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AROMATIC PLANTS AS ANTIFUNGAL AGENTS AGAINST ORAL CANDIDA STRAINS

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Introduction. The increasing resistance of *Candida* species to conventional antifungal agents necessitates the development of alternative therapies, especially in dentistry.

This study **aims to** assess the antifungal activity of hydroethanolic extracts from aromatic plants against *Candida albicans* and non-*albicans* species isolated from oral mucosal swabs of patients with oral candidiasis.

Methods. Thirteen plant extracts—laurel (*Laurus nobilis* L.), dwarf rosemary (*Rosmarinus officinalis* L.), ginger (*Zingiber officinale* Roscoe), turmeric (*Curcuma longa* L.), cinnamon bark (Ceylon Cinnamon) (*Cinnamomum verum* J. Presl), sweet basil (*Ocimum basilicum* L.), creeping thyme (*Thymus serpyllum* L.), wild marjoram (Oregano) (*Origanum vulgare* L.), tarragon (*Artemisia dracunculus* L.), black pepper (*Piper nigrum* L.), coriander (*Coriandrum sativum* L.), nutmeg (*Myristica fragrans* Houtt.), and chili pepper (*Capsicum frutescens* L.)—were prepared using 90% ethanol and tested against five clinical *Candida* strains (*C. albicans*, *C. tropicalis*, *C. lusitaniae*, *C. kefyr*, *C. lipolytica*) using the agar diffusion method. Fluconazole, chlorhexidine, decamethoxine, Stomatophyte, and Recutan served as control agents.

Results. Fluconazole showed the highest activity against all *Candida* spp. Among plant extracts, nutmeg and coriander were comparable to fluconazole in their activity against *C. tropicalis*. Creeping thyme and chili pepper exhibited broad-spectrum moderate activity against multiple strains, occasionally matching or surpassing the efficacy of decamethoxine and chlorhexidine. No plant extract demonstrated sufficient activity against *C. lusitaniae*.

Conclusions. A preliminary *in vitro* assessment of plant extracts, particularly nutmeg, coriander, creeping thyme, and chili pepper, showed promising antifungal activity against this limited panel of clinical isolates.

Keywords: Antifungal Agents, *Candida*, Plant Extracts, Candidiasis.

Introduction

Candida fungi are part of the oral cavity's opportunistic microbiota, with *C. albicans*—characterized by the highest pathogenic potential—accounting for 80-90% of oral candidiasis cases [1]. At the same time, there has been a consistent trend toward a greater role of *C. non-albicans* species in the development of opportunistic infections, with species such as *C. tropicalis* identified in approximately 20% of cases [1, 2]. In addition, the rising prevalence of antibiotic-resistant *Candida spp.*- associated complications has become a major concern [3].

Fluconazole is one of the most recommended and widely prescribed antifungal agents for *Candida* infections. Like other triazole antifungals, it inhibits lanosterol 14 α -demethylase, a cytochrome P450-dependent enzyme that demethylates lanosterol to generate ergosterol, an essential component of the fungal cell membrane. Ergosterol depletion and simultaneous accumulation of methylated sterols disrupt fungal cell membrane function, arresting fungal cell growth [4].

Recently isolated *Candida* strains from patients with oral candidiasis exhibit high resistance to conventional antifungal antibiotics and synthetic antimycotics, underscoring the urgent need for the development of new antifungal medications. Due to structural and biochemical similarities between fungal and human cells, the current antifungal armamentarium is limited, and only a small proportion is routinely used in dental practice. Additionally, most conventional antifungals are associated with undesirable, even toxic, side effects and often exhibit suboptimal pharmacodynamic and pharmacokinetic properties in the host organism [2; 5; 6]. These challenges underscore the importance of not only developing next-generation synthetic antifungal agents but also exploring the potential use of herbal medicines as alternatives [6].

Aromatic medicinal plants are widely used in medicine and are promising for treating and preventing fungal infections due to their diverse pharmacological properties [7; 8]. When taken as prescribed, herbal medicines have limited side effects and are low risk for the development of microbial resistance [8]. Thus, the purpose of this study was to determine the antifungal activity of hydroethanolic extracts from spicy and aromatic plants against clinical strains of yeast-like fungi of the genus *Candida* (*C. albicans* and *C. non-albicans*).

Methods

Approval of the Bioethics Committee

The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Ivano-Frankivsk National Medical University (protocol No. 148/24, dated 03.12.2024). All participants provided written informed consent for their participation and the use of their clinical isolates for research purposes.

Plant materials

In this study, the following thirteen raw plant materials were used: leaves of laurel (*Laurus nobilis* L.) and dwarf rosemary (*Rosmarinus officinalis* L.), rhizomes of ginger (*Zingiber officinale* Roscoe) and turmeric (*Curcuma longa* L.), cinnamon bark (Ceylon Cinnamon) (*Cinnamomum verum* J. Presl), herbs of sweet basil (*Ocimum basilicum* L.), creeping thyme (*Thymus serpyllum* L.), wild marjoram (Oregano) (*Origanum vulgare* L.), tarragon (*Artemisia dracunculus* L.), fruit of black pepper (*Piper nigrum* L.), coriander (*Coriandrum sativum* L.), nutmeg (*Myristica fragrans* Houtt.), chili pepper (*Capsicum frutescens* L.).

Extract preparation

The extract from the mentioned plant materials was prepared in 90% aqueous ethanol. The extraction was conducted using the maceration method, in accordance with the requirements of the State Pharmacopoeia of Ukraine (SPhU), at room temperature for 2 weeks (raw material-to-solvent ratio 1:10).

Antifungal Medications

Comparison drugs were fluconazole (25 μ g paper disks, Farmaktiv LLC, Ukraine), solutions of antiseptics—0.05% chlorhexidine bigluconate and 0.2% decamethoxine, and commonly used in dental practice herbal medicinal products—Recutan (Galychpharm JSC, Ukraine) and Stomatophyte (Phytopharm Klenka S. A., Poland). Recutan is a liquid extract of chamomile flowers (*Matricaria chamomilla* L.) in 50% ethanol. Stomatophyte is a liquid extract of a mixture of plant raw materials: chamomile flowers (*Matricaria chamomilla* L.), oak bark (*Quercus robur* L.), sage leaves (*Salvia officinalis* L.), arnica herb (*Arnica montana* L.), peppermint herb (*Mentha piperita* L.), thyme herb (*Thymus vulgaris* L.) and calamus rhizomes (*Acorus calamus* L.) in 70% ethanol.

Study participants

A total of 5 patients with oral candidiasis were enrolled in this study. The patients were recruited consecutively from the Department of Orthopedic Dentistry, Dental Center, and Ivano-Frankivsk National Medical University, between December 2024 and January 2025. The mean age was 64 years (range 60-72), with a male:female ratio of 4:1.

Inclusion criteria were: age ≥ 18 years; presence of clinical signs of oral candidiasis confirmed by positive microscopic examination of an oral mucosal swab for yeast-like cells; and ability to provide written informed consent.

Exclusion criteria were: systemic antifungal therapy within the preceding 30 days; use of topical antifungal agents or antiseptic mouthrinses within 7 days; treatment with systemic broad-spectrum antibiotics within 30 days; known severe immunodeficiency (e.g., advanced HIV infection, ongoing chemotherapy); uncontrolled diabetes mellitus; and any other acute oral mucosal disease unrelated to candidiasis.

Swab collection procedure: Oral mucosal swabs were collected from clinically affected sites (e.g., dorsal tongue, buccal mucosa, palate, or commissures) using sterile cotton swabs. Each swab was gently rolled over the lesion surface, then suspended in 2 ml of sterile saline, and inoculated onto Sabouraud agar and the chromogenic medium ChromID Candida (bioMérieux, France).

Candida strains

The isolated five strains of yeast-like fungi (*C. albicans* and *C. non-albicans*) were identified based on a comprehensive analysis of their morphological, cultural, and biochemical properties. Specifically, 40 biochemical tests were performed for each strain using the VITEK 2 system with the VITEK 2 YST ID card (bioMérieux, France).

In total, five clinical isolates of *Candida* were included in the study: *Candida albicans* isolate and four non-*albicans* species, namely *C. tropicalis*, *C. lusitaniae*, *C. kefyr* and *C. lipolytica*.

Antifungal drug profiles for these strains were determined using the ATB FUNGUS 3 (bioMérieux, France) microdilution test, with EUCAST (Version 12.0, 2025-06-26) interpretation. All strains were resistant to 5-Flucytosine (MIC ≥ 16 $\mu\text{g/Lm}$) and sensitive to Amphotericin B (MIC ≤ 1 $\mu\text{g/mL}$). *C. albicans* and *C. tropicalis* strains demonstrated high-level azole resistance (MIC Fluconazole $> 128\mu\text{g/mL}$, Itraconazole > 4 $\mu\text{g/mL}$, Voriconazole > 8 $\mu\text{g/mL}$). *C. lipolytica* strains demonstrated low-level azole resistance (MIC sensitive Fluconazole $32\mu\text{g/mL}$, Itraconazole > 0.5 $\mu\text{g/mL}$, Voriconazole 1 $\mu\text{g/mL}$). *C. lusitaniae* and *C. kefyr* strains were sensitive to Fluconazole (MIC < 1 $\mu\text{g/mL}$) and Voriconazole (MIC < 0.06 $\mu\text{g/mL}$), but varied in Itraconazole sensitivity (MICs 0.25 $\mu\text{g/mL}$ for *C. lusitaniae*, and < 0.06 $\mu\text{g/mL}$ for *C. kefyr*).

Antifungal susceptibility testing

The anti-*Candida* activity of the extracts was evaluated using the agar-gel diffusion micro-method. Each plant extract-strain combination was tested in quadruplicate. Petri dishes were filled with 30 mL of Sabouraud agar (Farmaktiv LLC, Ukraine) and placed on a flat, strictly horizontal surface. After the medium solidified, wells with a 4.0 mm diameter were punched using a special punch with smooth edges. The agar surface was then uniformly inoculated with test culture suspensions at a concentration of 1×10^7 CFU/mL. Subsequently, 20 μL of each test extract or solution was added to the wells. For the control, 20 μL of the extractant (90% ethanol) was introduced into separate wells. The diameters of fungal growth inhibition zones were evaluated 48 hours after incubation at 37 °C.

Digital images of cultures were captured and analyzed using ImageTool 2.0 (UTHSCSA ImageTool 2.0, The University of Texas Health Science Center in San Antonio, ©1995-1996). Antifungal activity was conditionally classified as weak (≤ 10 mm), moderate (11–15 mm), or strong (≥ 16 mm), based on the diameter of the inhibition zone.

Statistical analysis

Statistical analysis was performed in R. The mean and standard deviation of the diameters of fungal growth inhibition zones were calculated, and further assessment was performed using an ANOVA test with post-hoc analysis (Tukey Post-hoc Test). The p-value < 0.05 was considered significant.

Results

Fluconazole exhibited the strongest fungistatic activity against all *Candida* spp., with the highest inhibition zones for *C. lusitaniae*, but notably lower values for *C. tropicalis*. A fungicidal effect was observed only for *C. lusitaniae* and *C. kefyr*.

For *C. albicans*, among control agents, only decamethoxine showed moderate activity; chlorhexidine did not differ significantly but remained at the upper threshold of low efficacy. Laurel, ginger, dwarf rosemary, Ceylon cinnamon, coriander, and chili pepper had an effect similar to that of decamethoxine, though not significantly. Wild marjoram and nutmeg demonstrated moderate activity, comparable to decamethoxine, dwarf rosemary, and cinnamon, but significantly lower than other aforementioned plant extracts.

In *C. tropicalis*, the fungistatic activity of coriander and nutmeg, showing the highest activity among plant extracts, did not significantly differ from that of fluconazole and decamethoxine; nutmeg approached the upper threshold of moderate efficacy. The next most active group included sweet basil, turmeric, and black pepper, all demonstrating strong moderate activity.

For *C. lusitaniae*, only control drugs (fluconazole, chlorhexidine, and decamethoxine) showed moderate to high efficacy; plant extracts demonstrated either weak (nutmeg—highest) or no significant activity.

In *C. kefyr*, chlorhexidine and decamethoxine demonstrated moderate effects. Creeping thyme reached the upper range of moderate activity without a significant difference from decamethoxine; other extracts did not achieve comparable levels.

For *C. lipolytica*, decamethoxine and creeping thyme exhibited moderate-high activity, followed by nutmeg and chili pepper. Other extracts remained within the moderate-low or low activity ranges.

Discussion

Our findings demonstrated significant anti-*Candida* activity of extracts from several aromatic plants traditionally used in medicine. Aromatic plants are characterized by a high content of essential oils, which include terpene compounds, organic acids and alcohols, their esters, phenols, aldehydes, and other volatile substances with antifungal activity.

In our study, the *Laurus nobilis* L. extracts, though significantly less efficacious than fluconazole, still demonstrated moderate antifungal activity against *C. albicans*. While notably higher in activity than other control medications, it did not significantly differ from decamethoxine. Activity against *C. tropicalis* was markedly lower but did not differ significantly from that of chlorhexidine. These findings are partially consistent with Peixoto et al. [9], who reported that laurel essential oil, attributable to its content of myrcene, carvacrol, and eugenol, exhibited fungicidal activity against *C. albicans*, *C. glabrata*, *C. krusei*, and *C. tropicalis*, associated with changes in membrane ionic permeability and fungal cell wall biosynthesis inhibition. A significant constituent (31.9%) of laurel essential oils is eucalyptol (1,8-cineole), which exhibits high antibiofilm activity against *C. albicans* [10; 11]. Considering our results and the laurel essential oil's ability to inhibit biofilm formation [10; 11], it may be a promising candidate for inclusion in future mouthwash formulations.

Ginger has been shown to possess antioxidant, anti-inflammatory, and antitumor properties [12]. Our results demonstrated antifungal activity against *C. albicans* at the level of decamethoxine and against *C. tropicalis* at the level of chlorhexidine. Our tested solution results were comparable to those of the 50% concentration aqueous extract reported by Al-Ghanayem et al. [13]. Despite the absence of effect on other strains, the findings support further *in vitro* and *in vivo* studies of ethanolic ginger extract in the context of candidiasis.

The *in vitro* antifungal effects of rosemary (*Rosmarinus officinalis* L.) have been demonstrated against *C. albicans*, *C. dubliniensis*, *C. glabrata*, *C. krusei*, and *C. tropicalis* [14; 15]. Additionally, an *ex vivo* clinical study confirmed the ability of rosemary extract to abruptly reduce the number of viable microbial cells within biofilms formed in the oral cavity of healthy individuals [16]. However, our study revealed only moderate *Rosmarinus officinalis* L. antifungal activity, similar to that of decamethoxine, laurel, and ginger extracts against *C. albicans*. This effect is likely due to the high concentrations and synergic activity of 1,8-cineole and α -pinene in *Rosmarinus officinalis* L. [11]. Nevertheless, its efficacy against other *Candida* strains was markedly lower, suggesting a strain-specific response. It has also been demonstrated that rosemary essential oil enhances the antifungal efficiency of fluconazole against multidrug-resistant *C. auris*, through synergistic effects associated with its major constituents (eucalyptol, camphor, and borneol) [17]. Overall, in light of previous studies, these findings indicate the need for further investigation of rosemary preparations as potential adjuvants to conventional antifungal therapy.

Table 1. Anti-*Candida* activity of aromatic plant extracts prepared in 90% ethanol

No.	Antifungal agent			Inhibition Zone Diameter, mm				
				<i>C. albicans</i>	<i>C. tropicalis</i>	<i>C. lusitaniae</i>	<i>C. kefyr</i>	<i>C. lipolytica</i>
Comparison Drugs								
1	Fluconazole (fungistatic)			21.17±0.42 ^a	16.17±0.41 ^a	28.95±0.84 ^a	23.58±0.54 ^a	19.65±1.07 ^a
2	Fluconazole (fungicidal)			NA	NA	18.65±0.26 ^b	20.30±0.39 ^b	NA
3	Chlorhexidine 0.05%			9.62±0.45 ^{bcde}	10.07±0.44 ^{bc}	13.95±0.40 ^c	11.75±0.88 ^c	18.45±0.52 ^a
4	Decamethoxine 0.2%			11.79±0.69 ^{b fgh}	16.27±0.38 ^a	13.00±0.35 ^c	12.96±0.38 ^{cd}	14.17±0.62 ^b
5	Stomatophyte			6.73±0.56 ⁱ	6.09±0.45 ^d	6.14±0.38 ^{de}	6.27±0.62 ^e	6.94±0.12 ^{cd}
6	Recutan			NA	NA	NA	NA	4.20±0.08 ^e
7	Ethanol 90%			NA	5.79±0.25 ^d	5.57±0.55 ^{dh}	5.72±0.45 ^e	6.85±0.82 ^{cd}
Plant Extracts								
	Common name	Botanical name (Authority)	Plant part					
1	Laurel	<i>Laurus nobilis</i> L.	Leaves	14.14±0.80 ^f	8.59±1.00 ^{bef}	NA	6.04±0.51 ^e	4.33±0.15 ^e
2	Ginger	<i>Zingiber officinale</i> Roscoe	Rhizomes	14.09±1.07 ^f	10.65±0.73 ^{cg}	NA	NA	NA
3	Dwarf rosemary	<i>Rosmarinus officinalis</i> L.	Leaves	12.43±0.92 ^{fgh}	8.36±0.31 ^{ef}	8.91±0.77 ^{gh}	10.47±0.74 ^f	10.02±0.43 ^{fg}
4	Cinnamon (Ceylon Cinnamon)	<i>Cinnamomum verum</i> J. Presl	Bark	12.44±1.08 ^{fgh}	5.70±0.37 ^d	5.26±0.53 ^{df}	6.46±0.36 ^e	9.33±0.35 ^f
5	Sweet basil	<i>Ocimum basilicum</i> L.	Herb	7.57±1.66 ^{ci}	14.05±0.68 ^{hi}	5.53±0.61 ^{df}	10.47±0.46 ^f	7.66±0.12 ^{cd}
6	Creeping thyme	<i>Thymus serpyllum</i> L.	Herb	8.99±0.41 ^{cdi}	9.32±0.85 ^{bce}	8.87±0.75 ^{gh}	13.98±0.15 ^d	14.58±0.36 ^b
7	Wild marjoram (Oregano)	<i>Origanum vulgare</i> L.	Herb	11.50±0.73 ^{begh}	5.68±0.22 ^d	4.75±0.47 ^f	6.43±0.28 ^e	6.80±0.29 ^{cd}
8	Turmeric	<i>Curcuma longa</i> L.	Rhizomes	9.41±0.57 ^{cde}	12.69±0.48 ^{hj}	8.03±0.45 ^{gi}	8.61±0.46 ^g	10.77±0.45 ^g
9	Black pepper	<i>Piper nigrum</i> L.	Fruit	7.89±1.20 ^{cdi}	13.42±0.75 ^{hj}	5.68±0.34 ^{df}	4.42±0.20 ^h	6.56±0.38 ^c
10	Tarragon	<i>Artemisia dracunculus</i> L.	Herb	7.28±0.62 ^{ci}	7.68±0.42 ^f	7.32±0.21 ^{ei}	9.62±0.52 ^{fg}	5.01±0.47 ^e
11	Coriander	<i>Coriandrum sativum</i> L.	Fruit	13.69±1.50 ^{fg}	15.98±0.72 ^a	7.54±0.38 ⁱ	6.61±0.61 ^e	7.98±0.24 ^d
12	Nutmeg	<i>Myristica fragrans</i> Houtt.	Fruit	10.20±0.72 ^{bdeh}	14.97±0.92 ^{ai}	9.71±0.49 ^h	9.59±0.49 ^{fg}	11.24±0.32 ^{gh}
13	Chili pepper	<i>Capsicum frutescens</i> L.	Fruit	12.80±1.01 ^{fg}	12.07±0.30 ^{gi}	8.20±0.30 ^{gi}	8.54±0.23 ^g	12.20±0.76 ^h

Notes: Data are presented as mean ± standard deviation. Superscript letters indicate the results of Tukey's post-hoc test. Within each column, values that share at least one common letter do not differ significantly ($p \geq 0.05$), whereas values with no letters in common differ significantly ($p < 0.05$); NA – no activity (effect ≤ 4 mm)

Cinnamon (*Cinnamomum verum* J. Presl) is a well-known medicinal plant with established antimicrobial activity, largely attributed to cinnamaldehyde and other phenylpropanoids present in its essential oil [18-19]. It is widely used as a promising antimicrobial agent in dentistry [20]. Several studies reported its antifungal effects against *C. albicans*, including activity against fluconazole-resistant strains [21-23]. In our study, Ceylon cinnamon bark extract demonstrated moderate activity against *C. albicans*, comparable with decamethoxine, *Laurus nobilis* L., *Zingiber officinale* Roscoe, and *Rosmarinus officinalis* L., but showed limited or no efficacy against other *Candida* strains.

The essential oil of *Ocimum basilicum* L. has been reported to possess broad-spectrum antibacterial activity and to inhibit *C. albicans* more effectively than fluconazole [24]. In our study, however, its efficacy against *C. albicans* was weak, and no relevant activity was observed against *C. lusitaniae*. Instead, the oil demonstrated the highest activity against *C. tropicalis*, comparable to decamethoxine and significantly higher than chlorhexidine. Although estragole and linalool, both recognized for their antifungal properties [25], were present in high amounts, these discrepancies are likely attributable to variations in essential oil composition across cultivars from different regions [26].

Significant activity of *Origanum vulgare* L. against various *Candida* spp. due to both antibacterial and antifungal effects was reported [27; 28]. Conversely, we find that the hydroethanolic extract only moderately inhibited *C. albicans* growth and showed weak or no activity against non-*albicans* species, despite the presence of carvacrol and thymol, which have strong fungicidal activity [29]. The discrepancies between their findings and ours may be attributed to differences in experimental settings, including the geographical origin of plant material, cultivation practices, harvesting time, and preparation method. Furthermore, the concentration of carvacrol and thymol in oregano essential oil can reach up to 10% [29], which suggests that the preparations used in our study may have contained lower amounts, resulting in reduced antifungal efficacy.

Curcumin, a lipophilic phenol present in the rhizomes of turmeric (*Curcuma longa* L., *Zingiberaceae*), exhibits antifungal activity against *C. albicans* and *C. tropicalis* [30] by inducing reactive oxygen species (ROS) formation, triggering apoptosis, and interfering with the ergosterol biosynthesis pathway, ultimately inhibiting hyphal growth [31]. Beyond its direct antifungal effects, curcumin has been reported to synergistically enhance the activity of azoles and, particularly, polyenes against *C. albicans*, and to inhibit biofilm formation or disrupt preformed biofilms [32]. In our study, the antifungal activity of the hydroethanolic rhizome extract of *Curcuma longa* is likely attributable to curcumin. Its efficacy against *C. albicans* was comparable to that of chlorhexidine but significantly lower than that of decamethoxine. Against *C. tropicalis*, the extract demonstrated higher activity than chlorhexidine but comparable to *Ocimum basilicum*, *Piper nigrum*, and *Capsicum frutescens*, reflecting a moderate yet notable antifungal potential. This differential activity may be related to species-specific susceptibility and the concentration of bioactive compounds in the hydroethanolic extract.

The essential oil extracted from black pepper is characterized by a high content of total phenolic compounds, flavonoids, and proanthocyanidins, promoting its strong antioxidant, hepatoprotective, and antifungal properties [33]. *Piper nigrum* L. exhibited the highest antifungal activity against *C. tropicalis*, primarily due to the presence of the alkaloid piperine, which induces oxidative stress in fungal cells by destabilizing mitochondrial membranes, ultimately leading to cell cycle arrest and apoptosis [34]. Although black pepper essential oil has shown significant synergism with fluconazole against fluconazole-resistant *C. albicans* [34], in our study, it demonstrated only low standalone activity, comparable to chlorhexidine. This discrepancy may be attributed to differences in extraction methods, active compound concentrations, or strain-specific susceptibility, highlighting the importance of these factors in determining antifungal efficacy. At the same time, our findings revealed an acceptable level of activity against *C. albicans*, greater than that of chlorhexidine but lower than that of decamethoxine.

The antifungal potential of tarragon (*Artemisia dracuncululus* L.) against *C. albicans* has been confirmed in a study on the treatment of skin wounds. It is explained by its antioxidant and anti-inflammatory effects [35]. Estragole has been identified as a major compound in tarragon essential oil [36] and exhibits high antifungal properties [25]. However, in our study, tarragon did not demonstrate a notable effect against any of the assessed strains. This discrepancy may, once again, be attributed to the method of extract preparation and concentration of active compounds, geographical origin, or cultivation practices.

Coriander has demonstrated antifungal activity, attributed mainly to its monoterpenes and sesquiterpenes, which act synergistically and may disrupt fungal membranes by binding to ergosterol and increasing ionic permeability [37]. Barbosa et al. reported a dose-dependent reduction of *Candida* biofilm biomass by up to ~70% [38]. In our study,

coriander extract showed relatively strong activity against *C. tropicalis* and moderate activity against *C. albicans*, both of which were similar to decamethoxine.

Nutmeg (*Myristica fragrans*) has demonstrated antimicrobial, antiseptic, and disinfectant properties, as well as antioxidant and analgesic effects [39]. However, data on its antifungal activity is limited. In our study, nutmeg exhibited the highest activity against *C. lipolytica*, although it did not surpass decamethoxine or chlorhexidine. Against *C. tropicalis*, its efficacy was comparable to that of decamethoxine and fluconazole (fungistatic concentrations), consistent with recent reports demonstrating strong anticandidal activity and synergistic interactions of *Myristica fragrans* oil with fluconazole [40]. The antifungal potential of nutmeg may be attributed to bioactive compounds such as myristicin, elemicin, and eugenol [41].

Capsicum frutescens (chili pepper) contains capsaicinoids (notably capsaicin and dihydrocapsaicin), phenolics and saponins [42]. Besides its *in vitro* anticandidal activity via ergosterol biosynthesis inhibition, membrane integrity disruption, and biofilm biomass reduction, capsaicin has also been shown to potentiate fluconazole activity [43]. In our study, moderate inhibition of *C. albicans*, *C. tropicalis*, and *C. lipolytica* was observed, consistent with these reports; the observed potency likely depends on the extraction method and the concentrations of capsaicinoids and saponins in the preparation [42]. Moreover, the efficacy against *C. albicans* was similar to that of decamethoxine; against *C. tropicalis*, activity was intermediate and comparable to that of chlorhexidine and decamethoxine. However, chili pepper showed significantly lower activity against *C. lipolytica* than the agents above.

Taken together, our findings add several novel aspects to the existing literature on plant-derived antifungal agents. Thus, the results of this preliminary study provide a direct, head-to-head comparison of 13 hydroethanolic extracts of widely used aromatic plants with commonly used oral antiseptics and fluconazole, under the same experimental conditions and using the same clinical oral isolates. Moreover, in contrast to many previous studies that focused almost exclusively on *C. albicans*, we examined both *C. albicans* and four non-albican species (*C. tropicalis*, *C. parapsilosis*, *C. krusei*, and *C. lusitaniae*). We demonstrated clear species-specific differences in susceptibility patterns. It allowed comparative *in vitro* evidence for several extracts that have been less extensively studied in the specific context of oral *Candida* infections and dentistry to be presented.

Several limitations of this study should be acknowledged. First, only five clinical isolates (one for each *Candida* species) were included, which limits the generalizability of the findings and prevents us from capturing inter-strain variability. Second, although EUCAST-based microdilution testing with ATB FUNGUS 3 was used to characterize the antifungal drug profiles of these isolates, the comparative evaluation of plant extracts with antifungal medications in this study relied solely on an agar diffusion (zone of inhibition) assay at a single extract concentration. Considering zone diameters cannot be directly translated into MIC values, clinical breakpoints, or therapeutic equivalence, these findings should be interpreted with caution. Third, we did not assess cytotoxicity, pharmacokinetic properties, biofilm-associated susceptibility, or formulation aspects of the most active extracts. As a result, present data should be regarded as preliminary *in vitro* screening results identifying promising plant extracts for subsequent MIC-based, mechanistic, and *in vivo* studies, rather than as a basis for clinical recommendations.

To conclude, this preliminary *in vitro* study demonstrated that hydroethanolic extracts of aromatic plants possess antifungal activity against clinical isolates of *C. albicans* and non-albicans strains. Activity comparable to that of fluconazole was observed only with nutmeg and coriander against *C. tropicalis*. In addition, creeping thyme and chili pepper showed the most promising antifungal effects, in some cases comparable to or exceeding the efficacy of chlorhexidine. However, their antifungal activity was generally inferior to fluconazole. None of the plant extracts demonstrated sufficient efficacy against *C. lusitaniae*. These findings highlight the potential of the aforementioned plant extracts as candidates for further *in vitro* investigation.

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