

Antifungal essential oils in dental practice

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ABSTRACT

Introduction: The World Health Organization (WHO) has recently included fungi in the list of priority pathogens. The pathogenic yeast C. albicans is responsible for candidiasis in the mouth, throat and esophagus due to its high antifungal resistance and responsible for the number of deaths. In recent years there has been a considerable increase in interest in the practice of phytotherapy, mainly due to the emergence of new fungal strains resistant to antifungals. Herbal compounds have been used in medicine and dentistry for centuries. A classic example is the use of clove oil to treat tooth decay, and eugenol, its main active ingredient, is still used today in daily dental practice. They have been widely studied for their therapeutic grade, for biological and pharmacological tests and for their chemical constituents. Objective: In this integrative review study, the effects of essential oils, their potential benefits for use and their constituents on fungal micromorphology will be evaluated regarding their biological properties in the context of oral health care, helping to expand the knowledge of their mechanisms of action, in addition to provide an overview of the current literature. Methodology: Two indexed search databases Lilac and Pubmed were consulted in March 2024. The words "DENTISTRY" AND "VOLATILE OILS" and "antifungal" and Boolean AND were used, and 11 articles were found that were analyzed. Inclusion criteria: be in agreement with the proposed theme, in the free articles version. Exclusion criteria: not agreeing with the proposed theme. Results: The resident microbiota of the mouth is quite diverse, eight species of the genus Candida were considered pathogenic, and Candida tropicalis and Candida krusei, are associated with the pathological process, especially to promote the formation of biofilms and increase drug resistance. The herbal medicines used for the treatment of oral diseases in the studies showed antifungal activity and can also be used as an antiseptic. Conclusion: According to the literature reviewed, many plants and their chemical compounds have antifungal action. Scientific studies prove the effectiveness of essential oils, considered an herbal medicine and its advantages in relation to allopathic medicines used in Dentistry and are considered promising agents for the development of new bioproducts applicable in the clinical routine.

Keywords: Dentistry, Volatile oils, Antifungal.

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INTRODUCTION

The World Health Organization (WHO) recently included fungi on the list of priority pathogens. The pathogenic yeast *C. albicans is* responsible for candidiasis in the mouth, throat and esophagus due to its high antifungal resistance and responsible for the number of deaths (1).

In addition, it can cause superficial and systemic infections in individuals when mucosal barriers are broken or when the immune system is compromised (2), inducing the development of a spectrum of pathologies, compromising the quality of life and survival time of patients. (3)

Both in medicine and dentistry, herbal compounds have been used for centuries and in recent years there has been a considerable increase in interest in this practice, mainly due to the appearance of new fungal strains resistant to antifungals. (1) (4)

A classic example in dentistry of an herbal medicine is the use of clove oil to treat dental caries, common since the sixteenth century and eugenol, its main active ingredient is still used today. (1) (4)

The eugenol mentioned belongs to a class called terpene, which is a natural carbonic compound, and more than 30,000 types of terpenes have been described in the literature. Monoterpenes, belonging to a class of terpenes, can be found in plants such as true lavender (*Lavandula angustifolia*) or basil (*Ocimum basilicum*). Currently, we can find more than 1,500 documented monoterpenes with various biological and therapeutic properties. (1)

All of these compounds are hydrocarbons and with their oxygenated derivatives can exist in the form of various chemical classes, including aldehydes, ketones, alcohols, oxides, esters, amines, amides, phenols, nitrogen and sulfur compounds, and heterocycles (5)

Thus, essential oils (EO) have been widely studied for their therapeutic grade, biological and pharmacological tests, and for their chemical constituents. These have generated potential results highlighting antimicrobial, anti-inflammatory, antitumor, antioxidant and other activities. (4) (5)

The objective of this study was to evaluate the effects of essential oils, the potential benefits of their use and their constituents in fungal micromorphology regarding their biological properties in the context of oral health care, helping to expand the knowledge of their mechanisms of action, in addition to providing an overview of the current literature.

MATERIAL AND METHOD

Two indexed search databases, Lilac and Pubmed, were consulted in March 2024, analyzing the last five years. The words "DENTISTRY", "VOLATILE OILS", "ANTIFUNGAL" and Boolean AND were used, and eleven articles were found. Inclusion criteria: be in agreement with the proposed theme, in the free version of articles. Exclusion criteria: not agreeing with the proposed theme.



We found 11 articles that were read the abstracts and, when necessary, their entirety, which occurred 5 times due to the length of the subject.

RESULT AND DISCUSSION

In this article, we analyze the biological properties, practical use and applications of essential oils in the care of recurrent fungal pathologies in the dental environment in the context of oral health care in order to expand knowledge about natural substances that may eventually help in daily practice.

According to table 1, the articles can be analyzed according to their descriptions: author, year, study, objective, methodology, and conclusion.

AUTHOR	YEAR	STUDY	MAGAZINE	OBJECTIVE	METHODOLOGY	RESULT
Potocka W,	2023	Current and	Vol. 28,	This narrative	The review was	Monoterpe
Assy Z,		Potential	Molecules.	literature review	carried out using the	nes have
Bikker FJ,		Applications of	Multidisciplina	provides an overview	PubMed, Web and	been
Laine ML		Monoterpenes	ry Digital	of the biological	Science, Scopus and	shown to
		and Their	Publishing	properties and current	Google Scholar until	have
		Derivatives in	Institute	and potential	August 2023.	antifungal,
		Oral Health	(MDPI)	applications of selected	They used keywords	antiviral,
				Monoterpenes and	related to	and anti-
				their derivatives in oral	(monoterpene),	inflammato
				health.	(monoterpenes),	ry
					(monoterpenoid),	properties,
					(monoterpenoids),	making
					(volatile compound),	them
					(volatile oil) E	versatile
					(antimicrobial),	for various
					(antiseptic),	application
					(antibacterial),	S
					(antiviral),	demonstrat
					(antifungal),	ing
					(anticancer), (anti-	promising
					inflammatory),	potential
					(analgesic),	for
					(antinociceptive),	application
					(oral hygiene), (oral	s in future
					health), (oral),	research.
					(mouth), (halitosis),	
					(dentistry),	
					(dentistry),	
					(dentistry),	
					(dentistry),	
					(dental treatment),	
					(periodontal	
					diseases),	
					(periodontitis),	
					(gingivitis), (mucosal	
					lesions),	
					(dry mouth),	
					(xerostomia), (saliva),	
					(salivary flow),	
					(salivation),	

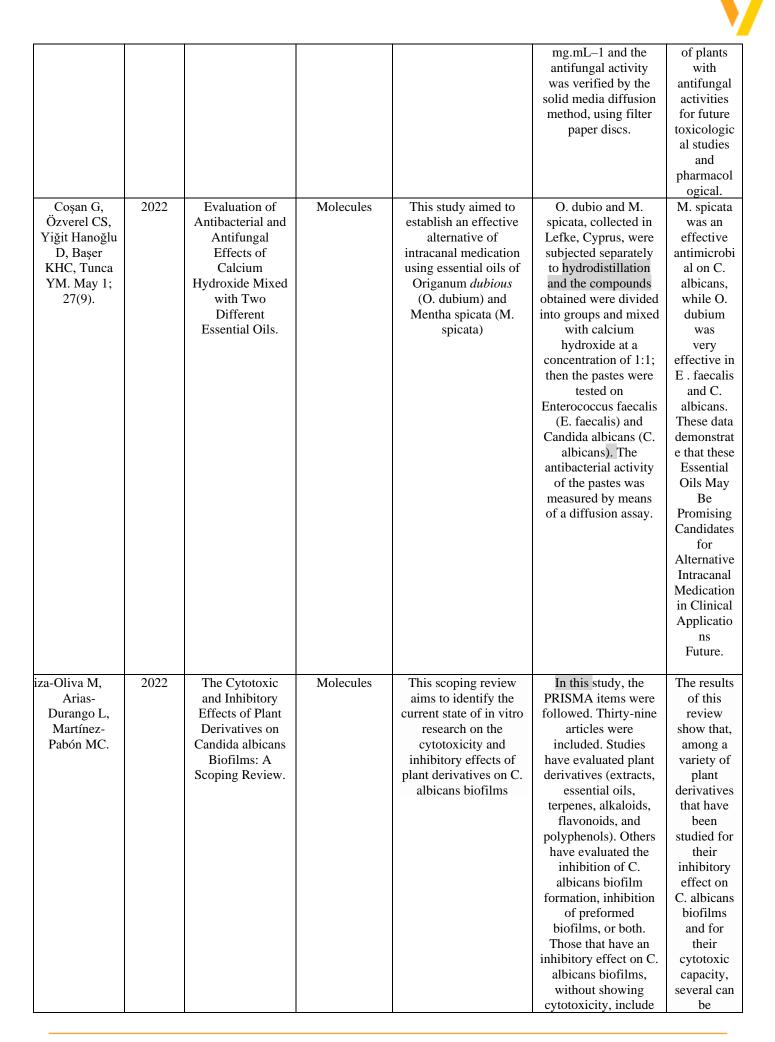
Table 1. Summary of the articles of the review -São Paulo - 2023

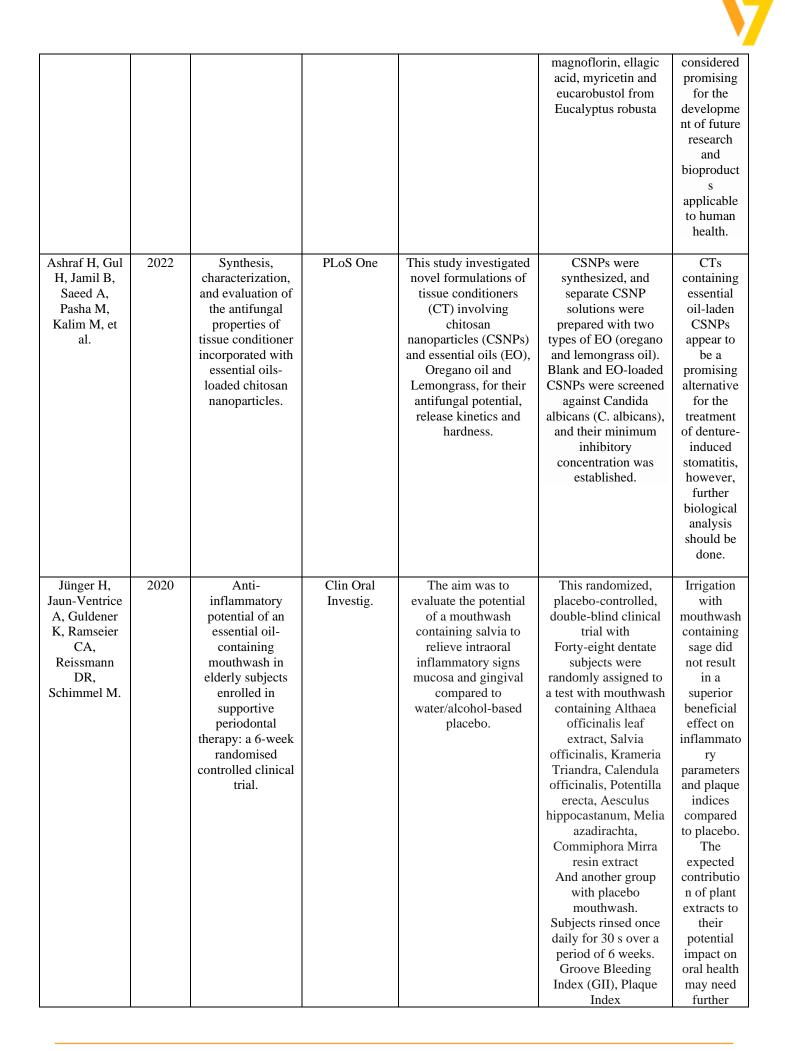


					(hyposalivation), (lateral effects), (allergy)(allergic reaction), (toxicity), (toxic).	
Marie-Pier Veilleux and Daniel Grenier	2019	Determination of the effects of cinnamon bark fractions on Candida albicans and oral 4pitelial cells.	BMC Complement Altern Med.	Cinnulin PF® did not reduce the growth of C. albicans, cinnamon bark oil exhibited high antifungal content and activity with minimum inhibitory concentrations and minimum fungicides in the range of 0.039 to 0.078%. Cinnamon oil was active against a preformed biofilm of C. albicans and Cinnulin PF® prevented biofilm formation and attenuated its adhesion to oral epithelial cells. The efficacy of cinnamon oil and Cinnulin PF® did not show significant cytotoxicity against oral epithelial cells	A microplate dilution assay was used to determine cytotoxicity to oral epithelial cells through cellular metabolic activity. The integrity of the tight junctions of gingival keratinocytes was evaluated by determining the transepithelial electrical resistance. TNFα-stimulated IL-6 and IL-8 secretion from epithelial cells were quantified by ELISA.	For its ability to attenuate the growth, biofilm formation and adhesion property of C. albicans, to reinforce the function of epithelial barrier, and to exert anti- inflammato ry properties the two fractions of cinnamon (essential oil, Cinnulin PF) ® investigate d in the present study may be promising agents for the treatment of oral infections involving C. albicans.
CID-Chevesic C, Meller- Sepulveda A, Zara Ja, López-Muoz R, Children's R, Budini M, et al.	2022	Origanum vulgare L. essential oil inhibits virulence patterns of Candida spp. and potentiates the effects of fluconazole and nystatin in vitro.	BMC Complement Med Ther	The antivirulence effect of Origanum vulgare L. (O-EO) essential oil against Candida spp. was evaluated.	The effect of O-OE was evaluated on ATCC reference strains of C. albicans and non-albicans Candida on biofilm proliferation. in 24 wells .The minimum inhibitory concentration (MIC) was determined by the broth microdilution assay	This study demonstrat es that o- EO interacted synergistic ally with fluconazol e and nystatin. Itsuse may be considered

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					and the adhesion to microplates by the crystal violet (CV) assay.	to improve antifungal treatment against Candida spp.
Trindade LA, Cordeiro LV, de Figuerêdo Silva D, Figueiredo PTR, de Pontes MLC, de Oliveira Lima E, et al.	2022	The antifungal and antibiofilm activity of Cymbopogon nardus essential oil and citronellal on clinical strains of Candida albicans.	Brazilian Journal of Microbiology.	He investigated the antifungal and antibiofilm activity of Cymbopogon essential oil (EO) in association with miconazole and chlorhexidine in clinical strains of Candida albicans. They analyzed the mechanism of action of C. nardus EO and citronellal subsequently.	The antifungal activity (MIC/MFC) and antibiofilm effects of <i>C. nardus</i> EO and citronellal were determined by the microdilution method, and their mechanism(s) of action by sorbitol and ergosterol assays. They were also tested for possible association with standard drugs using the checkered technique. Miconazole and chlorhexidine were the positive controls and the assays were performed in triplicate.	<i>C. nardus</i> EO and citronellal showed strong antifungal and antibiofilm activities against C. albicans
de Sousa DP, Damasceno ROS, Amorati R, Elshabrawy HA, de Castro RD, Bezerra DP, et al.	2023	Essential Oils: Chemistry and Pharmacological Activities	Vol. 13, Biomolecules. Multidisciplina ry Digital Publishing Institute	This review presents the main mechanisms of pharmacological action of essential oils and their components in various biological systems, the relationship between chemical aspects and the bioactivity of these products.Antioxidant, anti-inflammatory, antitumor, and antimicrobial (antiviral, antifungal) activities are discussed.	The search was performed in PubMed/MEDLINE, and the studies were selected according to its relevance and the objectives of this review. The terms used were: "anti-inflammatory"; "antioxidant"; "cancer"; "chemistry of essential oils"; "tumo(u)r"; "antibacterial"; "essential oils"; "antifungal"; "antifungal"; "antimicrobials"; "antiviral". The search was restricted to English and experimental studies.	The multiplicit y of pharmacol ogical properties of oils occurs due to the chemical diversity in their compositio n and their ability to interfere with biological processes at the cellular and multicellul ar level via interaction with various biological targets. These natural products

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de Morais MC, Perez- Castillo Y, Silva VR, de Souza Santos L, Soares MBP, Bezerra DP, et al	2021	Cytotoxic and antifungal amides derived from ferulic acid: Molecular docking and mechanism of action	Biomed Res Int.	A series of ten amides was obtained by coupling reactions using the reagents (benzotriazole-1- yloxy) tripyrrolidinophosphon ium hexafluorophosphate (PyBOP) and N,N'- dicyclohexylcarbodiim ide (DCC). All Compounds were identified based on their IR, 1H-MRI and 13C, HRMS data and yields ranging from 43.17% to 91.37%. The compounds were submitted to cytotoxic tests by the alamar blue technique and antifungal screening by broth microdilution method for determination of minimum inhibitory concentration (MIC).	Amides 10 and 11 exhibited the best result in both biological evaluations, with compound 10 being the most potent and selective in HL-60 cancer cells, with no cytotoxicity in healthy cells. This amide had antifungal activity in all strains and had the lowest MIC against Candida albicans and Candida tropicalis.	could be a promising source for the developme nt of new drugs. The present study demonstrat ed that compounds 10 and 11 can be used as a basis for drug developme nt in the future.
Oliveira De Alencar Menezes T, Braga AC, Alves A, Maria J, Vieira S, Fernandes De Menezes SA, et al.	2009	In vitro evaluation of the antifungal activity of essential oils and extracts of plants from the Amazon region on Candida albicans strain	Rev Odontol UNESP.	The objective of this study was to evaluate in vitro the antifungal activity of oils and extracts extracted from plants in the Amazon region and determine the minimum inhibitory concentration of the species that showed antifungal activity against the standard strain of <i>Candida albicans</i>	The antifungal activity of <i>Copaifera</i> <i>multijuga</i> , <i>Carapa</i> <i>essential oils</i> <i>Guyanese</i> , <i>Piper</i> <i>aduncum</i> and <i>Piper</i> <i>hispidinervum</i> were evaluated by the diffusion method in solid in dilutions of 32 to 2% to determine the minimum inhibitory concentration. Extracts of <i>Annona glabra</i> , <i>Azadiractha indica</i> , <i>Bryophyllum</i> <i>calycinum</i> , <i>Eleutherine plicata</i> , <i>Mammea americana</i> , <i>Psidium guajava</i> and <i>Syzygium aromaticum</i> were tested at concentrations of 500, 250.125 and 62.5	Based on the results presented, it was found that the extracts of <i>Eleutherin</i> <i>e plicata</i> , <i>Psidium</i> <i>guajava</i> and <i>Syzygium</i> <i>aromaticu</i> <i>m</i> have a potential inhibitory effect on the growth of <i>Candida</i> <i>albicans</i> , serving as a guide for the selection





	(PLI), tooth staining, investigati xerostomia, and on.
	degree of stomatitis were assessed at
	baseline and after 6 weeks.

The resident microbiota of the mouth is quite diversified and within this microbiological complexity, there are at least twenty genera and approximately ninety species of yeasts isolated and among these, eight species of the genus Candida were considered pathogenic: *Candida albicans, Candida guilliermondii, Candida kefyr, Candida krusei, Candida tropicalis, Candida parapsilosis, Candida viswanathii and Candida glabrata.* Among the species of the genus Candida, the most isolated from the oral cavity is *Candida albicans* (6).

And in the articles they mention that Candida tropicalis and Candida krusei, are associated with the pathological process, especially to promote the formation of biofilms and increase drug resistance. (3)

Candidiasis is considered an opportunistic fungal disease and commonly found in clinical dental practice, causing oral candidiasis and prosthetic stomatitis, especially Candida albicans, the most pathogenic species in humans. (2) It has also been reported to infect oral mucositis lesions in patients suffering from head and neck cancer and receiving chemotherapy and radiation treatments. (7,8) However, the presence of this fungus is not necessarily indicative of disease, as it can be isolated in about 40% of healthy individuals in various age groups (2,9)

When a cell population adheres to an abiotic or biological surface, Candida *spp biofilms* are formed, and produce an extracellular matrix (ECM), which protects them from the host's immune system and external factors, such as antifungals. (10)

Regarding the treatment of candidiasis, a large number of drugs obtained through organic synthesis have been used, such as antiseptics based on tincture of iodine, gentian violet, salicylic and benzoic acid, sulfamide derivatives, dyes, quinones and polyene antifungals (nystatin, amphotericin). In addition to these, antifungals such as azoles (ketoconazole, econazole, sulconazole, miconazole, clotrimazole and fluconazole) and amphotericin B are also used (9).

Many of these antifungals have undesirable adverse effects or may induce the emergence of resistant Candida species, especially in immunocompromised individuals. tag. (2,3,9) The mechanisms of resistance to antifungals are: the sequestration of drugs by the extracellular polymer matrix (EPM), the increase in drug efflux, high cell density, the presence of persistent cells, and activation of the responsive stress pathway. (11)

Chlorhexidine, despite being considered the gold standard, has the best result of minimum inhibitory concentration MIC and minimum antifungal concentration MFC, but when used in the



long term it has adverse effects such as taste changes, oral peeling, unpleasant taste and tooth pigmentation. (11)

For these reasons, the development of new drugs is necessary to prevent candidiasis/candidemia infection and the search for therapeutic alternatives such as plant derivatives (2,3,9).

In this context, natural phytotherapy products such as essential oils could be considered a new strategy to inhibit biofilms and potentiate conventional antifungals against Candida spp. (10)

The use of herbal medicines is an ancient practice, recognized by the WHO and their use in the treatment of oral diseases presents, according to scientific studies, antimicrobial, antiinflammatory and antifungal activities against the main oral microorganisms. (8) tag. (7,10)

One study evaluated C. *sativum* essential oil significantly reduced the development of hyphae, pseudohyphae, chlamydoconia, and blastoconids in *Candida albicans*. The essential oil mentioned has in its chemical composition a significant amount of linalool and a smaller amount of gamma-terpinene, which has antifungal action against several strains of fungi. (5)

Another study found that the extracts of *Eleutherine plicata, Psidium guajava and Syzygium aromaticum* showed a potential inhibitory effect on the growth of *Candida albicans*., serving as a guide, selecting plants with antifungal activities for future toxicological and pharmacological studies. (9)

Some studies have identified that essential oils extracted from Melaleuca alternifolia and β citronellol had an inhibitory effect of more than 60% on the formation of clinical *C. albicans* biofilms . (2)

The essential oil of *Baccharis tridentata Vahl* and the essential oil of Frankincense are composed of α -thujene, an inhibitor of leukocyte elastase and degrader of glycosaminoglycans, being the majority in the former, also presenting inhibition of topoisomerases I and II- α that stimulate apoptosis, in addition to antioxidant and fungitoxic activity. (12)

Preparations of twenty-three plants showed activity equal to or greater than 50% against biofilms of C. albicans in biofilm formation (BF) or preformed biofilm (PB), being seven essential oils and eight extracts being some of the plant families found: Myrtaceae (Eucalyptus robusta, Melaleuca alternifolia, Eugenia uniflora, Eugenia leitonii, Eugenia brasiliensis), Asteraceae (printed Santolina, Artemisia judaica), Arecaceae (Daemonoropsdraco), Campanulaceae (Adenophora triphylla), Combretaceae (Buchenavia tomentosa), Dioscoreaceae (Dioscorea genus), Lamiaceae (Vitex gardneriana), Lauraceae (Cinnamomum burmannii, Cinnamomum verum, Cryptocarya mandioccana, Cryptocarya moschatta), Lythraceae (Punica granatum sarcotesta), Magnoliaceae (Magnolia officinalis), Menispermaceae (Fibraurea recisa), Piperaceae (Piper claussenianum), Poaceae (Cymbopogon citratus) and Papaveraceae. (2)



Salvia officinalis (sage) has been used in medicine and dentistry for hundreds of years and a recent study demonstrated an effect against *Candida albicans*. (6) As well as several other studies have shown that the terpenoid citronellal is the main phytoconstituent in *C. Nardus* EO and that they were able to inhibit 100% of the growth of *C. albicans*, in addition to presenting low toxicity in human epithelial cells. (11)

In a comparative study between Cinnulin PF® and cinnamon bark oil, the former did not reduce the growth of *C. albicans*, while the latter exhibited high content of antifungal activity with minimum inhibitory concentrations and minimum fungicidal concentrations in the range of 0.039 to 0.078%. Cinnamon oil was also active against a preformed biofilm of *C. albicans*. Cinnulin PF®, on the other hand, prevented biofilm formation by *C. albicans* and attenuated its adhesion to oral epithelial cells. And both did not show significant cytotoxicity against the oral epithelium. (10)

Recently, the effect of *Lavandula dentata L*. and reported a high antibiofilm effect against C. *albicans strains*. A subspecies of essential oil of *Origanum vulgare L*. has gained attention in recent years, demonstrating a potent anti-candida effect, which may be related to the presence of carvacrol in its composition. The presence of several molecules in the essential oil could act simultaneously against different pharmacological targets. (10)

It is cited in a study that approximately 70% of prosthesis users had "prosthetic stomatitis" and often caused by colonization by *Candida albicans (C. albicans)*. Different therapeutic options are indicated for its treatment: replacement of ill-fitting prostheses, improvement of oral and prosthetic hygiene, use of local or systemic antifungals, and use of tissue conditioners. To maintain proper prosthesis hygiene and minimize microbial colonization, several antimicrobial agents were added to the tissue conditioners: metal oxides, photocatalysts, silver nanoparticles, zeolite, chlorhexidine, fluconazole, nystatin, miconazole, clotrimazole and chitosan. And the incorporation of essential oils such as (13) (13) *Melaleuca alternifolia* (tea tree oil), oregano oil (*Origanum vulgare*) and lemongrass oil (*Cymbopogan citratus*) showed significant antibacterial and antifungal activity. The latter showed greater antifungal action and very promising for the treatment of prosthetic stomatitis (13) (13)

In tenacious or secondary endodontic infections related to periradicular lesions, it is found in 7–18% *of C. albicans in the* root canal. (14) *M. spicata* was shown to be an effective antimicrobial agent in *C. albicans*, while *O. dubium* was shown to be very effective in *E. faecalis* and *C. albicans*. These data demonstrate that essential oils may be promising alternative compounds for intracanal drugs in future routine clinical applications. (14)

There has been an increase in antifungal resistance in recent years, a problem compounded by the slowness with which new antifungals have been developed. Recent reports estimate that yeasts of the genus *Candida* are responsible for 400,000 new cases of life-threatening candidiasis each year,



with mortality rates of up to 40–60%, even with antifungal treatment. In addition, there is an increase in non-albicans Candida species as causative agents of emerging infections that are often more resistant than C. *albicans strains*, making the search for new pharmacological strategies urgent (10)

CONCLUSION

According to the literature reviewed, many plants and their chemococcal compounds have antifungal action. Scientific studies prove the effectiveness of essential oils, considered an herbal medicine, and their advantages in relation to allopathic medicines used in dentistry.

Herbal medicines can contribute to the treatment and control of fungal diseases, and may or may not be used concomitantly with allopathic medicines, and it is important that the health professional knows their pharmacological action, as well as their adverse effects and contraindications. They can be considered promising for the development of future research and the development of new drugs.



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