ÓLEOS ESSENCIAIS E EXTRATOS ALCOÓLICOS: UMA COMPARAÇÃO DA ATIVIDADE ANTIFÚNGICA CONTRA Candida spp.

ESSENTIAL OILS AND ALCOHOLIC EXTRACTS: A COMPARISON OF ANTIFUNGAL ACTIVITY AGAINST Candida spp.

ACEITES ESENCIALES Y EXTRACTOS ALCOHÓLICOS: UNA COMPARACIÓN DE LA ACTIVIDAD ANTIFÚNGICA CONTRA Candida spp

https://doi.org/10.56238/sevened2025.021-044

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RESUMO

A crescente resistência de Candida spp. aos antifúngicos convencionais, como azóis e polienos, representa um desafio clínico relevante, sobretudo em infecções oportunistas que acometem pacientes imunocomprometidos. Esse cenário tem estimulado a busca por terapias alternativas baseadas em compostos naturais, que apresentam menor toxicidade e risco reduzido de induzir resistência. Este estudo teve como objetivo realizar uma análise comparativa da atividade antifúngica de óleos essenciais e extratos alcoólicos de diferentes plantas medicinais frente a cepas de Candida, com ênfase em Candida albicans e espécies não-albicans, como C. tropicalis, C. krusei e C. glabrata, conhecidas por sua capacidade de formar biofilmes e resistir a tratamentos convencionais. Foram revisados estudos publicados entre 2020 e 2025, envolvendo compostos amplamente utilizados na medicina tradicional. Entre os óleos essenciais investigados, destacam-se os de Melaleuca alternifolia (árvore-do-chá), rico em terpinen-4-ol, e Cymbopogon citratus (capim-limão), composto por citral e geraniol. Já entre os extratos alcoólicos, foram incluídos Syzygium cumini (jambolão), rico em flavonoides e taninos, e Ziziphus joazeiro (joazeiro), com saponinas e compostos fenólicos. Os resultados apontam que os óleos essenciais apresentaram atividade antifúngica superior, mesmo em baixas concentrações (geralmente <1%), além de expressivo efeito antibiofilme. Os extratos alcoólicos também demonstraram eficácia, embora com necessidade de concentrações mais elevadas. Acredita-se que a

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lipofilicidade dos óleos favoreça sua ação na membrana fúngica. Conclui-se que ambos os extratos possuem potencial terapêutico, mas os óleos essenciais, sobretudo os ricos em monoterpenos, destacam-se como alternativas mais potentes e promissoras no desenvolvimento de fitoterápicos antifúngicos, especialmente contra cepas resistentes e infecções recorrentes.

Palavras-chave: Óleos essenciais. Extratos alcoólicos. Candida albicans. Antifúngico natural. Fitoterapia.

ABSTRACT

The increasing resistance of Candida spp. to conventional antifungals, such as azoles and polyenes, represents a relevant clinical challenge, especially in opportunistic infections that affect immunocompromised patients. This scenario has stimulated the search for alternative therapies based on natural compounds, which present lower toxicity and reduced risk of inducing resistance. This study aimed to perform a comparative analysis of the antifungal activity of essential oils and alcoholic extracts of different medicinal plants against Candida strains, with emphasis on Candida albicans and non-albicans species, such as C. tropicalis, C. krusei and C. glabrata, known for their ability to form biofilms and resist conventional treatments. Studies published between 2020 and 2025 involving compounds widely used in traditional medicine were reviewed. Among the essential oils investigated, those of Melaleuca alternifolia (tea tree), rich in terpinen-4-ol, and Cymbopogon citratus (lemongrass), composed of citral and geraniol, stand out. Among the alcoholic extracts, Syzygium cumini (jambolão), rich in flavonoids and tannins, and Ziziphus joazeiro (joazeiro), with saponins and phenolic compounds, were included. The results indicate that the essential oils presented superior antifungal activity, even at low concentrations (generally <1%), in addition to a significant antibiofilm effect. The alcoholic extracts also demonstrated efficacy, although requiring higher concentrations. It is believed that the lipophilicity of the oils favors their action on the fungal membrane. It is concluded that both extracts have therapeutic potential, but essential oils, especially those rich in monoterpenes, stand out as more potent and promising alternatives in the development of antifungal phytotherapeutics, especially against resistant strains and recurrent infections.

Keywords: Essential oils. Alcoholic extracts. Candida albicans. Natural antifungal. Phytotherapy.

RESUMEN

La creciente resistencia de Candida spp. a los antifúngicos convencionales, como los azoles y los polienos, representa un desafío clínico relevante, especialmente en infecciones oportunistas que afectan a pacientes inmunodeprimidos. Este escenario ha estimulado la búsqueda de terapias alternativas basadas en compuestos naturales, que presentan menor toxicidad y menor riesgo de inducir resistencia. Este estudio tuvo como objetivo realizar un análisis comparativo de la actividad antifúngica de aceites esenciales y extractos alcohólicos de diferentes plantas medicinales contra cepas de Candida, con énfasis en Candida albicans y especies no albicans, como C. tropicalis, C. krusei y C. glabrata, conocidas por su capacidad para formar biopelículas y resistir tratamientos convencionales. Se revisaron estudios publicados entre 2020 y 2025 que involucran compuestos ampliamente utilizados en la medicina tradicional. Entre los aceites esenciales investigados, destacan los de Melaleuca alternifolia (árbol del té), rico en terpinen-4-ol, y Cymbopogon citratus (limoncillo), compuesto por citral y geraniol. Entre los extractos alcohólicos, se incluyeron Syzygium cumini (jambolão), rico en flavonoides y taninos, y Ziziphus joazeiro (joazeiro), con saponinas y compuestos fenólicos. Los resultados indican que los aceites esenciales presentaron una actividad antifúngica superior, incluso a bajas concentraciones (generalmente <1%), además de un significativo efecto antibiofilm. Los

extractos alcohólicos también demostraron eficacia, aunque requiriendo concentraciones más altas. Se cree que la lipofilicidad de los aceites favorece su acción sobre la membrana fúngica. Se concluye que ambos extractos tienen potencial terapéutico, pero los aceites esenciales, especialmente aquellos ricos en monoterpenos, se destacan como alternativas más potentes y prometedoras en el desarrollo de fitoterapéuticos antifúngicos, especialmente contra cepas resistentes e infecciones recurrentes.

Palabras clave: Aceites esenciales. Extractos alcohólicos. Candida albicans. Antifúngico natural. Fitoterapia

INTRODUCTION

Candidiasis is an opportunistic infection caused by fungi of the genus Candida, with Candida albicans being the most common species. However, non-albicans species such as C. glabrata, C. krusei, and C. tropicalis have also emerged as relevant agents, especially in hospital settings and in patients with immunosuppression. The high incidence of these infections, added to the growing resistance to conventional antifungals, such as fluconazole and amphotericin B, highlights the need for new therapeutic alternatives (Domingues and Paiva., 2021).

Pharmacognosy and ethnopharmacology have played a fundamental role in the scientific validation of traditional knowledge, allowing the identification, isolation and characterization of bioactive compounds with therapeutic potential. These areas of knowledge not only rescue the ancestral use of medicinal plants, but also enable the application of this knowledge in the formulation of new phytopharmaceuticals (Farias., et al 2024).

Essential oils and alcoholic extracts of medicinal plants have emerged as promising natural alternatives, with widely studied antimicrobial properties. Compounds such as monoterpenes (present in Melaleuca alternifolia and Cymbopogon citratus) and flavonoids (common in the alcoholic extracts of Syzgium cumini and Ziziphus joazeiro) are recognized for their antifungal activity (Carneiro et al., 2024).

Herbal medicines, defined as medicines obtained from plant raw materials, such as extracts, essential oils, and tinctures, have stood out as promising therapeutic alternatives in the treatment of fungal infections. Its complex composition, rich in secondary metabolites with antimicrobial properties, provides a multifactorial action, which goes beyond the simple inhibition of fungal growth. Unlike synthetic antifungals, which usually have unique mechanisms of action, herbal medicines act through diverse and synergistic pathways, which contributes to their effectiveness and less propensity to develop microbial resistance (Ferreira, 2022).

In addition to direct antifungal activity, herbal medicines also demonstrate the ability to modulate the host's inflammatory response, favoring the recovery of affected tissues. This integrative approach has been shown to be especially relevant in view of the therapeutic limitations imposed by the formation of fungal biofilms, which reduce the penetration and efficacy of conventional agents. In this context, herbal medicines represent a valuable complementary strategy in the fight against fungal infections, especially in view of the progressive increase in resistance to synthetic drugs and the low toxicity they present (Berla, 2022).

The present study aimed to perform a comparative analysis of the antifungal activity of essential oils and alcoholic extracts against Candida spp., highlighting its efficacy, the proposed mechanisms of action and the possible clinical applications as alternatives to conventional treatments. The rationale for conducting this study is based on the increasing fungal resistance to available synthetic antifungals, especially in the treatment of infections caused by Candida albicans and non-albicans species. In view of this scenario, it is essential to investigate alternative therapies, of natural origin, that have proven efficacy, lower toxicity, and potential for clinical use in dealing with these recurrent and difficult-to-manage infections.

METHODOLOGY

This work is a qualitative and comparative literature review, whose objective was to analyze studies published between 2020 and 2025 that investigated the antifungal activity of natural substances of plant origin against strains of the genus Candida spp., through in vitro laboratory tests.

The search for articles was performed in the PubMed, SciELO, Web of Science and Scopus databases, using the following descriptors, combined by Boolean operators ("AND" and "OR"):"Candida spp.", "antifungal activity", "essential oils", "alcoholic extracts", "biofilm".

Articles that met the following criteria were included, such as availability of the full text, which obtained a clear description of the methodology for extracting natural compounds, identification of the strain(s) of Candida spp. used, containing standardized antifungal assays (in vitro) and presenting a robust experimental design, using appropriate controls and appropriate statistical methods.

Studies were excluded from articles that did not specify the concentrations of the extracts or compounds tested; they did not detail the statistical procedures adopted; evaluated natural compounds exclusively in association with synthetic drugs, making it impossible to analyze the activity of products of plant origin in isolation.

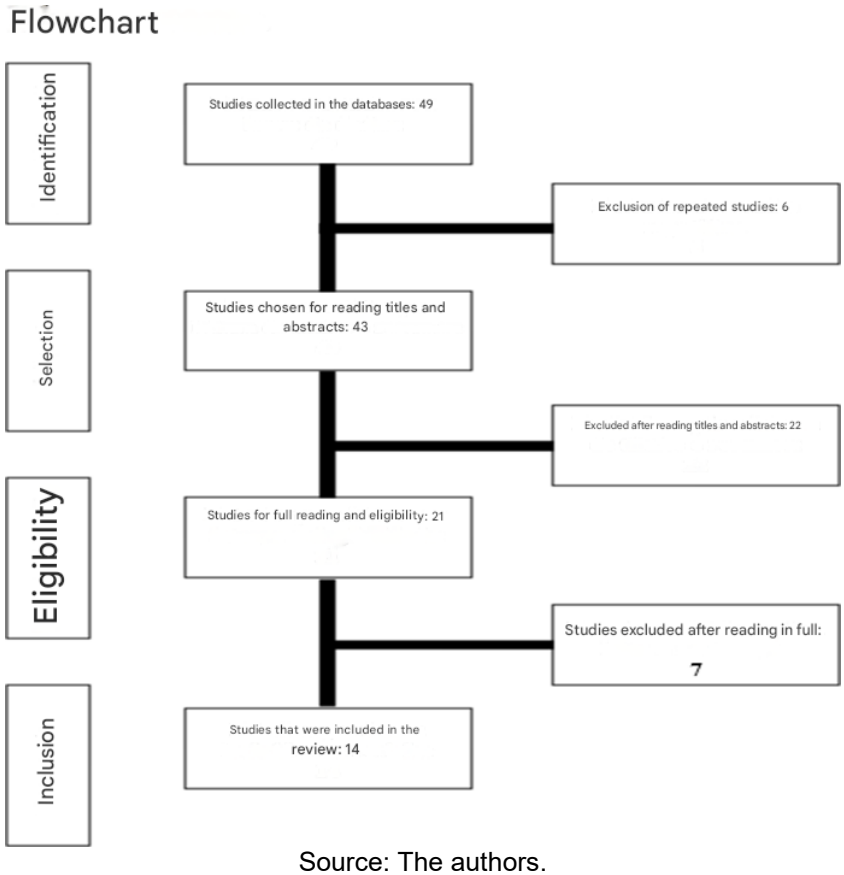
The selection of articles was conducted in two stages: a) Reading of titles and abstracts, with application of the previously established inclusion and exclusion criteria; b) Full reading of the eligible articles, to confirm adherence to the criteria and relevance to the objectives of the review.

The data from the selected studies were extracted in a systematic way and organized in a table containing the following information as the title of the article; Authors; year of publication; study objective; description of the methodology used (including type of

extract, extraction method, strains tested, and antifungal techniques employed); Main results and conclusions.

The data analysis was conducted in a descriptive, interpretative and critical way, seeking to identify methodological patterns, efficacy of natural compounds against Candida spp. strains, in addition to pointing out gaps, limitations and trends observed in the scientific literature.

The synthesis of the findings was carried out through an integrative and critical approach, allowing the comparison of the methods employed, the results obtained and the contributions of each study to the advancement of knowledge in the area of antifungal agents of plant origin. Whenever relevant, the results were organized into thematic categories, facilitating comparative analysis between the reviewed studies.



Source: The authors.

RESULTS AND DISCUSSION

The genus Candida comprises commensal yeasts that normally inhabit the oral mucosa, gastrointestinal tract, and genitourinary tract of humans. Under conditions of immunosuppression or microbiota imbalance, these yeasts can become pathogenic and cause mucocutaneous and systemic infections. The most frequently isolated species is Candida albicans, but other species such as C. glabrata, C. krusei, and C. tropicalis have

gained prominence, mainly because they have greater resistance to conventional antifungals (Carneiro et al., 2024).

The formation of biofilms is one of the main virulence factors of Candida, giving it increased resistance to drugs and protection against the immune response. These complex structures make it difficult for drugs to penetrate and are associated with recurrent and chronic infections (Silva, 2024).

Antifungal resistance occurs through multiple mechanisms, such as overexpression of efflux pumps, changes in the ergosterol biosynthesis pathway, and mutations in drug target sites. In addition, Candida's ability to form biofilms contributes to up to 1000 times greater resistance compared to planktonic forms, being a therapeutic challenge (Santos, 2024).

The results extracted from the analyzed studies indicate that both essential oils and alcoholic extracts demonstrate antifungal activity against Candida strains, but with significant differences in potency and scope.

The choice of the broth microdilution method to determine the Minimum Inhibitory Concentration (MIC) and Minimum Fungicidal Concentration (CFM) is based on the fact that it is considered the gold standard according to the guidelines of the Clinical and Laboratory Standards Institute (CLSI, 2023). The studies also included biofilm formation assays in 96-well plates, allowing the evaluation of the interference of the tested compounds in the adhesion and structuring of fungal communities. Statistical analysis was performed mainly by ANOVA and Tukey's test, aiming at the comparison between the experimental and control groups.

The essential oil of Melaleuca alternifolia showed a Minimum Inhibitory Concentration (MIC) of 0.312 µg/mL and a Minimum Fungicide Concentration (MFC) of 1.25 µg/mL for C. albicans, in addition to effective inhibition of biofilm formation, even at low concentrations. Similarly, Cymbopogon citratus oil demonstrated MIC of 0.5 µg/mL, also with strong antibiofilm action, as shown in the table below.

TABLE 1 COMPARISON OF ANTIFUNGAL ACTIVITY OF ESSENTIAL OILS AGAINST Candida spp.

Essential oil	Part used	Extraction method	MIC for Candida spp.	Effect observed	Other Microorganisms Tested	Additional observations
Lemongrass (*Cymbopogon citratus*)	Sheets	Hydrodistillation (steam distillation) using Clevenger apparatus	0,281–1,125 µg/mL	High antifungal activity	*Candida albicans*, *C. dubliniensis*, *C. tropicalis*, *C. glabrata*,	Potential use as a preventive or therapeutic herbal medicine
Melaleuca (*Melaleuca alternifolia*)	Sheets	Usually by steam distillation (not specified in the article)	*C. albicans*: 0,312 µg/mL; *C. krusei*: 0,312 µg/mL	High antifungal/antibiofilm activity	Candida krusei	CFM: 1.25 µg/mL (C. albicans), 0.625 µg/mL (C. krusei); Promising as a therapeutic alternative

Source:The authors.

These effects are attributed to the presence of monoterpenes such as terpinen-4-ol and citral, hydrophobic compounds that destabilize the fungal cell membrane, causing cell lysis and changes in ATP production.

On the other hand, the alcoholic extracts of Syzgium cumini (jambolão) and Ziziphus joazeiro (joazeiro) showed relevant antifungal action, but with MIC ranging from 2 to 5 mg/mL, showing lower potency when compared to essential oils. Despite this, they have also demonstrated the ability to inhibit the formation of biofilms and alter the morphology of fungal cells, mainly due to the presence of flavonoids, tannins and alkaloids as shown in the table below:

TABLE 2- COMPARISON OF ANTIFUNGAL ACTIVITY OF EXTRACTS AGAINST Candida spp.

Alcoholic extract	Part used	Extraction method	MIC for Candida spp.	Effect observed	Other Microorganisms Tested	Additional observations
Joazeiro (*Ziziphus joazeiro*)	Bark	Infusion with 93.8% cereal alcohol, for 15 days at 4°C	*C. albicans*: 150 µg/mL	Antifungal activity confirmed in vitro	*Staphylococcus aureus* (CIM: 2 µg/mL)	Low cytotoxicity; presence of flavonoids and saponins
Jambolan (Syzygium cumini)	Sheets	Not specified in detail (laboratory use)	*Candida spp.* 500 mg/mL	Moderate growth inhibition at 250 mg/mL	Bacillus cereus (no inhibition)	Antioxidant potential; presence of flavonoids and polyphenols

Source:The authors.

A relevant factor observed was the greater efficacy of essential oils against strains of C. krusei, normally resistant to traditional antifungals. Tea tree oil, for example, showed a CFM of 0.625 µg/mL against this species, reinforcing its therapeutic potential.

Essential oils showed superiority in terms of antifungal potency and antibiofilm action, while alcoholic extracts showed greater phytochemical complexity and lower potential toxicity, and may be useful as adjuvants in therapeutic formulations.

The findings support the feasibility of using natural compounds as an alternative or complement to conventional antifungals, especially in view of the alarming increase in the resistance of Candida strains to first-line drugs, such as fluconazole and amphotericin B. This resistance compromises the efficacy of current treatments and imposes the urgent need for new therapeutic strategies.

Compounds extracted from medicinal plants such as the monoterpenes present in essential oils of Melaleuca alternifolia and Cymbopogon citratus, or the flavonoids and tannins found in alcoholic extracts of species such as Syzygium cumini and Ziziphus joazeiro have demonstrated significant antifungal activity in laboratory studies.

Table 3 - Main sources analyzed

Article Title:	Journals:	Country:	Language:	Year of publication:
Antimicrobial evaluation of the alcoholic extract of *Syzygium cumini* on *Bacillus cereus* and *Candida spp*. and biosurfactant production	(Undergraduate Monograph – Federal University of Campina Grande)	Brazil	Portuguese	2022
Antifungal activity of *Cymbopogon citratus* (DC) Stapf against yeasts of the genus *Candida spp*.	Fitos Magazine	Brazil	Portuguese	2021
Antifungal and antibiofilm activity of tea tree essential oil against candida species	Pedagogical Notebook Magazine	Brazil	Portuguese	2024
Study of the in vitro antimicrobial action of joazeiro alcoholic extract on *Candida albicans* and *Staphylococcus aureus*	Periodicals Brazil: Scientific Research	Brazil	Portuguese	2024

Source:The authors.

CONCLUSION

This study reinforces the therapeutic potential of essential oils and alcoholic extracts as natural antifungal agents against Candida spp. strains. Essential oils, especially those of Melaleuca alternifolia and Cymbopogon citratus, have shown greater antifungal potency, with low MICs and effective action against the formation of biofilms. Alcoholic extracts, such as those of Syzgium cumini and Ziziphus joazeiro, showed relevant efficacy, especially due to phytochemical complexity and lower toxicity.

Although essential oils stand out for their more direct and rapid action, alcoholic extracts have important benefits, being especially promising in combination formulations or

in prolonged use. The use of these compounds as alternative therapies or adjuvants to conventional antifungals shows promise, especially in cases of drug resistance.

Future studies should go beyond in vitro analyses, incorporating in vivo research to understand the bioavailability, metabolism and real efficacy of natural substances in the body. In addition, it is essential to conduct toxicological tests to identify possible adverse effects, establish safe doses, and avoid unwanted drug interactions.

The standardization of extraction methods is also essential, since the variation in the technique used can directly impact the concentration of bioactive compounds, compromising the reproducibility of the results and therapeutic efficacy. Recent studies highlight that the absence of standardization is one of the main barriers to the clinical translation of herbal medicines, reinforcing the need for robust protocols that ensure quality, safety, and efficacy in the development of products based on natural compounds.

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