Review article

Promising potential of the antifungal action of essential oils and its challenges: a systematic review

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SUMMARY

Introduction: Fungal infections have increased, especially in immunocompromised patients, while therapeutic options have decreased due to resistance to available antifungals. The World Health Organization (WHO) warns of the urgent need for new therapies. In this context, essential oils (EOs) have been the subject of study to find new treatments. **Objective:** A systematic review was carried out to investigate the antifungal activity of EOs according to the Cochrane Handbook guidelines (2023). The search, selection and extraction of data of interest were carried out in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) in articles selected in biomedical databases (Pubmed/Medline, Scopus, Virtual Health Library, ScienceDirect and Online Electronic Scientific Library - SciELO). The descriptors used were defined by Medical Subject Heading (MeSH) and Descriptors in Health Sciences (DeCS). **Results:** Of the 419 articles initially found, 35 were included in the review. Most studies (54.2%) were conducted in Brazil, investigating mainly aromatic plants such as lemongrass, oregano, and citronella. Although EOs have shown antifungal activity in some studies, research has revealed a lack of standardization in testing methods and a paucity of studies for certain pathogens. However, some EOs have shown significant potential against *Candida* spp., *Aspergillus* spp., and dermatophytes. **Conclusion:** There is a growing interest in investigating EOs as therapeutic alternatives against resistant fungal infections. However, more research is needed, especially to explore less studied plants to identify promising new antifungal agents.

Keywords: Volatile oil; phytochemical compounds; antifungal agent

RESUMO

Potencial promissor da ação antifúngica dos óleos essenciais e seus desafios: uma revisão sistemática

Introdução: As infecções fúngicas aumentaram, especialmente em pacientes imunocomprometidos, enquanto as opções terapêuticas diminuíram devido à resistência aos antifúngicos disponíveis. A Organização Mundial da Saúde (OMS) alerta para a necessidade urgente de novas terapias. Nesse contexto, os óleos essenciais (OEs) têm sido objeto de estudo para encontrar novos tratamentos. **Objetivo:** Foi realizada uma revisão sistemática para investigar a atividade antifúngica de OEs de acordo com as diretrizes do *Cochrane Handbook* (2023). A busca, seleção e extração dos dados de interesse foram realizadas de acordo com o *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA) em artigos selecionados em bases de dados biomédicas (Pubmed/Medline, Scopus, Biblioteca Virtual em Saúde, *Science Direct* e *Online Electronic Scientific Library* - SciELO). Os descritores utilizados foram definidos pelo *Medical Subject Heading* (MeSH) e Descritores em Ciências da Saúde (DeCS). **Resultados:** Dos 419 artigos encontrados inicialmente, 35 foram incluídos na revisão. A maioria dos estudos (54,2%) foi conduzida no Brasil, investigando principalmente plantas aromáticas, como capim-limão, orégano e citronela. Embora os OEs tenham demonstrado atividade antifúngica em alguns estudos, a pesquisa revelou uma falta de padronização nos métodos de teste e uma escassez de estudos para certos patógenos. No entanto, alguns OEs mostraram potencial significativo contra *Candida* spp., *Aspergillus* spp. e dermatófitos. **Conclusão:** Há um interesse crescente em investigar EOs como alternativas terapêuticas contra infecções fúngicas resistentes. No entanto, mais pesquisas são necessárias, especialmente para explorar plantas menos estudadas para identificar novos agentes antifúngicos promissores.

Palavras-chave: Óleo volátil; compostos fitoquímicos; agente antifúngico

RESUMEN

Potencial prometedor de la acción antifúngica de los aceites esenciales y sus desafíos: una revisión sistemática

Introducción: Las infecciones por hongos han aumentado, especialmente en pacientes inmunocomprometidos, mientras que las opciones terapéuticas han disminuido debido a la resistencia a los antifúngicos disponibles. La Organización Mundial de la Salud (OMS) advierte de la urgente necesidad de nuevas terapias. En este contexto, los aceites esenciales (AEs) han sido objeto de estudio para encontrar nuevos tratamientos. **Objetivo:** Se llevó a cabo una revisión sistemática para investigar la actividad antifúngica de los AEs según las directrices del Manual Cochrane (2023). La búsqueda, selección y extracción de datos de interés se realizaron de acuerdo con el *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA) en artículos seleccionados en bases de datos biomédicas (Pubmed/Medline, Scopus, Biblioteca Virtual em Saúde, *Science Direct* y Biblioteca Científica Electrónica en Línea - SciELO). Los descriptores utilizados fueron definidos por *Medical Subject Heading* (MeSH) y *Health Sciences Descriptors* (DeCS). **Resultados:** De los 419 artículos encontrados inicialmente, 35 fueron incluidos en la revisión. La mayoría de los estudios (54,2%) se realizaron en Brasil, investigando principalmente plantas aromáticas, como limoncillo, orégano y citronela. Aunque los AEs han demostrado actividad antifúngica en algunos estudios, las investigaciones han revelado una falta de estandarización en los métodos de prueba y una escasez de estudios para ciertos patógenos. Sin embargo, algunos AEs han mostrado un potencial significativo contra *Candida* spp., *Aspergillus* spp. y dermatofitos. **Conclusión:** Existe un interés creciente en investigar los AE como alternativas terapéuticas contra las infecciones fúngicas resistentes. Sin embargo, se necesita más investigación, especialmente para explorar plantas menos estudiadas e identificar nuevos agentes antifúngicos prometedores.

Palabras clave: Aceite volátil; compuestos fitoquímicos; agente antifúngico

1. INTRODUCTION

Antimicrobial resistance (AMR) is one of the biggest challenges of the 21st century, with an imminent risk of a lack of treatment for even minor infections [1]. In this context, the need for research aimed at finding potentially active substances, that have characteristics such as non-toxic and coming from renewable sources [2], stands out.

In this sense, the plant kingdom is considered extremely relevant and plants are an alternative, as they produce many bioactive compounds whose activity has not yet been completely clarified. Furthermore, the use of compounds derived from plants brings the advantage of resource availability, especially in Brazil [3].

It has been reported that many plants have active natural substances, exerting, for example, antimicrobial action. Among plant-derived products, essential oils (EOs) play a prominent role, with use in various industrial segments, including food and pharmaceuticals. Furthermore, they are environmentally friendly, that is, they degrade quickly in soil and water, and are low toxic to humans [4].

EOs are considered plant secondary metabolites and can be found in the leaves, flowers, stems, buds, seeds, fruits, roots, or bark of many plants [5]. The most commonly used extraction methods for EOs can be hot (steam distillation, hydro-diffusion and hydrodistillation) or cold (solvents), and their respective products can vary in their activity due to the type and stereochemistry of their molecules [4] and the extraction method used can account for the variation in its activity due to the types of molecules and their stereochemical structures [6].

According to Bilia *et al.* [7], various compounds are found in EOs, including hydrocarbons (monoterpenes, sesquiterpenes) and oxygenated ones (alcohols, ethers, esters, ketones, aldehydes, phenols, lactones, and others), which may be phenolic or terpenic. Phenols and terpenes are related to the antifungal action of EOs. The literature shows that phenolic compounds and sesquiterpenes have potential activity against fungi, with fungicidal or fungistatic activity depending on the concentration used [8,9].

The number of fungal infections has increased, particularly in immunocompromised patients, largely due to the indiscriminate use of antibiotics and greater access to therapies that alter the immune system [8-10]. Therefore, the availability of therapeutic options for the treatment of these fungal infections has been decreasing, since both yeast-like fungi, such as *Candida auris* [10], and filamentous fungi with a high level of resistance or even complete resistance to all classes of available antifungal drugs [11]. This fact led the World Health Organization [12] to publish a list that warns of resistant fungi that must be monitored and for which new therapies must be urgently sought. For example, in this list *C. auris* and *Candida albicans* are mentioned as critical priorities, the latter considered one of the main and most frequent etiological agents of fungal infections.

Therefore, it is necessary to increase knowledge about the antifungal potential of highly relevant bioactive compounds. Therefore, this work aims to report the findings of a systematic review on the antifungal potential of EOs found in the literature, which may help and encourage new research and the use of these compounds in the fight against fungal infections.

2. MATERIAL AND METHODS

2.1. Search strategy

A systematic review was conducted according to the Cochrane Handbook guidelines [13]. The research, selection, and extraction of data of interest were carried out according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [14]. Articles that aimed to investigate the antifungal activity of essential oils were searched from biomedical databases (Pubmed/Medline, Scopus, Virtual Health Library, ScienceDirect, and Online Electronic Scientific Library - SciELO). The descriptors used were defined by Medical Subject Heading (MeSH) (descriptors in English) and Descriptors in Health Sciences (DeCS) (descriptors in Portuguese and Spanish), being: ("Volatile Oils" OR "Oil, Essential" OR "Essential Oil" OR "Oils, Essential" OR "Essential Oils" OR "Volatile Oil" OR "Oil, Volatile") AND ("Agents, Antifungal" OR "Therapeutic Fungicides" OR "Fungicides, Therapeutic" OR "Antifungal Agent" OR " Agent, Antifungal" OR "Antibiotics, Antifungal" OR "Antifungal Antibiotics'). The descriptors were combined using the AND and OR symbols between them, being inserted in the search tabs of each base according to their characteristics and limitations. Limits were established for articles published in Portuguese, Spanish, and English, published until December 2023.

2.2. Eligibility criteria

The general selection criteria for studies obtained after searching previously defined databases was determined by the "PVE" strategy, as follows: "Population" – plants; "Variable": antifungal activity; "Study": studies using essential oils.

2.3. Exclusion criteria

Review articles, notes, emails, editorials, letters, works presented at scientific events, and articles that did not present original material were excluded. Furthermore, other articles were excluded based on the following criteria: (i) studies that do not identify fungi at the genus or species level; (ii) studies that did not present the minimum inhibitory concentration (MIC) for EOs. If the study complies with the inclusion criteria, but the original text is not available, the corresponding author was contacted by email up to 3 times (with an interval of 14 days between them), and the study was excluded if it was not sent after the last contact.

The selected articles were subjected to a full analytical reading to identify and extract the variables of interest: reference, study location, studied plant, origin, identification of the fungus, EO's concentration, and MIC obtained. The data were summarized in a table for subsequent critical analysis.

3. RESULTS AND DISCUSSION

In this study, a systematic review of the literature was conducted to investigate the activity of essential oils against fungi. As shown in Figure 1, 419 articles were retrieved in the initial search in the selected databases. After excluding repeated studies, 407 were screened according to the exclusion criteria. After reading the title, keywords, and summary, 332 articles were excluded and the remaining 75 continued to read the full text. At this stage, 40 articles were excluded after evaluating their agreement with the defined eligibility criteria, and the remaining 35 articles were included in this review.

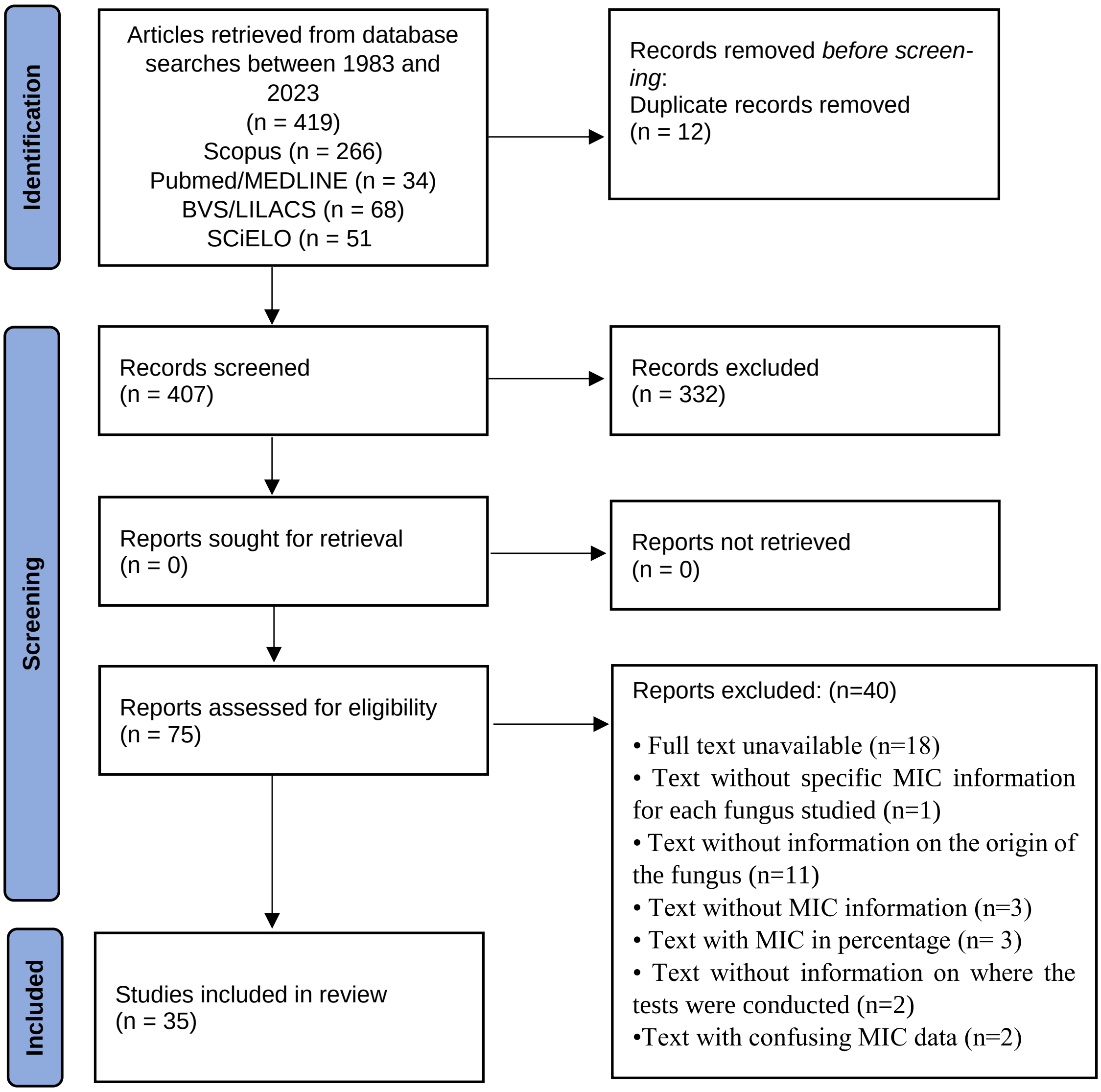

Figure 1. Flowchart of articles selected for the systematic review according to the PRISMA criteria.

Although the selection period was not limited, it was observed that only from 2005 (Table 1) were studies found that covered the topic of this review, with a greater number of publications from 2015 (21/34) onwards. As reviewed by Suleyman and Alangaden [15], fungal infections have increased, especially healthcare-associated infections (HAIs), due to the greater number of immunocompromised patients due to chronic diseases with the consequent need for organ transplants, prolonged use of therapy antibacterial and invasive medical devices. In parallel, antifungal resistance is also growing, which is an additional challenge, combined with the toxicity of the already limited therapeutic options [16]. Therefore, new strategies for the treatment of these infections have to be sought and, in this context, EOs tend to be more explored.

Table 1. Antifungal activity of essential oils extracted from different plants.

Study reference	**Study location**	**Essential oil study plant/ popular name/ basic composition according to the authors**	**Genus or species of fungus/origin**	**Essential oil activity concentration**
Lemos *et al*. [17]	Brazil	*Ocimum gratissimum*/ manjericão/ eugenol	*Cryptococcus neoformans* (clinical isolate)	CIM_{50} and CIM_{90} 250 μg/mL
Fontenelle *et al*. [18]	Brazil	*Croton nepetifolius*/ marmeleiro vermelho/ methyl eugenol and bicyclogermacrene *Croton argyrophylloides*/ marmeleiro prateado/ spatulenol and biciclogermacrene *Croton zehntneri*/ canela-brava/ methyl-chavicol and anethole	*Candida albicans* *Candida tropicalis* *Microsporum canis* (veterinary isolates)	*C. nepetifolius*: *C. albicans* and *C. tropicalis* undetected activity *M. canis* > 5000 μg/mL *C. argyrophylloides*: *C. albicans and C. tropicalis* undetected activity *M. canis* 9 - > 19 μg/mL *C. zehntneri:* *C. albicans* > 5000 μg/mL *C. tropicalis* 2500 μg/mL *M. canis* 620 – 1250 μg/mL
Cleff et *al*. [19]	Brazil	*Origanum vulgare*/ oregano/ carvacrol	*Sporothrix schenckii* (clinical isolate human and veterinary)	250 μl/mL
Souza *et al*. [20]	Brazil	*Origanum vulgare*/ orégano/carvacrol and thymol *Origanum majorana*/ marjoram and terpinen-4-ol	*Candida albicans* ATCC-7645 *Candida tropicalis* LM-14 *Cryptococcus neoformans* FGF-5 *Aspergillus flavus* LM-02 *Aspergillus fumigatus* IPP-21 *Trichophyton rubrum* ATCC-28184 *Trichophyton mentagrophytes* LM-64 *Microsporum gypseum* ATCC 184 *Microscoporum canis* LM-36 *Cladosporium herbarium* ATCC 26362 (reference strains)	*O. vulgare*: 80 μg/mL (except for *T. mentagrophytes* and *M. gypseum*) *O. majorana:* 160 μL/mL (except for *T. rubrum, M. canis, C. herbarium* and *A. fumigatus*)
Custódio *et al*. [21]	Brazil	*Pimenta pseudocaryophyllus*/ louro-cravo/ eugenol *Tynanthus micranthus*/ cipó-cravo/ eugenol	*Candida albicans* *Candida krusei* (clinical isolate)	*P. pseudocaryophylus:* 4 μL/mL *T. micranthus*: 17 μL/mL
Anaruma *et al*. [22]	Brazil	*Cymbopogon citratus*/ capim-limão/ geranial and neral	*Colletotrichum gloeosporioides* (vegetable isolate)	0.25 μg/mL

Deus *et al*. [23]	Brazil	*Copaifera multijuga*/ copaiba/ α-copaene, caryophyllene oxide and β-caryophyllene	*Aspergillus flavus* IOC-3974 *Aspergillus niger* IOC-200 *Aspergillus tamarii IOC*-186, IOC-187 *Aspergillus terreus* IOC-217 *Candida guilliermondii* IOC-2889 *Candida tropicalis* IOC-3610 *Candida parapsilosis* IOC-2882 (reference strains)	*A. flavus* 0.08 mg/mL *A. niger* 0.1 mg/mL *A. tamarii* 0.3 – 0.5 mg/mL *A. terreus* 0.3 mg/mL *C. guilliermondii* 0.1 mg/mL *C. tropicallis* 0.5 mg//mL *C. parapsilosis* 0.1 mg/mL
Castro, Lima [24]	Brazil	*Ocotea odorifera*/ canela-sassafrás/ NA *Rosmarinus officinalis*/ alecrim/ NA	*Candida albicans* ATCCs 90028, 76615, 76645, 76485,13803, LM-42V, 18F, MD-37, LM-968, ICB-12 *Candida tropicalis* ATCC-13803 and LM-708, 14, 028, 37, 13, 759. (reference strains)	*O. odorífera:* *C. albicans* 2.5 – 5.0 mg/mL *C. tropicalis* 2.5 - > 5.0 mg/mL *R. officinalis:* *C. albicans* 2.5 - > 5.0 mg/mL *C. tropicalis* ≥ 5 mg/mL
Khosravi *et al*. [25]	Iran	*Cuminum cyminum*/ cominho/ pinene, cineole and linalool *Nigella sativa*/ cominho preto/ trans-anethole and p-cymene *Ziziphora clinopodioides*/ tomilho de folha estreita/ pulegone, 1,8-cineole and limonene	*Aspergillus fumigatus* ATCC 16913 *Aspergillus flavus* ATCC 16013 (reference strains)	*C. cyminum:* *A. fumigatus* and *A. flavus* CIM_{90} 0.25 – 1.5 mg/mL *N. sativa:* *A. fumigatus* CIM_{90} 1.5 mg/mL *A. flavus* CIM_{90} 1.5 – 2.0 mg/mL *Z. clinopodioides:* *A. fumigatus* CIM_{90} 0.5 – 1.5 mg/mL *A. flavus* CIM_{90} 1.5 mg/mL
Pereira *et al*. [26]	Brazil	*Cymbopogon winterianus*/ citronella de java/ citronellal and geraniol	*Trichophyton rubrum* (clinical isolate)	CIM_{50} 312 μg/mL
Oliveira *et al*. [27]	Brazil	*Cymbopogon winterianus*/ citronella de java/ citronellal and geraniol	*Candida albicans* ATCCs: 76485, ATCC 76615, ATCC 13803, LMV 42, ICB 12, M101, LM 968, LM 68, LM 16, LM 018, LM 023, LM 601, LM 290, LM 052, LM 087 (reference strains)	78 – 625 μg/mL
Tadić *et al*. [28]	Serbia	*Sideritis scardica*/ chá grego da montanha/ hexadecanoic acid, myristicin, menthol, caryophyllene oxide and τ-muurolol	*C. albicans* (clinical isolate)	2.560 μg/mL
Vizcaya *et al*. [29]	Venezuela	*Vismia baccifera* subsp. dealbata/ caryophyllene oxide and β-caryophyllene	*C. albicans* ATCC 90028 *C. glabrata* ATCC 90030 *C. tropicalis* ATCC 50658 *C. krusei* ATCC 6258 *Candida parapsilosis* ATCC 22019 (reference strains) *Cryptococcus neoformans* (clinical isolate)	*C. albicans, C. tropicalis, C. parapsilosis, C. neoformans* 1000 μg/mL *C. glabrata* 200 μg/mL *C. krusei* 160 μg/mL

Aguiar *et al*. [30]	Brazil	*Cymbopogon nardus*/ ci-tronela/ citronellal *Corymbia citriodora*/ euca-lipto-limão/ citronellal	*Aspergillus* spp. *Pyricularia grisea* *Colletotrichum musae* (isolated from plants and fruits)	*C. nardus*: *Aspergillus* spp. – 100 ppm *P. grisea* – 100 ppm *C. musae* – 50 ppm *C. citriodora:* *Aspergillus* spp. – 200 ppm *P. grisea* – 200 ppm *C. musae* – 50 ppm
Bogavac *et al*. [31]	Serbia	*Coriandrum sativum*/ co-entro/ linalyl acetate and linalol *Thymus vulgaris*/tomilho/ thymol	*Candida albicans* (clinical isolate) *Candida albicans* ATCC 10231 (reference strains)	*C. sativum:* *C. albicans* 0.11 - > 0.45 µl/mL *C. albicans* 10231 > 0.45 µl/mL *T. vulgaris:* *C. albicans* and *C. albicans* 10231 0.11 µl/mL
Costa *et al*. [32]	Brazil	*Ocimum selloi*/ alfavaca-anis/ methyl chavicol	*Alternaria alternata* CML 184 *Colletotrichum gloeosporioides* CML 459 *Moniliophthora perniciosa* CEPLAC 1188 (reference strains)	*A. alternata, C. gloeosporioides* > 1000 ppm *M. perniciosa* 250-500 ppm
Nasci-mento *et al*. [33]	Brazil	*Piper arboreum*/ pa-riparoba/ curcumene, cis-cadin-4-en-7-ol and germacrene	*Microsporum gypseum* URM6199 *Epidermophyton floccosum* URM 3182 (reference strains)	*M. gypseum* 156.25 µg/mL *E. floccosum* 62.5 µg/mL
Brito *et al*. [34]	Brazil	*Lippia sidoides*/ alecrim pimenta/ thymol	*Candida albicans* LM 62 *Candida tropicalis* LM 20 *Candida krusei* LMBM 01 and LMBM 02. (reference strains)	*C. krusei* 01 – 128 µg/mL *C. albicans* 62 – 256 µg/mL *C. tropicalis* 20 – 128 µg/mL
Baptista *et al*. [35]	Brazil	*Eucalyptus smithii*/ euca-lipto/ α-pinene, ϱ-cy-mene, 1,8-cineole, linal-ool, terpinen-4-ol and α-terpineol	*Microsporum canis* ATCC 32903 *Microsporum gypseum* ATCC 14683 *Trichophyton mentagrophytes* ATCC 9533 *T. mentagrophytes* ATCC 11481 *Trichophyton rubrum* CCT 5507 (reference strains)	*M. canis* ATCC32903 500 µg/mL *M. gypseum* ATCC 14683 1000 µg/mL *T. mentagrophytes* ATCC 9533 250 µg/mL *T. mentagrophytes* ATCC 11481 125 µg/mL *T. rubrum* CCT 5507 62.5 µg/mL

Houël *et al*. [36]	French Guiana	*Achetaria guianensis*/ NA *Cymbopogon citratus*/ capim-limão/ geranial and neral *Mikania micrantha*/ cipó-amargo/NA *Otacanthus azureus*/ erva copaíba/ β-copaen-4-α-ol, α-humulene, α-copaene, myrtenal, viridiflorol and trans-pinocarveol *Piper hispidum*/ falso jaborandi/ curzerene, furanosesquiterpenes and β-caryophyllene *Protium heptaphyllum*/ amescla/ limonene, α-pinene, β-pinene, p-cymene, trans-carveol, β-myrcene and carvone *Vouacapoua americana*/ NA *Andira aubletii*/ acapu/ NA	*Trichophyton mentagrophytes* LMGO 1931 *Microsporum gypseum* LMGO 10 *Microsporum canis* LMGO 22 (reference strains)	*Microsporum gypseum:* > 500 µg/mL *Achetaria guianensis* 16 µg/mL *Cymbopogon citratus* 250 µg/mL *Mikania micrantha* 16 µg/mL *Otacanthus azureus* 125 µg/mL *Piper hispidum* 62 µg/mL *Protium heptaphyllum*, *Vouacapoua Americana*, and *Microsporum canis* > 500 µg/mL *Achetaria guianensis* 62 µg/mL *Cymbopogon citratus* > 500 µg/mL *Mikania micrantha* 125 µg/mL *Otacanthus azureus* 500 µg/mL *Piper hispidum* 62 µg/mL *Protium heptaphyllum* 500 µg/mL *Vouacapoua americana* *Trichophyton mentagrophytes:* > 500 µg/mL *Achetaria guianensis* 8 µg/mL *Cymbopogon citratus* 125 µg/mL *Mikania micrantha* > 8 µg/mL *Otacanthus azureus* 62 µg/mL *Piper hispidum* 31 µg/mL *Protium heptaphyllum* 62 µg/mL *Vouacapoua Americana*
Pinheiro *et al*., [37]	Brazil	*Laurus nobilis*/ louro/ isoeugenol, myrcene, chavicol and methyl eugenol	*Cryptococcus neoformans* FCF10, LM, 0109, LM 310, LM 2601, LM 2301, LM1909 and LM 0310 (reference strains)	256 µg/mL
Cavalcanti *et al*. [38]	Brazil	*Mentha arvensis*/ hortelã japonesa/ NA *Pimpinella anisum*/ anis verde/ NA *Eucalyptus citriodora*/eucalipto limão/ NA *Cymbopogon winterianus*/java citronela/ NA	*Candida albicans* ATCC 289065 *Candida krusei* ATCC 40042 *Candida tropicalis* ATCC40147 (reference strains)	*C. albicans:* 1.25 µg/mL *M. arvensis* and *E. citriodora* 5 µg/mL *P. anisum* 625 µg/mL *C. winterianus* *C. krusei:* 2.5 µg/mL *M. arvensis* and *C. winterianus* 5 µg/mL *P. anisum* and *E. citriodora* *C. tropicalis:* 2.5 µg/mL *M. arvensis* and *E. citriodora* 10 µg/mL *P. anisum* 1.25 µg/mL *C. winterianus*
Bukvicki *et al*. [39]	Serbia	*Thymus algeriensis*/ maralina do campo/ carvacrol	*Aspergillius fumigatus* (clinical isolate) *Penicillium aurantiogriseum.* (isolated from food) *Aspergillius versicolor* ATCC 11730, *Aspergillius ochraceus* ATCC12066, *Aspergilius niger* ATCC 6275, *Trichoderma viride* IAM 5061, *Penicillium funiculosum* ATCC 36839, *Penicillium ochrochloron* ATCC 9112. (reference strains)	*A. fumigatus, A. ochraceus, A. niger, T. viride, P. funiculosum, P. ochrochloron* 0.01 mg/mL *A. versicolor* 0.04 mg/mL *P. aurantiogriseum* 0.02 mg/mL

Gadban *et al*. [40]	Argentina	*Tagetes filifolia*/ cravinho da serra/ anethole	*Colletotrichum truncatum* *Trichoderma harzianum* (isolated from grains and soil)	*C. truncatum* 4000 µl/L *T. harzianum* 7400 µl/L
Hosseini *et al*. [41]	Iran	*Allium sativum*/alho/allyl trisulfide, diallyl disulfide and diallyl sulfide *Rosmarinus officinalis*/ alecrim/ α-pinene, bornyl acetate, camphor and 1,8-cineole	*Colletotrichum nymphaeae* CCTUCCh32 (reference strains)	*A. sativum* CIM_{50}: 3.74 -10.10 µL/L *R. officinalis* CIM_{50}: 43.77 -75.49 µL/L
Elgat *et al*. [42]	Egypt	*Citrus aurantium*/ laranja da terra/ linalyl acetate, α-terpineol, linalool, neryl acetate, geranyl acetate and caryophyllene *Eucalyptus camaldulensis*/ eucalipto vermelho/ inalool and 1,8-cineole *Citrus sinensis* /laranjeira/limonene	*Aspergillus flavus* AFI375 *Aspergillus niger* FC24771 *Aspergillus terreus* V0103 *Fusarium culmorum* CBS128,537. (reference strains)	*C. aurantium:* *A. flavus* 25 µL/mL *A. niger* 8 µL/mL *A. terreus, F. culmorum* 12 µL/mL *E. camaldulensis:* *A. flavus* 12 µL/mL *A. niger* 7 µL/mL *A. terreus* 10 µL/mL *F. culmorum* 8 µL/mL *C. sinensis:* *A. flavus* 12 µL/mL *A. niger, A. terreus, F. culmorum* 6 µL/mL
Abdullahi *et al*. [43]	Malasia	*Zingiber officinale*/ gengibre/isoeugenol	*Fusarium oxysporum* *Pyricularia oryzae* *Colletotrichum falcatum* *Ganoderma boninense* *Rigidoporus microporus* (isolated from plants)	1 µL/mL
Sobrinho *et al*. [44]	Brazil	*Vernonia chalybaea*/ cambarazinho-roxo/ β-caryophyllene	*Trichophyton rubrum* LABMIC 0201; LABMIC 0202; LABMIC 0203 and LABMIC 0204. (reference strains)	1,25 mg/mL
Oliveira *et al*. [45]	Brazil	*Lippia gracilis*/ alecrim-selvagem/ carvacrol and thymol	*Fusarium oxysporum* URM6704 *Fusarium solani* URM6749 *Colletotrichum gloeosporioides* URM6176 Colletotrichum lindemuthianum URM5771. (reference strains)	*F. oxysporum, F. solani* 0.625 mg/mL *C. gloeosporioides*, *C. lindemuthianum* 0.31 mg/mL
Pusceddu *et al*. [46]	Italy	*Thymus capitatus*/ tomilho de creta/ carvacrol *Thymus herba-barona*/ tomilho-alcarávia/carvacrol *Cinnamomun zeylanicum*/ canela da índia/ e-cinnamaldehyde	*Ascosphaera apis* 3136 (reference strains)	*T. capitatus*, *T. herba-borona* 100 µg/mL *C. zeylanicum* 200 µg/mL

Marinas *et al*. [47]	Romania	*Amorpha fruticosa*/ falso indigo/ linalool, citronellol, β -caryophyllene, caryophyllene oxide, α- and γ -muurolene, germacrene D, δ - cadinene and τ -cadinol	*Candida famata* *Candida albicans*, *Candida utilis* (clinical isolate) *Candida famata* CMGBy.14 *Candida albicans* ATCC 101103 (reference strains)	*C. famata* 945 – 14.75 mg/mL *C. albicans* 393 – 7.38 mg/mL *C. utilis* 15 – >29.50 mg/mL C. famata CMGBy.14 > 29.50 mg/mL *C. albicans* ATCC 101103 7.38 mg/mL
Tripathi, Yami, Shukla [5]	India	*Ageratum conyzoides*/ erva de são joão/alkaloids, coumarins, flavonoids, chromenes, benzofurans, sterols and terpenoids *Lantana camara* /cambará/alkaloids, phenolics, terpenoids, phytosterols, tannins and saponins *Litsea cubeba* /pimenta chinesa/ citral *Piper mullesua*/ NA	*Alternaria alternata* MTCC 149 *Mucor haemilis* MTCC 157 *Helminthosporium solani* MTCC 1899 *Humicola grisea* MTCC 352 *Botrytis cinerea* MTCC 359. (reference strains)	*A. conyzoides:* *A. alternata* 500 ppm *H. solani* 300 ppm *M. haemilis, H. grisea, B. cinerea* 400 ppm *L. camara:* *A. alternata* 200 ppm *M. haemilis, H. solani* 300 ppm *H. grisea, B. cinerea* 400 ppm *L. cubeba:* *A. alternata, H. grisea* 300 ppm *M. haemilis* 400 ppm *H. solani, B. cinerea* 200 ppm *P. mullesua:* *A. alternata, H. grisea* 400 ppm *M. haemilis* 200 ppm *H. solani, B. cinerea* 300 ppm
Vuko *et al*. [3]	Croatia	*Dittrichia viscosa*/ tádega/ 1,8-cineole and caryophyllene oxide	*Candida albicans* ATCC 90029 *Aspergillius niger* food isolate	*C. albicans* CIM_{50}: 2.8 mg/mL *A. niger* CIM_{50}: 0.09 mg/mL
Cibanal *et al*. [48]	Argentina	*Origanum vulgare*/ oregano/ carvacrol and thymol	*Penicillium allii*/ vegetable isolate	1,5 μL/mL
Valková *et al*. [4]	Slovakia	*Cymbopogon citratus*/ capim-limão/ citral, geraniol and 1,8-cineole	*Candida albicans* CCM 8261, *Candida krusei* CCM 8271, *Candida glabrata* CCM 8270 *Candida tropicalis* CCM 8223 (reference strains)	*C. albicans* CIM_{50}: 212.35 μL/mL *C. krusei* CIM_{50}: 196.18 μL/mL *C. glabrata* CIM_{50}: 205.26 μL/mL *C. tropicalis* CIM_{50}: 208.34 μL/Ml

Of the 35 articles included (Table 1), 19 (54.2%) are from Brazilian studies, three from Argentina, and one from French Guiana, which suggests a superiority of interest in the antifungal activity of EOs in the Americas, but also marked in several parts of the world [49].

Of the EOs analyzed for their antifungal activity, it was noted that most studies focused on aromatic plants, with emphasis on herbs and spices. The genera *Eucaliptus, Origanum, Piper* and *Cymbopogon* stand out, the latter being the most discussed and referenced in studies from Brazil (five), Slovakia and French Guiana. In fact, according to Butzge *et al.* [50] this genus stands out, with the species *Cymbopogon citratus* (lemongrass) and *Cymbopogon winterianus* (citronella) related to various biological activities, including antifungal.

Regarding the fungi included in the research, the majority were reference strains, but human, veterinary, and plant isolates were also included. However, it was observed that five articles included both the reference strain and the isolates above. The use of a reference strain has the advantage of providing a complete phenotypic description of the species, favoring the selection of the microorganism based on the hypothesis of biological activity. However, the inclusion of microorganisms of human, veterinary, and environmental origin microorganisms can promote differences in results considering the adaptation attributes that they are using [51].

Of the yeast-like fungi, *Candida spp* and *Cryptococcus neoformans* were included in 16/35 articles, and among the filamentous fungi, dermatophytes (*Trichophyton* spp., *Epidermophyton floccosum*, and *Microscoporum* spp.) and *Aspergillus* spp. Most of the work carried out in Brazil was also explored (Table 1). These fungi, in addition to *Fusarium* spp. and other agents of opportunistic mycoses (*Penicillium* spp., *Alternaria alternata*, *Mucor haemilis*, among others) are extremely important in the human clinic, especially in cases of invasive infections facilitated by numerous risk factors related to the patient's clinical history [15].

Interestingly, considering the wide distribution of the disease caused by it among humans and animals, especially the increase in cases in southern Brazil [52], only one study [19] investigated the activity of OE on *Sporothrix schenckii*. Furthermore, the report of resistance of this fungus to itraconazole, one of the first treatment options for the infection [53], indicates a gap in the investigation of the antifungal activity of EOs against this pathogen. In this review, it was noted that only the EO of *Origanum vulgare* (oregano) was studied for this purpose.

The EOs for which antifungal action was investigated originated from different plants and it was observed that there is no standardization regarding the concentration unit of the EO to be tested, which makes analysis and categorization as good or bad antifungal activity difficult also references in literature are not found for all units.

However, in most studies (21/35), concentration units in μg/mL (12/35) or mg/mL (9/35) were adopted, allowing a more precise analysis of the results. This is because Kuete [54] classified biocompounds based on their antimicrobial activity as significant (MIC < 100 μg/mL), moderate (100 < MIC ≤ 625 μg/mL), or weak (MIC > 625 μg/mL), while Mbaveng *et al.* [55] considered a MIC below 10 μg/mL to be significant, moderate between 10 and 100 μg/mL, and low when greater than 100 μg/mL.

Thus, considering the articles subject to analysis based on these references, it was observed that only 12 (34.2%) studies were able to demonstrate significant antifungal activity according to the categorization of Kuete [54]. Considering a study carried out by Mbaveng *et al*. [55], which we will use for analysis in this review, the scenario of potential antifungal candidates is more drastic with only five (14.2%) articles included, three of which are articles from Brazil [18, 34, 36, 38, 39]. In these studies, antifungal activity was identified in EOs from plants commonly found in Brazil (*C. citratus, L. medoides* Cham, *C. winterianus, E. citriodora* and *M. arvensis*), against fungi of great clinical relevance, including *C. albicans, C. krusei, C. tropicalis*, *A. fumigatus, A. niger*, in addition to the dermatophytes *M. canis* and *T. mentagrophytes* (Table 1). These results highlight Brazil's potential in researching new bioactive compounds with antifungal properties.

Moderate activity (MIC 10 - 100 μg/mL) [55] was attributed to EOs in nine (25.7%) articles [18, 20, 23, 27, 34-36, 39, 46]. In these studies, emphasis is placed on the activity of OE from oregano, lemongrass, copaiba, and citronella against *Candida* spp and *Aspergillus* spp. (Table 1), which despite the "moderate" classification could be explored for use in association with other compounds after investigating synergism between them, a strategy supported by Cordisco *et al*. [56].

Interestingly, some authors have shown an absolute lack of EO activity against filamentous and yeast-like fungi [18, 24, 25, 28, 30, 47] reporting that concentrations of EOs ≥ 2,000 μg/mL from plants with some known antimicrobial activity, including rosemary, lemon eucalyptus, and cumin, under the conditions used in the studies cited, do not have antifungal action.

Five studies (14.3%) determined the MIC_{50} or MIC_{90}, which are not considered ideal parameters for antimicrobial evaluation by Kuete [54] considering the possible heterogeneity of the population included. Even so, all studies found high MIC values, that is, with moderate or low antifungal activity of EOs, extracted from plants with reports of antimicrobial activity, such as *Cymbopogon* spp., *O. gratissimum*, and *C. cyminum*. Also, these studies included both clinical isolates and reference strains, which suggests that regardless of the origin of the fungus, the antifungal activity of these EOs is not even significant.

Furthermore, two studies also investigated the antifungal action of compounds in ppm concentration, but when converting the results into μg/mL it was observed that the EOs of the plants studied (Table 1) showed good antifungal activity, varying, for example, from 0.2 – 0.5 μg/mL [5]. Completing the relevance of these findings, it should be mentioned that the action was demonstrated against *B. cinerea* and *A. alternata*, important phytopathogens [57], the latter being related to the worsening of respiratory diseases in humans [58].

It should be noted that, although most authors consider that there is a basic component in the EO that could be related to the antifungal action (Table 1), even when the same EO is studied by more than one author, it was not possible to make inferences about the antifungal action and the composition of the EO. This is because the fungal agents included in the studies were very diverse in terms of type (yeast-like and filamentous) and origin (reference species and human, animal or plant isolates), making it impossible to compare the antifungal activity obtained without bias.

This review has some limitations due to the non-uniformity of the studies, especially related to the terroir of the plants originating from the EOs, the extraction methods, and the experimental conditions, especially the concentrations studied. It is known that as essential oil is a secondary metabolite of plants, this variation in antimicrobial potential is expected. However different studies show antifungal activity at low concentrations, while others show no activity at high concentrations of the same plant. Therefore, different factors may be associated with this variation, such as the MIC assessment methods used, the use of standard and correct protocols, and the microorganisms used, among others. However, the data from this work indicate that different OEs are promising antifungals and that, due to the high content of different phytochemical compounds in the composition of the same oil, fungal resistance is less likely. Therefore, given the context of fungi resistance to available drugs, more research must be conducted to establish the best concentrations, essential oils, and the resistance mechanism of these fungi.

4. CONCLUSION

Based on the analysis of the reviewed articles, we can conclude that there is a growing interest in investigating the antifungal activity of EOs against fungal pathogens, especially those resistant to conventional treatments. However, there is a significant gap in research related to the evaluation of EOs against certain fungi, as demonstrated by the scarcity of studies specific to certain pathogens. This gap highlights the need for future research to explore the potential of EOs as effective therapeutic alternatives against resistant fungal infections. Furthermore, these investigations must consider a wide range of essential oils, including those derived from less explored plants, to identify promising new antifungal agents.

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