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Phytotherapy in oral candidiasis: A review of the most important native Iranian medicinal plants effective against *Candida albicans*, the cause of oral thrush. *A review*

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Abstract

Introduction and purpose: Oral thrush, a mucocutaneous infection caused by an overgrowth of Candida albicans, manifests as white, curd-like lesions on oral mucosal surfaces, often accompanied by burning sensations and altered taste perception. Conventional treatment modalities primarily rely on antifungal medications, while adjunctive therapies include topical saline or sodium bicarbonate rinses and rigorous oral hygiene practices. The current investigation seeks to elucidate and document the indigenous medicinal flora of Iran that is employed in the treatment of oral thrush induced by *Candida albicans*.

Methodology: In this review article, a search was made in Web of Science, PubMed, Magiran, SID, Scopus, and Google Scholar databases using keywords such as medicinal plants, extract, essential oil, traditional medicine, candidiasis, and *Candida albicans*. Articles that were not relevant were removed and finally, relevant articles were used for literature review.

Results: A variety of medicinal herbs, including Purple Coneflower, Persica, Matrica, Cinnamol, Jaftex, Green Cumin, Lemon Balm, Green Tea, Valerian, Oregano, Water Hyacinth, Ginger, Jujube, Hatchet Vetch, Sumac, Blue Mint Bush, Dandelion, Zaatar, Yarrow, Ephedra, Danish Thyme, Cinnamon, Curly Catnip, Barberry, Myrtle, Garlic, Kah-makki and Putar, Black Caraway, Nettle, Chamomile, Tarragon, Harmala, Lavender, Honey Garlic, Asafoetida (Devil's Dung), and Saffron, are indigenous to Iran. These plants demonstrate an anti-candidal effect against Candida albicans in the oral cavity, particularly when compared to commercial mouthwashes and standard chemical treatments.

Conclusion: Medicinal plants offer a promising therapeutic approach to oral thrush due to their inherent antibacterial, antifungal, and anti-inflammatory properties. Herbal mouthwashes containing phytochemicals derived from plants like thyme, chamomile, and sage can effectively

alleviate oral thrush symptoms and suppress Candida overgrowth. As a natural and well-tolerated alternative to synthetic antifungals, these mouthwashes can be employed as adjunctive or primary treatments for oral candidiasis.

Keywords: Infectious Disease, Fungal infection, Yeast, *Candida albicans*, Medicinal plants, Indigenous, Iran

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Introduction

Infectious diseases emerge when pathogenic microorganisms, such as viruses, bacteria, fungi, parasites, and yeasts, successfully invade and colonize the human body (Fauci, 2001; Gorbach, 2004). These diseases often exhibit contagious properties, spreading readily among individuals through various transmission routes (Fauci, 2001). Fungal infections, a prevalent global health concern, occur when the host's immune system is unable to contain the proliferation of pathogenic fungi. Notably, *Candida albicans*, a yeast species, is a significant human fungal pathogen, often existing as a commensal organism within the human microbiome (Bongomin et al., 2017, Talapko et al. 2021).

Candida albicans is a dimorphic fungus capable of existing as both yeast and hyphal forms, allowing for adaptation to diverse host environments (5). As a commensal organism, it forms part of the normal human microbiota. However, under conditions of immune compromise, *C. albicans* can transition from a benign commensal to a pathogenic state, resulting in candidiasis (6). This opportunistic fungal infection can affect various mucosal and cutaneous surfaces, including the oral cavity, gastrointestinal tract, and genitourinary system. Notably, *C. albicans* is a significant cause of morbidity and mortality in immunocompromised individuals (7).

Oral candidiasis, commonly referred to as thrush, is a fungal infection primarily caused by *Candida albicans*. Clinically, it manifests as white, pseudomembranous lesions on the oral mucosa, often accompanied by burning sensations, pain, xerostomia, and dysphagia (7).

The management of oral candidiasis typically involves antifungal agents such as fluconazole, clotrimazole, miconazole, nystatin, and amphotericin B (8). The

emergence of antifungal resistance, particularly among *Candida albicans* strains, has necessitated the development of alternative therapeutic strategies due to the limitations and toxicities associated with conventional antifungal drugs (9, 10, 11).

Medicinal plants, rich in bioactive compounds, have been traditionally employed for the treatment of various diseases, including infections (12-14). Compared to synthetic drugs, these botanicals often exhibit a more favorable safety profile, contributing to their widespread use (15-17). The accessibility and affordability of medicinal plants have positioned them as viable alternatives to conventional treatments for many individuals (18).

The antifungal properties of medicinal plants have established them as viable alternatives for the treatment of fungal infections, including candidiasis. These plants contain bioactive compounds that inhibit fungal growth and proliferation (19). Given the increasing prevalence of antifungal resistance, there is a growing interest in exploring plant-based therapies. This study aims to identify and document Iranian medicinal plants with potential antifungal activity against *Candida albicans*.

Method

A comprehensive literature search was conducted utilizing the keywords "medicinal plants," "extracts," "essential oils," "traditional medicine," "candidiasis," and "Candida albicans" within the Web of Science, PubMed, Magiran, SID, Scopus, and Google Scholar databases. Irrelevant studies were excluded, and the remaining articles were subjected to a thorough review.

Results

The results of our study showed that for candida albicans, the cause of oral thrush, the medicinal plants Purple Coneflower, Persica, Matrica, Cinnamol, Jaftex, Green Cumin, Lemon Balm, Green Tea, Valerian, Oregano, Water Hyacinth, Ginger, Jujube, Hatchet Vetch, Sumac, Blue Mint Bush, Dandelion, Zaatar, Yarrow, Ephedra, Danish Thyme, Cinnamon, Curly Catnip, Barberry, Myrtle, Garlic, Kah-makki and Putar, Black Caraway, Nettle, Chamomile, Tarragon, Harmala, Lavender, Honey Garlic, Asafoetida (Devil's Dung), and Saffron are used.

Additional information about medicinal plants effective against oral thrush (Candida albicans) is specified in Table No. 1.

Table 1. Medicinal plants native to Iran effective against Candida albicans, the cause of oral thrush

Plant Name	Scientific Name	Family	Type	Effect	Ref.
Purple coneflower	*Echinacea purpurea*	Asteraceae	Essential oil	The obtained results showed that the minimum inhibitory concentration of sorghum extract on *Candida alicens* was 150 mg/mL. Clotrimazole ointment, with concentrations of 200 and 150 mg/mL, has demonstrated the most significant inhibitory effects in animal models, as derived from the extract of *Echinacea purpurea*.	20
Persica Matrica Cinnamol		Asteraceae	Essential oil	The mean MIC for *C. albicans* for chlorhexidine, Persica, Matrica, and Cinnamon was 0.098%, 25.0%, 10.417%, 6.25% and 3.125%, .respectively	21
Jaftex	*Jaftex*		Essential oil	The average minimum inhibitory concentration (MIC) for *Candida albicans* was recorded at 0.0625 mg/mL. This indicates that *Candida albicans* shows a higher sensitivity to Jaftex herbal mouthwash.	22
Green cumin, Lemon balm, and Green tea	*Cuminum cyminum Melissa officinalis Camellia sinensis*	Apiaceae Lamiaceae Theaceae	Aqueous extract	The aqueous extract of *C. sinensis* exhibited an average growth inhibition diameter of 6.33 millimeters (mm), while the essential oil of *C. cyminum* demonstrated a significantly larger inhibition diameter of 40.33 mm. In contrast, the aqueous extract of *M.*	23

				officinalis did not exhibit any growth inhibition after 48 hours. Among the tested compound mouthwashes 1 to 5, mouthwash 5 proved to be the most effective against *Candida albicans*, with a measurement of 184.911 and statistical significance indicated by F=0.001 and P<0.001.	
Valerian or Garden heliotrope	*Valeriana officinalis*	Caprifoliaceae	Methanolic extract	The ethanolic extract of valerian demonstrated complete inhibition of the *Candida albicans* fungus, with a non-growth halo diameter ranging from 12 to 20 mm.	24
Oregano	*Origanum vulgare*	Lamiaceae	Aqueous and Alcoholic extract	The mean diameter of the growth halo surrounding the discs with both aqueous and alcoholic extracts of oregano, across all tested concentrations, was notably smaller than that of nystatin (P<0.001).	25
Water-hyacinth	*Eichhornia crassipes*	Pontederiaceae	Methanolic and Aqueous extract	The investigated methanolic and aqueous extracts had an inhibitory effect on *Candida albicans* at concentrations of 50 and 100 mg/ml.	26
Ginger	*Zingiber officinale*	Zingiberaceae	Aqueous extract	The disk diffusion method revealed that the inhibition zone for ginger mouthwash measures 3.18 mm ± 1, while nystatin exhibits a zone of 3.28 mm ± 1.0 mm (P<0.0001). In conclusion, the findings of this study suggest that ginger mouthwash (Vi-one) may be more effective	27

				than nystatin extract in inhibiting the growth of *Candida albicans* under laboratory conditions.	
Jujube	*Ziziphus jujuba*	Rhamnaceae	Methanolic, Ethanolic, and Aqueous extract	The results showed that the concentration of 100 mg/ml of all aqueous, ethanolic, methanolic, and dichloromethane extracts did not affect Streptococcus mutans/MFC and *Candida albicans*.	28
Hatchet vetch	*Securigera securidaca*	Fabaceae	Methanolic extract	The microemulsion derived from the methanolic extract of the *Securigera securidaca*, at a concentration of 0.01%, demonstrated notable anti-candidal activity. This formulation exhibited the highest level of inhibition against *Candida albicans*.	29
Sicilian sumac	*Rhus coriaria*	Anacardiaceae	Aqueous extract	The aqueous extract of *Rhus coriaria*, regardless of concentration, did not show any inhibitory effect on the growth of *Candida albicans*. However, the ethanolic extract at a concentration of 60 mg/ml successfully inhibited the growth of *Candida albicans* after 24 hours.	30
Blue mint bush	*Ziziphora clinopodioides*	Lamiaceae	Ethanolic extract	The minimum inhibitory concentration (MIC) of the plant was in the range of 25.6 to 125.3 mg/ml and MFC, MBC was from 5.12 to more than 100 mg/ml.	31
Dandelion	*Taraxacum officinale*	Asteraceae	Ethanolic extract	Fluconazole and nystatin showed more antifungal effects than the ethanolic	32

				extract of dandelion root in all three *Candida albicans* fungal strains.	
Grey echinophora	*Echinophora cinerea*	Apiaceae	Aqueous extract	The antifungal properties of Grey echinophora may be effective in treating skin conditions caused by various fungi, although this study was conducted in a controlled culture setting.	33
Zaatar or thyme	*Origanum Syriacum*	Lamiaceae	Essential oil	Zaatar oil had a significant effect on oral *Candida albicans* and at a dose of 150 µg/ml it had an anti-Candida albicans effect.	34
Yarrow	*Achillea millefolium*	Asteraceae	Methanolic extract	The MIC of Yarrow methanolic extract with a dose of 2.67 ± 2.55 µg/ml affects *Candia albicans*, the cause of oral stomatitis.	35
Ephedra or Brigham tea	*Ephedra major*	Ephedraceae	Aqueous extract	The MIC of Ephedra extract at a dosage of 11.67 ± 0.58 µg/ml demonstrates an impact on *Candida albicans*, which is responsible for oral stomatitis.	36
Danish thyme	*Thymus danensis*	Lamiaceae	Essential oil	The average area of *Candida albicans* non-growth aura between groups consuming thyme solution was 0.43 ± 0.53 mm.	37
Thyme and Cinnamon	*Thymus vulgaris and Cinnamomum verum*	Lamiaceae Lauraceae	Essential oil	The sensitivity of Candida albicans isolates ATCC10231 to the essential oils of garden thyme and cinnamon and nystatin was obtained as 120 µg/ml MIC, 340 µg/ml MIC, and 1 µg/ml MIC respectively.	37
Curly catnip and Catnip	*Nepeta Crispa L. and Nepeta Cataria*	Lamiaceae Lamiaceae	Essential oil	The results of a study showed that the minimum lethal concentration of fungi was 4	39

				micrograms/ml for Curly catnip and 6 micrograms/ml for catnip.	
Barberry, Cinnamon, Myrtle, and Garlic	*Berberis vulgaris, Cinnamomum verum, Myrtus communis, and Allium sativum*	Berberidaceae Lauraceae Amaryllidaceae	Ethanolic extract	A study showed that the minimum inhibitory concentration or MIC for *Candida albicans* was 10 mg ml^{-1} for barberry extract, 1.25 mg ml for white cinnamon extract, 11 mg ml^{-1} for the plant extract, and In the case of garlic extract, it was 0.07 mg ml and mg ml^{-1}, respectively, and in the case of fluconazole, it was 3.6 mg ml-1 and 3.1 mg ml^{-1}, and in the case of ketoconazole, it was equal to 2.3 mg ml^{-1} for both cases.	40
Kah-makki and Putar	*Cymbopogon olivieri*	Gramineae	Ethanolic extract	The ethanol extract of Kah-makki and Putar, administered at a concentration of 45 micrograms/ml, resulted in a growth inhibition halo with a diameter of 13 mm.	41
Black caraway and Stinging nettle	*Nigella sativa and Urtica dioica*	Ranunculaceae and Urticaceae		The hydroalcoholic extract of Black caraway and Stinging nettle had MIC of 25 mg/ml, respectively.	
Chamomile	*Matricaria chamomilae*	Asteraceae	Aqueous extract	The chamomile extract exhibited a halo diameter of 9.8 mm against Candida albicans, whereas the chlorhexidine mouthwash produced a larger average halo of 16.5 mm.	42
Wild tarragon	*Artemisia dracunculus*	Asteraceae	Aqueous extract	Tarragon leaf extract with a dose of 5 mg has an inhibitory effect on the growth of *Candia*	43

				albicans, the cause of oral thrush.	
Harmala and Lavender	*Peganum harmala and Lavandula angustifolia*	Nitrariaceae Lamiaceae		The findings indicated that both extracts exhibit antifungal properties. A study revealed that a concentration of 1000 mg/ml of methanolic extract from Harmala and a concentration of 500 mg/ml of methanolic extract from lavender were effective against Candida fungus.	44
Honey garlic	*Nectaroscordum tripedale*		Aqueous Extract	The analysis of the aqueous extract from the plant on both clinical samples and the standard fungal sample reveals that concentrations of 5, 10, 20, and 40 mg/ml have minimal impact on *Candida albicans*. However, at a concentration of 80 mg/ml, there is a complete absence of growth halo when compared to the lower concentrations, which exhibited more significant effects.	45
Asafoetida - devil's dung	*Ferula assa foetida*	umbelliferae	Aqueous Extract	The aerial branch extract of Asafoetida devil's dung, demonstrated a complete inhibition of *Candida albicans* growth and eradicated all viable Candida cells at this concentration (MFC). Furthermore, the aqueous extract of Asafoetida yielded minimum inhibitory concentrations of 0.273 mg/ml and 4.4 mg/ml, corresponding to 50% and 90% growth inhibition of Candida,	46

				respectively.	
Saffron crocus	*Crocus sativus*	Iridaceae	Aqueous Extract	A significant difference was observed between the effect of alcoholic and aqueous extracts of saffron and nystatin on *Candida albicans* compared to chlorhexidine mouthwash and P<0.01.	47

Discussion

Traditional medicine has effectively managed fungal infections, including candidiasis, through the utilization of medicinal plants. These botanicals possess antifungal properties that contribute to symptom alleviation and immune system enhancement (48). By offering a natural and often safer alternative to synthetic drugs, traditional medicine has played a crucial role in preventing and managing fungal diseases (49).

Several Iranian medicinal plants, including oregano, ginger, blue mint bush, grey echinophora, thyme, and saffron, possess antimicrobial properties (49-52). Additionally, cumin, green tea, jujube, sumac, dandelion, yarrow, and garlic have demonstrated antimicrobial activity in laboratory studies (53-56).

These plants contain a variety of bioactive compounds, such as flavonoids, terpenoids, phenolics, alkaloids, sulfides, fatty acids, and tannins, which contribute to their antifungal and antimicrobial effects (57, 58).

These compounds target multiple stages of fungal growth and reproduction, inhibiting fungal adherence to mucosal surfaces and modulating host immune responses (59, 60). Consequently, medicinal plants offer promising therapeutic potential for the management and prevention of *Candida albicans* infections.

Conclusion

The integration of herbal anti-Candida albicans products into clinical practice holds significant promise for the management of fungal infections, particularly oral candidiasis. Characterized by natural composition and favorable safety profiles, these herbal formulations directly target *Candida albicans*, effectively inhibiting fungal growth and reducing infection severity.

Clinical research supporting the efficacy and safety of these products has demonstrated reduced adverse effects compared to conventional antifungal agents, thereby enhancing patient adherence. Upon rigorous scientific and commercial validation, herbal anti-Candida albicans products can serve as valuable adjuncts to standard therapies, improving overall treatment outcomes and promoting public health.

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