mirabilis* (*P. mirabilis*). This inhibitory activity was linked to the high content of saturated and unsaturated fatty acids in the plant extract, with linoleic acid, oleic acid, and palmitic acid identified as the primary antimicrobial constituents [73].

Furthermore**,** Dehestani *et al*. [74] reported potent antimycobacterial activity against *Mycobacterium tuberculosis* (*Mtb*) for both the dichloromethane and *n*-butanol fractions of *Crinitaria grimmii* and the dichloromethane and ethyl acetate fractions of *Linum album*. Similarly, *Hypericum scabrum* L. and *Echinops*

[DOI: 10.61882/JoMMID.14.1.1]

was moderately active against the H37Rv strain of *Mtb*, with a MIC of 12.5 µg/mL [58]. Jahanpour *et al*. [75] evaluated the inhibitory activity of several ethanolic extracts—including those from *Peganum harmala* seeds, pomegranate (*Punica granatum*) peel, *Digitalis* sp. leaves, *Rosa canina*, and *Berberis vulgaris*—against clinical isolates of *Mtb*, using isoniazid and rifampin as positive controls. At a concentration of 200 mg/mL (crude extract), the ethanolic extracts of *P. harmala* seeds and *P. granatum* peel exhibited significant activity against all *Mtb* isolates, with mean inhibition zones of 18.7 and 18.8 mm, respectively, comparable to isoniazid (19.2 mm) and rifampin (18.8 mm) [75]. A summary of the antibacterial properties of the plants discussed in this section is provided in Table 1.

Table 1. Summary of Iranian medicinal plants with reported antibacterial activity.

Plant species	Common/Persian name	Geographical distribution in Iran	Target bacteria	Reference(s)
Allium sativum L.	Sir (Garlic)	Various regions	*Pseudomonas aeruginosa*	[57, 94-98]
Artemisia spicigera	Dermane sonbulei	Northern and northwestern Iran	*Staphylococcus aureus*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, *Escherichia coli*	[30-43]
Berberis integerrima Bunge	Zereshk vahshi	Gorgan, Azerbaijan, Isfahan, Yasuj, Lorestan, Fars, Tehran, Kerman, Yazd, Semnan, Khorasan	*Staphylococcus aureus*, *Escherichia coli*	[50-56]
Berberis vulgaris	Zereshk	Khorasan, Azerbaijan, Gilan, Mazandaran, Tehran, Fars	*Mycobacterium tuberculosis*	[75]
Crinitaria grimmii	Kasni	Mountainous regions and Khorasan Razavi	*Mycobacterium tuberculosis*	[74]
Datura stramonium	Tature	Temperate regions	*Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*	[47, 48]
Digitalis sp.	Gole angoshtane (Foxglove)	Forested and humid regions	*Mycobacterium tuberculosis*	[75]
Dracocephalum kotschyi	Daraq Sorkh, Zarin Giah	Gorgan, Mazandaran, Hamedan, Kermanshah, Fars, Tehran, Semnan, Isfahan	*Bacillus subtilis*	[29]
Echinophora platyloba	Khosharize	Kurdistan, Semnan, Tehran, Isfahan	*Staphylococcus aureus*, *Listeria monocytogenes*, *Salmonella* serovar *Typhimurium*, *Escherichia coli*, *Bacillus subtilis*, *Pseudomonas aeruginosa*	[30-43, 65]
Echinops ritrodes	Shekar tighan	Gorgan, Mazandaran, Azerbaijan, Kurdistan, Isfahan, Fars, Khorasan, Tehran	*Mycobacterium tuberculosis* H37Rv	[58]
Eremostachys azerbaijanica Rech.	Sonbol Biabani Azarbaijani	North-West (East and West Azerbaijan)	*Staphylococcus aureus*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, *Escherichia coli*	[30-43]
Eremostachys macrophylla	Sonbol Biabani	North-West (West Azerbaijan, Kurdistan, Kermanshah)	*Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*	[44, 45]
Eucalyptus camaldulensis	Eucalyptus	South and South-West (Kerman, Khuzestan)	*Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*	[47, 48, 57]
Ferula assafoetida	Anghoze	Khorasan Razavi, Baluchestan, Kerman, etc.	*Listeria monocytogenes*	[71]
Foeniculum vulgare	Razianeh (Fennel)	North and North-West (Caspian Sea provinces)	*Staphylococcus aureus*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, *Escherichia coli*	[30-43]
Gontscharovia popovii	Avishan esteko	Mountainous and dry regions	*Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli*, *Klebsiella pneumoniae*	[67]
Gundelia tournefortii L.	Kangar	Gorgan, Mazandaran, Gilan, Azerbaijan, Kermanshah, Ilam, Hamedan, etc.	*Staphylococcus aureus*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, *Escherichia coli*	[30-43]
Hymenocrater calycinus	Arvane	North, northeast, east, and center of Iran	*Bacillus cereus*	[1]
Hymenocrater longiflorus Benth.	Arvane Oramani	North-West and West	*Staphylococcus aureus*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, *Escherichia coli*	[30-43]
Hypericum scabrum L.	Ofarighon	Gilan, Mazandaran, Azerbaijan, Gorgan, Khorasan, Isfahan, Bakhtiari, etc.	*Bacillus cereus*, *Staphylococcus aureus*, *Streptococcus mutans*, *Staphylococcus epidermidis*, *Bacillus subtilis*, *Enterococcus faecalis*, *Salmonella* serovar Typhimurium, *Mycobacterium tuberculosis* H37Rv	[1, 58]

[DOI: 10.61882/JoMMID.14.1.1]

Hyssopus officinalis	Zufa (Hyssop)	Dry and hot southern regions	*Enterococcus faecalis*, *Pseudomonas aeruginosa*, *Escherichia coli*	[59]
Iris germanica	Zanbagh Rishedare Almani	Cultivated and wild North and West	*Staphylococcus aureus*, *Escherichia coli*	[50-56]
Juglans regia L.	Gerdoo (Walnut)	Temperate and mountainous regions	*Pseudomonas aeruginosa*	[62, 63]
Lavandula angustifolia	Ostookhodos (Lavender)	Various regions	*Staphylococcus aureus*, *Bacillus cereus*, *Bacillus megaterium*, *Bacillus subtilis*, *Micrococcus luteus*, β-hemolytic *Streptococcus* spp., *Salmonella* serovar Typhi, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Shigella boydii*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella* spp., *Proteus* spp.	[61]
Linum album	Katan sefid (White flax)	Azerbaijan, Kurdistan, Tehran, Isfahan, Bakhtiari, Fars, Hamedan, etc.	*Mycobacterium tuberculosis*	[74]
Malva sylvestris L.	Panirak (Common Mallow)	Isfahan, Fars, Hamedan, Baluchestan, Kerman, Tehran, Mashhad	*Pectobacterium carotovorum* (formerly *Erwinia carotovora*), *Staphylococcus aureus*, *Streptococcus agalactiae*, *Enterococcus faecalis*	[69]
Marrubium vulgare L.	Gandnai koohii	Gorgan, Mazandaran, Azerbaijan, Kurdistan, Tehran, Kerman, Khorasan	*Staphylococcus aureus*, *Escherichia coli*	[50-56]
Matricaria chamomilla L.	Babone	Azerbaijan, Lorestan, Fars, Khuzestan, Tehran, Damavand, Alborz, etc.	*Pseudomonas aeruginosa*	[57]
Melissa officinalis	Badranj boie	Temperate regions	*Staphylococcus aureus*, *Bacillus cereus*, *Bacillus megaterium*, *Bacillus subtilis*, *Micrococcus luteus*, β-hemolytic *Streptococcus* spp., *Salmonella* serovar Typhi, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Shigella boydii*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella* spp., *Proteus* spp.	[61]
Mentha spp.	Nana (Mint)	Various regions; West (Ilam)	*Pseudomonas aeruginosa*	[55, 62, 63]
Micromeria hedgei Rech.	Morzangush	West (Zagros Mountains)	*Staphylococcus aureus*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, *Escherichia coli*	[30-43]
Moringa oleifera Lam.	Gaze roghani	Tropical and subtropical	*Staphylococcus aureus*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, *Escherichia coli*	[30-43]
Myrtus communis	Murd	North and West (Mazandaran, Gilan); West (Ilam)	*Staphylococcus aureus*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Streptococcus mutans*, *Porphyromonas gingivalis*	[30-43, 50-56, 62, 63, 72]
Nepeta spp.	Poonesa	Northern, Western, and North-West	*Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*	[50-56, 62, 63]
Olea europaea	Zeytoon (Olive)	North (Mazandaran), West, South	*Escherichia coli*, *Enterobacter aerogenes*, *Bacillus cereus*, *Listeria innocua*	[70]
Parietaria officinalis	Gosh, Moshe Tebbi	North and temperate (Caspian Sea region)	*Staphylococcus aureus*, *Escherichia coli*	[50-56]
Peganum harmala	Espand	Gorgan, Mazandaran, Azerbaijan, Isfahan, Fars, Khuzestan, etc.	*Mycobacterium tuberculosis*	[75]
Potentilla recta	Panje barg	Azerbaijan, Kurdistan, Kermanshah, Hamedan, Lorestan, Isfahan, etc.	*Staphylococcus aureus*, *Listeria monocytogenes*, *Escherichia coli*	[60]
Prosopis farcta	Kahorak, jeghjeghe	Hot and dry regions (southern Iran)	*Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*	[47, 48]
Pycnocycla bashagardiana Mozaff.	Sag Dandane Beshagardi	Bashagard region (Hormozgan province)	*Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*	[46]
Rosa canina	Nastaran	Gorgan, Mazandaran, Gilan, Azerbaijan, Hamadan, Kurdistan, etc.	*Mycobacterium tuberculosis*	[75]
Rosa damascena Herrm.	Golmohammadi	Kerman, Fars, Khuzestan, Isfahan, Kashan, East Azerbaijan	*Proteus mirabilis*	[73]
Salvia santolinifolia	Maryam Gooli Khaliji	West and North-West (Zagros Mountains)	*Staphylococcus aureus*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, *Escherichia coli*	[30-43]
Salvia sharifii	Maryam Goli Jonobi	Hot and dry region (south of Iran)	*Staphylococcus aureus*	[64]
Salvia spp.	Maryam goli	Zagros and Alborz regions	*Pseudomonas aeruginosa*	[55, 62, 63]
Satureja hortensis	Marzeh	Temperate and Southern regions	*Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*	[44, 45]
Satureja khuzestanica	Marze khuzestani	Khuzestan; West (Ilam)	*Pseudomonas aeruginosa*	[57, 94-98]

[DOI: 10.61882/JoMMID.14.1.1]

Satureja laxiflora C. Koch	Marzeh Koohi	South-West of Iran	*Staphylococcus aureus*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, *Escherichia coli*	[30-43]
Solanum nigrum L.	Tajrizi siah	Azerbaijan, Mazandaran, Gilan, Tehran, Hamedan, Isfahan, etc.	*Enterococcus faecalis*, *Pseudomonas aeruginosa*, *Escherichia coli*	[59]
Stachys lavandulifolia Vahl	Chaei koohii	Gorgan, Mazandaran, Isfahan, Azerbaijan, Fars, Hamedan, etc.	*Staphylococcus aureus*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, *Escherichia coli*	[30-43]
Tanacetum fisherae	Babuneh	North (Alborz Mountains)	*Bacillus subtilis*, *Enterococcus faecalis*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*	[66]
Thymus daenensis Celak.	Avishan Denay (Denay Thyme)	South and South-West (Fars, Bushehr)	*Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*	[42, 50-56, 62, 63]
Thymus spp.	Avishan	Temperate regions	*Pseudomonas aeruginosa*	[55, 62, 63]
Thymus vulgaris	Avishan (Common Thyme)	Cultivated and temperate North	*Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*	[44, 45]
Urtica dioica	Gazane (Nettle)	Temperate and mountainous regions	*Pseudomonas aeruginosa*	[62, 63]
Zataria multiflora	Avishan koohi (Mountain Thyme)	South and South-West (Fars, Bushehr, Hormozgan)	*Staphylococcus aureus*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Shigella flexneri*, *Klebsiella pneumoniae*, *Salmonella enterica*	[6, 28, 44, 45]
Ziziphora clinopodioides Lam.	Kakooti-koohi	Western and northwestern Iran (Zagros Mountains)	*Staphylococcus aureus*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, *Escherichia coli*	[30-43]
Zosima absinthifolia	Zarak koohi	West (Zagros Mountains)	*Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli*, *Salmonella* Typhi	[68]

Antiviral activity of medicinal plants

Viral pathogens cause numerous human diseases, including influenza, infections caused by herpes simplex virus (HSV), acquired immunodeficiency syndrome (AIDS), viral hepatitis, yellow fever, and coronavirus disease 2019 (COVID-19). Despite significant advances in antiviral pharmacotherapy, the treatment of viral diseases remains challenging due to limited treatment options, the rapid emergence of drug resistance, and the adverse side effects associated with synthetic agents [76, 77]. These challenges have stimulated renewed interest in natural resources, particularly medicinal plants, which possess significant potential for combating viral pathogens. This potential is rooted in the diverse array of bioactive compounds (*e.g*., flavonoids, alkaloids, tannins, saponins, terpenoids, and phenolic compounds), which mediate antiviral activity through various mechanisms, including inhibition of viral entry, suppression of genomic replication, inactivation of essential viral proteins, and modulation of the host's immune response [78, 79]. Consequently, the reported efficacy, favorable safety profiles, and cost-effectiveness of medicinal plants make them a valuable resource for developing novel phytopharmaceuticals to treat and prevent viral diseases [78].

Numerous studies have highlighted the antiviral activity of Iranian medicinal plants against common human viruses. For instance, various extracts and fractions from *Glycyrrhiza glabra*, *Myrtus communis*, *Melissa officinalis*, *Calendula officinalis*, *Salix alba*, and *Camellia sinensis* exhibited activity against influenza A virus *in vitro* [80]. Khanavi *et al*. evaluated the activity of essential oils from *Zataria multiflora* and *Origanum majorana*, traditionally used for respiratory ailments, against herpes simplex virus type 1 (HSV-1) [81]. The essential oil of *Z. multiflora*, rich in thymol (38%) and carvacrol (34.96%), and that of *O. majorana*, containing terpinen-4-ol (36.2%), both inhibited viral replication even at a dilution of 1:10,000 (*v/v*) [81]. Similarly, Ansari *et al*. demonstrated that extracts of *Teucrium polium* and *Ziziphora clinopodioides* exhibited time- and concentration-dependent inhibition of HSV-1 plaque formation [82]. The essential oil of *Matricaria chamomilla* L. has also shown promising antiviral activity against herpes simplex virus type 2 (HSV-2) *in vitro* [83, 84]. This activity is attributed to its complex mixture of constituents, which includes chamazulene, bisabolol derivatives, carvacrol, *p*-cymene, (*E*)- and (*Z*)-β-ocimene, (*E*,*E*)-farnesol, and en-yne dicycloethers, alongside flavonoids, coumarins, and hydroxycinnamic acids [83, 84]. Furthermore, Sharifi-Rad *et al*. [85] and Charostad *et al*. [86] demonstrated that extracts from *Ferula assafoetida* and *Veronica persica* inhibited both HSV-1 and HSV-2 replication by up to 80% and exhibited significant synergistic activity when combined with acyclovir [85, 86].

Beyond *in vitro* screening, research has also focused on herbal formulations and their clinical applications. Setarud (IMOD™), an herbal mixture containing extracts of *Tanacetum vulgare* (tansy), *Rosa canina* (dog rose), and *Urtica dioica* (nettle), has been used in Iran to treat patients with HIV [87]. Clinical trials have demonstrated

[DOI: 10.61882/JoMMID.14.1.1]

that treatment with IMOD™ led to significant increases in $CD4^+$ T-cell counts and improvements in lipid profiles, effects that may be linked to the formulation's immunomodulatory and antioxidant properties [87]. In addition to formulations, the anti-HIV activity of individual plants has also been explored; for instance, the anti-HIV activity of *Haplophyllum tuberculatum* has been attributed to alkaloids such as haplophyllin-A and haplophyllin-B [88]. Mahmoudi *et al*. conducted computational studies exploring the potential of Iranian medicinal plant compounds against SARS-CoV-2, the causative agent of COVID-19. Phytochemicals such as linarin, amentoflavone, (−)-catechin gallate, and hypericin—derived from plants such as *Hypericum perforatum*, *Humulus lupulus*, and *Hibiscus sabdariffa*—were analyzed for their binding affinity to key viral proteins [89]. These *in silico* models predicted that the compounds could inhibit essential viral targets, including the main protease ($3CL^{pro}$), RNA-dependent RNA polymerase (RdRp), and the spike (S) glycoprotein, which are critical for viral replication and entry [89, 90]. Beyond human viruses, the antiviral spectrum of Iranian plants also extends to phytopathogens. For example, extracts of *Bunium persicum* and *Zataria multiflora* inhibited tobacco mosaic virus (TMV) by 65.50% and 52.06%, respectively, under experimental conditions [91]. A summary of the antiviral properties of the plants discussed in this section is provided in Table 2.

Table 2. Summary of Iranian medicinal plants with reported antiviral activity.

Plant species	Common/Persian name	Geographical distribution in Iran	Target virus(es)	Reference(s)
Calendula officinalis	Gole hamishe bahar	Western and central regions of Iran	Influenza A virus	[80]
Camellia sinensis	Chaei sabz (green tea)	Gilan	Influenza A virus	[80]
Ferula assafoetida	Anghoze	Khorasan Razavi, Baluchestan, Kerman, *etc.*	Herpes simplex virus type 1(HSV-1), Herpes simplex virus type 2 (HSV-2)	[85, 86]
Glycyrrhiza glabra L.	Shirin baian	Larestan, Azerbaijan, Bakhtiari, Isfahan	Influenza A virus	[80]
Haplophyllum tuberculatum	Sadabi jonobi	Southeastern (Baluchistan)	Human immunodeficiency virus (HIV)	[88]
Hibiscus sabdariffa	Chaei torsh	Sistan and Baluchestan, Khuzestan	Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)	[89]
Humulus lupulus	Razak	Northern Iran (Gorgan, Chalus, Rasht, etc.)	SARS-CoV-2	[89]
Hypericum perforatum	Gole Raei	Alborz, Chalus, Mazandaran, western Iran	SARS-CoV-2	[89]
Matricaria chamomilla L.	Babone	Azerbaijan, Lorestan, Fars, Khuzestan, Tehran, etc.	HSV-2	[84, 83]
Melissa officinalis	Badranj boie	Temperate regions	Influenza A virus	[80]
Myrtus communis	Murd	North and West (Mazandaran, Gilan)	Influenza A virus	[80]
Nigella sativa	Siah dane (black seed)	Arak and Isfahan	Tobacco mosaic virus (TMV), HIV-1	[91, 92]
Origanum majorana L.	Marzangush	Hot and dry region	HSV-1	[81]
Rosa canina	Nastaran	Gorgan, Mazandaran, Gilan, Azerbaijan, etc.	HIV	[87]
Salix alba	Bide sefid (white willow)	Kurdistan, Hamedan, Lorestan, Kermanshah, Tehran	Influenza A virus	[80]
Tanacetum vulgare	Dokme talaei (tansy)	Temperate to subtropical regions	HIV	[87]
Teucrium polium	Kalpore	Gorgan, Azerbaijan, Kurdistan, Hamadan, Isfahan, etc.	HSV-1	[82]
Urtica dioica	Gazane (nettle)	Temperate and mountainous regions	HIV	[87]
Veronica persica Poir.	Shatare	Temperate and mountainous regions	HSV-1, HSV-2	[85, 86]
Zataria multiflora	Avishan koohi (mountain thyme)	South and South-West (Fars, Bushehr, Hormozgan)	HSV-1, TMV	[81, 91]
Ziziphora clinopodioides Lam.	Kakooti-koohi	North-West and West (Zagros Mountains)	HSV-1	[82]

Antiparasitic activity of medicinal plants

Parasitic organisms cause numerous diseases in both humans and animals, including malaria, leishmaniasis, and helminthiases, posing a significant global health burden. The growing resistance of parasites to conventional chemotherapeutics and the adverse effects associated with these agents have fueled increasing research into medicinal plants as a safer, more effective alternative for treating parasitic diseases. Many medicinal plants owe their antiparasitic activity to various bioactive constituents, such as alkaloids, flavonoids, tannins, and essential oil components, which act through diverse mechanisms to exert parasitostatic or parasitocidal effects [93].

In this context, a diverse collection of medicinal plants native to Iran's Ilam province has been documented for

[DOI: 10.61882/JoMMID.14.1.1]

both traditional use and efficacy against parasitic diseases [94-98]. This group includes species from genera such as *Centaurea*, *Echinops*, and *Tanacetum*, as well as specific plants like *Artemisia aucheri*, *Allium sativum*, *Zataria multiflora*, and *Myrtus communis*. The antiparasitic activity of these plants has been evaluated against numerous parasitic species, including *Giardia lamblia*, *Entamoeba histolytica*, *Trichomonas vaginalis*, *Leishmania* spp., and various intestinal helminths [94-98]. This activity is largely attributed to various bioactive This activity is largely attributed to various bioactive constituents, including phenolics, sesquiterpene lactones, tannins, terpenoids, and flavonoids, as well as essential oil compounds such as thymol, carvacrol, 1,8-cineole, and allicin, which exert cytocidal or cytostatic effects on parasites [94-99]. Among the documented activities, significant antileishmanial activity has been reported for several Iranian medicinal plants. Sharifi-Rad *et al*. demonstrated that alcoholic and methanolic extracts of *Veronica persica* were effective against *Leishmania major* (*L. major*) in both *in vitro* and *in vivo* models [100]. Similarly, a hydroalcoholic extract of *Rhus coriaria*, rich in tannins, flavonoids, and other phenolic compounds, potently inhibited promastigotes of *L. major* [101]. The potential of Iranian flora against *Toxoplasma gondii*, the causative agent of toxoplasmosis, has also been investigated. Ghanadian *et al*. [102] demonstrated that the hydroalcoholic extract of *Dracocephalum kotschyi* effectively reduced the growth and survival of *T. gondii* tachyzoites *in vitro* and *in vivo*. This dose-dependent effect, comparable to pyrimethamine (the standard drug) at specific concentrations, was attributed to the plant's bioactive flavonoids, polyphenols, and essential oils [102]. In another study, Montazeri *et al*. [103] evaluated the anti-*Toxoplasma* activity of several plants from the Brassicaceae family, including *Lepidium sativum*, *Brassica napus*, and *Sinapis arvensis*. These extracts successfully reduced the parasitic burden and increased survival rates in infected animal models, an effect attributed to their glucosinolate and flavonoid content [103]. Research has also identified effective compounds against the protoscolices of *Echinococcus granulosus*, the parasite responsible for hydatid cyst disease. For example, carvone ($C_{10}H_{14}O$), a monoterpenoid ketone found in the essential oils of *Mentha* spp., *Thymus* spp., and *Salvia rosmarinus*, rapidly induced dose- and time-dependent death of protoscolices [104]. The proposed mechanism of action involves the induction of programmed cell death (apoptosis-like processes) and the disruption of parasite cell membrane integrity and metabolic function [104]. The antiparasitic properties of the plants discussed in this section are summarized in Table 3.

Table 3. Summary of antiparasitic properties of Iranian medicinal plants.

Plant species	Common/Persian name	Geographical distribution in Iran	Target parasite(s)	Reference(s)
Achillea millefolium	Bomadaran	West (Ilam) and other regions	*Giardia lamblia*, *Entamoeba histolytica*, *Ichthyophthirius multifiliis*, *Trichomonas vaginalis*, *Acanthamoeba* spp., *Leishmania* spp., intestinal helminths	[94-98]
Allium sativum L.	Sir (garlic)	Various regions; West (Ilam)	*Giardia lamblia*, *Entamoeba histolytica*, *Trichomonas vaginalis*, *Acanthamoeba* spp., *Leishmania* spp., intestinal helminths	[94-98]
Artemisia aucheri	Dermane koohi	West (Ilam)	*Giardia lamblia*, *Entamoeba histolytica*, *Ichthyophthirius multifiliis*, *Trichomonas vaginalis*, *Acanthamoeba* spp., *Leishmania* spp., intestinal helminths	[94-98]
Brassica napus	Kolza	Temperate regions	*Toxoplasma gondii*	[103]
Centaurea spp.	Gole Gandom	West (Ilam)	*Giardia lamblia*, *Entamoeba histolytica*, *Ichthyophthirius multifiliis*, *Trichomonas vaginalis*, *Acanthamoeba* spp., *Leishmania* spp., intestinal helminths	[94-99]
Dracocephalum kotschyi	Daraq Sorkh, Zarin Giah	Gorgan, Mazandaran, Hamedan, Kermanshah, Fars, Tehran, etc.	*Toxoplasma gondii*	[102]
Echinops spp.	Shekar tighan	West (Ilam)	*Giardia lamblia*, *Entamoeba histolytica*, *Ichthyophthirius multifiliis*, *Trichomonas vaginalis*, *Acanthamoeba* spp., *Leishmania* spp., intestinal helminths	[94-98]
Eucalyptus camaldulensis	Eucalyptus	South and South-West; West (Ilam)	*Giardia lamblia*, *Entamoeba histolytica*, *Trichomonas vaginalis*, *Acanthamoeba* spp., *Leishmania* spp., intestinal helminths	[94-98]
Ferula assafoetida	Anghoze	Khorasan Razavi, Baluchestan, Kerman, etc.; West (Ilam)	*Giardia lamblia*, *Entamoeba histolytica*, *Trichomonas vaginalis*, *Acanthamoeba* spp., *Leishmania* spp., intestinal helminths	[94-98]
Foeniculum vulgare	Razianeh (fennel)	North and North-West; West (Ilam)	*Giardia lamblia*, *Entamoeba histolytica*, *Trichomonas vaginalis*, *Acanthamoeba* spp., *Leishmania* spp., intestinal helminths	[94-98]
Lepidium sativum	Shahi	Gilan, Gorgan, Mazandaran, Isfahan, Azerbaijan, Khuzestan, etc.	*Toxoplasma gondii*	[103]
Mentha spp.	Nana (mint)	Various regions; West (Ilam)	*Giardia lamblia*, *Entamoeba histolytica*, *Trichomonas vaginalis*, *Acanthamoeba* spp., *Leishmania* spp., intestinal helminths, *Echinococcus granulosus*	[94-99, 104]
Myrtus communis	Murd	North and West; West (Ilam)	*Giardia lamblia*, *Entamoeba histolytica*, *Ichthyophthirius multifiliis*, *Trichomonas vaginalis*, *Acanthamoeba* spp., *Leishmania* spp., intestinal helminths	[94-98]

[DOI: 10.61882/JoMMID.14.1.1]

Nigella sativa	Siah dane (black seed)	Arak, Isfahan; West (Ilam)	*Giardia lamblia*, *Entamoeba histolytica*, *Trichomonas vaginalis*, *Acanthamoeba* spp., *Leishmania* spp., intestinal helminths	[94-98]
Rhus coriaria	Sumagh	Widely grown in temperate regions	*Leishmania major*	[101]
Salvia rosmarinus	Rosemary	Various regions	*Echinococcus granulosus*	[104]
Satureja khuzestanica	Marze Khuzestani	Khuzestan; West (Ilam)	*Giardia lamblia*, *Entamoeba histolytica*, *Ichthyophthirius multifiliis*, *Trichomonas vaginalis*, *Acanthamoeba* spp., *Leishmania* spp., intestinal helminths	[94-98]
Scariola spp.	Kaho vahshi	West (Ilam)	*Giardia lamblia*, *Entamoeba histolytica*, *Trichomonas vaginalis*, *Acanthamoeba* spp., *Leishmania* spp., intestinal helminths	[94-98]
Sinapis arvensis	Khardal vahshi	Temperate to subtropical regions	*Toxoplasma gondii*	[103]
Tanacetum spp.	Babone Gavi	West (Ilam)	*Giardia lamblia*, *Entamoeba histolytica*, *Trichomonas vaginalis*, *Acanthamoeba* spp., *Leishmania* spp., intestinal helminths, Ichthyophthirius multifiliis	[98]
Thymus spp.	Avishan	Temperate regions	*Echinococcus granulosus*	[104]
Veronica persica Poir.	Shatare	Temperate and mountainous regions	*Leishmania major*	[100]
Zataria multiflora	Avishan koohi (mountain thyme)	South and South-West; West (Ilam)	*Giardia lamblia*, *Entamoeba histolytica*, *Trichomonas vaginalis*, *Acanthamoeba* spp., *Leishmania* spp., intestinal helminths	[94-98]

Antifungal activity of medicinal plants

The global incidence and severity of invasive fungal infections (IFIs) are rising, contributing to substantial mortality. Clinical management is hampered by the limited efficacy and significant toxicity of existing antifungal drugs. This challenge is compounded by the emergence of resistance to conventional antifungal agents (*e.g.*, fluconazole and amphotericin B), driving the search for natural alternatives. Among these alternatives, plant-derived compounds are being explored as potential chemosensitizing agents that may overcome or reverse fungal drug resistance [105].

The essential oil from the aerial parts of *Zhumeria majdae*, a member of the mint family (Lamiaceae), has demonstrated broad-spectrum antifungal activity [106]. This oil, which contains high concentrations of linalool (63.40%) and camphor (27.48%), was effective against a range of pathogenic fungi, including *Candida albicans* (*C. albicans*), *Trichophyton mentagrophytes*, *Aspergillus flavus*, *Trichophyton rubrum*, *Microsporum canis*, *Microsporum gypseum*, and *Epidermophyton floccosum* [106]. Similarly, the antifungal activity of *Otostegia persica* against *C. albicans* has been attributed to its terpenoid and phenolic compounds, which are proposed to act by disrupting the fungal cell membrane [49]. A substantial body of research has documented potent activity against *C. albicans* from numerous other Iranian plants. Notable examples include extracts and essential oils from *Hymenocrater longiflorus* Benth. [31], *Foeniculum vulgare* [33], *Micromeria hedgei* Rech. f. [34], *Ziziphora clinopodioides* Lam. [35], *Eremostachys azerbaijanica* Rech. f. [36], *Salvia santolinifolia* [37], *Satureja laxiflora* C. Koch [42], *Eremostachys macrophylla* [45], *Eucalyptus camaldulensis* [48], *Parietaria officinalis* [50], *Marrubium vulgare* L. [52], *Thymus daenensis Celak* [55], *Nepeta* spp. [56], *Myrtus communis* [54, 72], *Zataria multiflora*, *Thymus vulgaris*, *Satureja hortensis* [43, 44], and *Olea europaea* [107]. The activity of these plants against *Candida* spp. is directly linked to their phytochemical composition. For example, extracts from olive (*Olea europaea*) leaves, which are rich in polyphenols, flavonoids, and terpenoids, have demonstrated variable efficacy depending on plant cultivar and harvest season [107]. In addition, Khoshbakht *et al*. evaluated the antifungal activity of both the essential oil and a nanoemulsion formulation from three Iranian medicinal plants—*Zataria multiflora*, *Satureja khuzestanica*, and *Thymus daenensis*—against *C. albicans*. The nanoemulsion formulation exhibited significantly greater antifungal activity compared to the pure essential oil [108]. Ghavam *et al*. demonstrated that an extract of *Dracocephalum kotschyi* was more potent against *Aspergillus brasiliensis* and *C. albicans* than the conventional antifungal agent nystatin [29]. Similarly, *Dorema kopetdaghense*, a plant used in traditional medicine to treat suspected fungal infections, has demonstrated antifungal activity against pathogens such as *C. albicans*, *Aspergillus fumigatus*, and *Fusarium solani* [109]. This activity is attributed to its sesquiterpene lactones and phenolic compounds, which are proposed to exert antifungal effects by disrupting cell membrane integrity [109]. Furthermore, the essential oil of *Tanacetum fisherae*, which is predominantly composed of 1,8-cineole (79.9%), exhibited antifungal activity against *C. albicans* and *Saccharomyces cerevisiae* [66]. A rhizome extract of *Iris germanica* has also demonstrated antifungal activity against *C. albicans* and *Aspergillus niger*, an activity attributed to its high content of isoflavones, phenolic compounds, and essential oil components [51]. Moreover, *Pycnocycla bashagardiana* has shown significant antifungal activity against *C. albicans* and *Aspergillus* spp., an effect attributed to its content of monoterpenes and sesquiterpenes, including α-pinene, β -caryophyllene, and limonene [46]. Finally, pyranocoumarin compounds isolated from the roots of *Zosima absinthifolia* were active against *Candida kefyr* and *Fusarium* sp. [68]. A summary of the antifungal properties of the plants discussed in this section is presented in Table 4.

[DOI: 10.61882/JoMMID.14.1.1]

Table 4. Summary of Iranian medicinal plants with reported antifungal activity.

Plant species	Common/Persian name	Geographical distribution in Iran	Target fungus/fungi	Reference(s)
Dorema kopetdaghense	Doreh	Kopet-Dag mountain range, North-East	*Candida albicans*, *Aspergillus fumigatus*, *Fusarium solani*	[109]
Dracocephalum kotschyi	Daraq Sorkh, Zarin Giah	Gorgan, Mazandaran, Hamedan, Kermanshah, Fars, Tehran, etc.	*Candida albicans*, *Aspergillus brasiliensis*	[29]
Eremostachys azerbaijanica Rech.	Sonbol Biabani Azarbaijani	North-West (East and West Azerbaijan)	*Candida albicans*	[31, 33-37, 42-45, 48-50, 52, 54-56, 72, 107, 108]
Eremostachys macrophylla	Sonbol Biabani	North-West (West Azerbaijan, Kurdistan, Kermanshah)	*Candida albicans*	[31, 33-37, 42-45, 48-50, 52, 54-56, 72, 107, 108]
Eucalyptus camaldulensis	Eucalyptus	South and South-West (Kerman, Khuzestan)	*Candida albicans*	[31, 33-37, 42-45, 48-50, 52, 54-56, 72, 107, 108]
Foeniculum vulgare	Razianeh (fennel)	North and North-West (Caspian Sea provinces)	*Candida albicans*	[31, 33-37, 42-45, 48-50, 52, 54-56, 72, 107, 108]
Hymenocrater longiflorus Benth.	Arvane Oramani	North-West and West	*Candida albicans*	[31, 33-37, 42-45, 48-50, 52, 54-56, 72, 107, 108]
Iris germanica	Zanbagh Rishedare Almani	Cultivated and wild North and West	*Candida albicans*, *Aspergillus niger*	[51]
Marrubium vulgare L.	Gandnai Koohi, Farasion Sefid	Temperate North and West	*Candida albicans*	[31, 33-37, 42-45, 48-50, 52, 54-56, 72, 107, 108]
Micromeria hedgei Rech.	Morzangush	West (Zagros Mountains)	*Candida albicans*	[31, 33-37, 42-45, 48-50, 52, 54-56, 72, 107, 108]
Myrtus communis	Murd	North and West (Mazandaran, Gilan)	*Candida albicans*	[31, 33-37, 42-45, 48-50, 52, 54-56, 72, 107, 108]
Nepeta spp.	Poonesa	Northern, Western, and North-West	*Candida albicans*	[31, 33-37, 42-45, 48-50, 52, 54-56, 72, 107, 108]
Olea europaea	Zeytoon (olive)	North (Mazandaran), West, and South	*Candida albicans*	[31, 33-37, 42-45, 48-50, 52, 54-56, 72, 107, 108]
Otostegia persica	Gol Gavzaban Siah	South-East (Kerman and Bam)	*Candida albicans*	[31, 33-37, 42-45, 48-50, 52, 54-56, 72, 107, 108]
Parietaria officinalis	Gosh, Moshe Tebbi	North and temperate (Caspian Sea region)	*Candida albicans*	[31, 33-37, 42-45, 48-50, 52, 54-56, 72, 107, 108]
Pycnocycla bashagardiana Mozaff.	Sag Dandane Beshagardi	Bashagard region (Hormozgan province)	*Candida albicans*, *Aspergillus* spp.	[46]
Salvia santolinifolia	Maryam Gooli Khaliji	West and North-West (Zagros Mountains)	*Candida albicans*	[31, 33-37, 42-45, 48-50, 52, 54-56, 72, 107, 108]
Satureja hortensis	Marzeh	Temperate and Southern regions	*Candida albicans*	[31, 33-37, 42-45, 48-50, 52, 54-56, 72, 107, 108]
Satureja khuzestanica	Marze Khuzestani	Khuzestan	*Candida albicans*	[31, 33-37, 42-45, 48-50, 52, 54-56, 72, 107, 108]
Satureja laxiflora C. Koch	Marzeh Koohi	South-West	*Candida albicans*	[31, 33-37, 42-45, 48-50, 52, 54-56, 72, 107, 108]
Tanacetum fisherae	Babuneh	North (Alborz Mountains)	*Candida albicans*, *Saccharomyces cerevisiae*	[66]
Thymus daenensis Celak	Avishan Denay (Denay thyme)	South and South-West (Fars, Bushehr)	*Candida albicans*	[31, 33-37, 42-45, 48-50, 52, 54-56, 72, 107, 108]
Thymus vulgaris	Avishan (common thyme)	Cultivated and temperate North	*Candida albicans*	[31, 33-37, 42-45, 48-50, 52, 54-56, 72, 107, 108]
Zataria multiflora	Avishan koohi (mountain thyme)	South and South-West (Fars, Bushehr, Hormozgan)	*Candida albicans*	[31, 33-37, 42-45, 48-50, 52, 54-56, 72, 107, 108]
Zhumeria majdae	Mur khosh	South and South-West (Kerman, Hormozgan, Bam)	*Candida albicans*, *Trichophyton mentagrophytes*, *Aspergillus flavus*, *Trichophyton rubrum*, *Microsporum canis*, *Microsporum gypseum*, *Epidermophyton floccosum*	[106]
Ziziphora clinopodioides Lam.	Kakooti-Koohi	North-West and West (Zagros Mountains)	*Candida albicans*	[31, 33-37, 42-45, 48-50, 52, 54-56, 72, 107, 108]
Zosima absinthifolia	Zarak koohi	West (Zagros mountains)	*Candida kefyr*, *Fusarium* sp.	[68]

[DOI: 10.61882/JoMMID.14.1.1]

Nanotechnology applications for medicinal plants

In recent years, the combination of nanotechnology with medicinal plants has emerged as a promising strategy for combating antimicrobial-resistant pathogens. Nanoparticles (NPs) can act as effective drug carriers or independent antimicrobial agents due to their small size, high surface-area-to-volume ratio, enhanced penetration of microbial barriers, and unique physicochemical properties [110, 111]. When these NPs are combined with plant extracts, the resulting synergistic effects can increase therapeutic efficacy, lower the effective dose, and mitigate potential side effects [110, 111]. Numerous studies have demonstrated that metal NPs, including silver (AgNPs), gold (AuNPs), and copper (CuNPs), as well as carbon nanotubes (CNTs) and various metal oxide NPs, exhibit enhanced antibacterial, antifungal, and antiviral activity when combined with plant extracts from species such as *Zataria multiflora*, *Nigella sativa*,

Curcuma longa, and *Linum usitatissimum*, compared to either component alone [111-115]. In the green synthesis of NPs, plant-derived compounds can serve as both reducing agents (to reduce metal ions into their nanoparticulate form) and stabilizing agents (to prevent NP aggregation), thereby producing NPs with enhanced biocompatibility and improved safety [116]. This approach not only enhances the antimicrobial potential of medicinal plants but also facilitates the development of novel therapeutic agents, advanced antimicrobial packaging, and other biomedical applications. Indeed, the application of nanotechnology to medicinal plant processing represents a rapidly growing area in biotechnology and pharmaceutical research.

Mirbehbahani *et al*. developed a nanofibrous wound dressing composite incorporating an extract of *Artemisia annua*. This biocompatible material demonstrated no cytotoxicity while promoting the proliferation and attachment of fibroblast cells and exhibiting notable antibacterial activity against *S. aureus in vitro* [117]. Similarly, zinc oxide nanoparticles (ZnO NPs) were green-synthesized using an aqueous aerial extract of *Dracocephalum kotschyi*; these NPs demonstrated potent antibacterial and antifungal activity against *S. aureus, P. aeruginosa*, and *C. albicans* [118]. Ghaedi *et al*. investigated the synergistic antimicrobial effect of combining an extract from *Linum usitatissimum* (flax) with ZnO/Zn $(OH)_2$ NPs. The resulting composite demonstrated significantly enhanced inhibitory activity against *S. aureus*, *E. coli*, and *P. aeruginosa* compared to the extract alone [119]. The green synthesis of AgNPs using Iranian plant extracts represents an extensively studied approach for generating potent antimicrobial agents. For example, AgNPs synthesized using leaf extracts from *Callistemon citrinus* [120] and *Crocus sativus* [122], exhibited potent antibacterial activity against several pathogens, including *S. aureus*, *E. coli*, *Acinetobacter baumannii* (*A. baumannii*), and *P. aeruginosa.*

This broad-spectrum activity has been consistently reported across a wide range of plant sources. AgNPs produced with extracts from *Eruca sativa* (arugula)and *Spinacia oleracea* (spinach) were effective against *E. coli*, *S. aureus*, and *C. albicans* [121]. Similarly, AgNPs biosynthesized using an aqueous extract of *Kelussia odoratissima* (mountain celery) leaves demonstrated dose-dependent inhibition against various microorganisms, including the bacteria *S. aureus*, *B. cereus*, *E. coli*, *S. Typhimurium*, and *L. monocytogenes*, as well as the fungi *Aspergillus flavus*, *Penicillium expansum*, and *Claviceps purpurea* [123]. Extracts from *Sesamum indicum* (sesame) also yielded AgNPs with activity against the bacteria *B. subtilis*, *E. coli*, and *S. aureus*, as well as the yeasts *Saccharomyces cerevisiae* and *C. albicans* [124]. Quantitative analysis revealed that AgNPs synthesized from a hydroalcoholic extract of *Urtica dioica* (nettle) exhibited potent antibacterial activity, with MIC values of 11.71 µg/mL for *P. aeruginosa* and 23.4 µg/mL for *S. aureus* [125].

Nanofiber-based delivery systems have been developed to enhance the stability and efficacy of plant-derived essential oils. For example, Rahmatinia *et al*. [126] fabricated zein protein nanofibers as carriers for the essential oil of *Eucalyptus globulus* leaves. These nanofibers demonstrated potent antimicrobial activity against *E. coli*, *S. aureus*, and *P. aeruginosa*, and showed greater stability compared to the essential oil alone, highlighting their potential for medical applications and use as natural disinfectants in food packaging. In a similar approach, Rezaei *et al*. loaded an extract from *Artemisia sieberi* onto chitosan nanofibers produced via electrospinning. This composite exhibited stronger antimicrobial activity against *E. coli*, *S. aureus*, and *C. albicans* than the extract alone [127]. Green synthesis of metal oxide nanoparticles using Iranian plant extracts is another widely explored strategy. For example, Raja *et al*. demonstrated that ZnO NPs synthesized using a leaf extract from *Tabernaemontana divaricata* exhibited broad-spectrum antimicrobial activity against the bacteria *E. coli* and *S. aureus*, as well as notable antifungal activity against *C. albicans* [128]. Following a similar methodology, Omid *et al*. biosynthesized ZnO NPs using an aqueous extract of elderberry (*Sambucus ebulus*) leaves, demonstrating effective antibacterial activity against *S. aureus*, *B. subtilis*, *E. coli*, and *Salmonella enteritidis* (*S. enteritidis*) [129].

In a final example, Weisany *et al*. nanoencapsulated the essential oils of *Thymus vulgaris* and *Anethum graveolens* using CuNPs to enhance their antifungal activity against *Colletotrichum nymphaeae*, the causative agent of anthracnose in agricultural products. This nanoencapsulation process significantly enhanced antifungal activity compared to the unencapsulated essential oils, demonstrating its potential for controlling fungal phytopathogens in agriculture [130]. A summary of the nanotechnology applications discussed in this section is provided in Table 5.

[DOI: 10.61882/JoMMID.14.1.1]

Table 5. Nanotechnology applications of Iranian medicinal plants for antimicrobial activity.

Plant Species	Common/Persian name	Geographical distribution in Iran	Nanomaterial	Target organism(s)	Reference(s)
Anethum graveolens	Shevid	Kermanshah, Kerman, Hormozgan, etc.	CuNPs	*Colletotrichum nymphaeae*	[130]
Apium graveolens	Karafs (celery)	Temperate North and West	AgNPs	*Staphylococcus aureus*, *Bacillus cereus*, *Escherichia coli*, *Salmonella* serovar Typhimurium, *Listeria monocytogenes*, *Aspergillus flavus*, *Penicillium expansum*, *Claviceps purpurea*	[123]
Artemisia annua	Qinghao, Sweet wormwood	Gorgan	Nanofibrous composite	*Staphylococcus aureus*	[117]
Artemisia sieberi	Dermane dashti (Iranian wormwood)	Central and southern arid regions	Chitosan nanofibers	*Escherichia coli*, *Staphylococcus aureus*, *Candida albicans*	[127]
Callistemon citrinus	Shishe shor	Warm and temperate regions	AgNPs	*Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*	[120]
Crocus sativus	Zaferan (saffron)	Southeast (Khorasan), Isfahan, Qom	AgNPs	*Staphylococcus aureus*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*	[121]
Dracocephalum kotschyi	Daraq Sorkh, Zarin Giah	Gorgan, Mazandaran, Hamedan, Kermanshah, etc.	ZnO NPs	*Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Candida albicans*	[118]
Eucalyptus globulus	Eucalyptus	Coastal and temperate regions of the north	Zein protein nanofibers	*Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*	[126]
Euphorbia spp.	Ferfion, Shire sag	Various regions	ZnO/Zn(OH)2 NPs	*Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*	[119]
Linum usitatissimum	Katan (flax)	Warm and temperate regions	ZnO/$Zn(OH)_2$ NPs	*Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*	[119]
Raphanus sativus L.	Torob (radish)	Agricultural and indigenous regions	AgNPs	*Escherichia coli*, *Staphylococcus aureus*, *Candida albicans*	[121]
Sambucus ebulus L.	Aghti (elderberry)	Northern and western temperate regions	ZnO NPs	*Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli*, *Salmonella enteritidis*	[129]
Sesamum indicum	Konjed (sesame)	Hot and dry southwest and south	AgNPs	*Bacillus subtilis*, *Escherichia coli*, *Staphylococcus aureus*, *Saccharomyces cerevisiae*, *Candida albicans*	[124]
Spinacia oleracea	Esfenaj (spinach)	Temperate and cool regions	AgNPs	*Escherichia coli*, *Staphylococcus aureus*, *Candida albicans*	[121]
Tabernaemontana divaricata	Yas amameh	Tropical and subtropical South/Southeast	ZnO NPs	*Escherichia coli*, *Staphylococcus aureus*, *Candida albicans*	[128]
Thymus vulgaris	Avishan (common thyme)	Cultivated and temperate North	CuNPs	*Colletotrichum nymphaeae*	[130]
Urtica dioica	Gazane (nettle)	Temperate and mountainous regions	AgNPs	*Staphylococcus aureus*, *Pseudomonas aeruginosa*	[125]

Conclusion and future perspective

This review has highlighted the significant antimicrobial potential of numerous Iranian medicinal plants, underscoring the broad-spectrum activity of multiple species. For example, plants such as *Zataria multiflora*, *Thymus daenensis*, and *Myrtus communis* exhibited potent antibacterial and antifungal activity; notable antiviral activity was reported for *Glycyrrhiza glabra*, *Melissa officinalis*, and *Nigella sativa*; and significant antiparasitic activity was observed in extracts from *Linum album*, *Dracocephalum kotschyi*, and *Mentha* spp. These diverse biological activities are largely attributed to key phytochemicals, including thymol, carvacrol, linalool, and oleuropein. Beyond traditional extracts, the integration of nanotechnology with medicinal plants, particularly through the green synthesis of AgNPs and ZnO NPs, significantly enhances antimicrobial efficacy. This enhancement occurs via improved penetration of microbial barriers, targeted delivery of active compounds, and synergistic effects between NPs and phytochemicals.

While the traditional use of these plants is well established, additional interdisciplinary research is required to fully realize their therapeutic potential. Future research should prioritize the following areas. First, rigorous standardization of extraction methods is crucial to ensure consistent active compound concentrations, maintain product stability, and guarantee product quality [131]. Second, advanced analytical technologies, including liquid chromatography-mass spectrometry (LC-MS) and nuclear magnetic resonance (NMR) spectroscopy, coupled with bioinformatics and

[DOI: 10.61882/JoMMID.14.1.1]

biotechnology, are essential for precisely identifying bioactive compounds and elucidating their mechanisms of action [131]. These efforts are essential for developing novel drug leads capable of overcoming or circumventing existing resistance mechanisms. Third, comprehensive preclinical and clinical investigations are essential, including rigorous toxicological studies, pharmacokinetic and pharmacodynamic (PK/PD) profiling for dose optimization, and phased clinical trials to establish safety and efficacy in humans [132]. Finally, successful clinical translation requires assessments of environmental sustainability and the cost-effectiveness of extraction, purification, and large-scale production processes [132]. With strategic investment in interdisciplinary research, Iran's rich botanical heritage can be translated into a sustainable pipeline of novel, safe, and effective antimicrobial agents for the benefit of global health and the healthcare community [132].

ACKNOWLEDGMENT

The authors acknowledge the Pasteur Institute of Iran for institutional support and access to research databases.

CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest associated with this manuscript.

FUNDING

This research received no external funding.

AI DISCLOSURE

The authors confirm that no AI tools were used in the preparation of this manuscript.

DATA AVAILABILITY

As a review article, all data discussed are derived from previously published studies, fully cited in the References section.

AUTHORS' CONTRIBUTIONS

MSH: Conceptualization, supervision, resources, writing – original draft, writing – review & editing, validation, and data curation. HS: Investigation, writing – original draft. ER: Investigation, writing – original draft.

ETHICS STATEMENT

Not applicable. This is a review article and did not involve studies with human or animal subjects.

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Cite this article:
Sheikhpour M, Sakhi H, Rahimi E. Iranian Medicinal Plants with Antimicrobial Properties: A Narrative Review. J Med Microbiol Infect Dis, 2026; 14 (1): 1-18. DOI: 10.61882/JoMMID.14.1.1.

[DOI: 10.61882/JoMMID.14.1.1]