Clinical, Cosmetic and Investigational Dentistry

Dovepress

open access to scientific and medical research

Open Access Full Text Article

REVIEW

Effectiveness of Lemon Verbena (*Cymbopogon citratus*) in Oral Candidiasis: A Systematic Review

Katherine Cuenca-León[1–3], Miriam Lima-Illescas[1,2], Edisson-Mauricio Pacheco-Quito[1,2], Eleonor Vélez-León[1,2], Aránzazu Zarzuelo-Castañeda[3]

[1]Universidad Católica de Cuenca, Facultad de Odontología, Cuenca, 010105, Ecuador; [2]Grupo de Investigación: Innovación y Desarrollo Farmacéutico. Grupo de Investigación en Odontología, Facultad de Odontología, Jefatura de Investigación e Innovación, Universidad Católica de Cuenca, Cuenca, 010105, Ecuador; [3]Pharmaceutical Sciences Department, University of Salamanca, Salamanca, 37007, Spain

Correspondence: Katherine Cuenca-León, Universidad Católica de Cuenca, Facultad de Odontología, Avenida de las Américas, Cuenca, 010105, Ecuador, Email kcuencal@ucacue.edu.ec

Abstract: The rise of phytotherapy has enabled the utilization of various plant species for medicinal purposes, such as *Cymbopogon citratus* (*C. citratus*), providing solutions for oral pathologies, such as oral candidiasis. The PubMed, Web of Science, Scopus, and SciELO databases were searched. In vivo and in vitro studies on the action of *C. citratus* against oral candidiasis were included, and ROBINS-I was used to determine study quality and risk of bias. The search yielded 1922 articles, of which 10 met the inclusion criteria. Limited scientific evidence exists regarding the use of *C. citratus* for oral candidiasis. However, studies have indicated its potent antifungal effects. Further studies, preferably clinical trials, are necessary to confirm this effect and to enable its clinical use as a therapeutic option.

Keywords: systematic review, candidiasis, oral efficacy, phytotherapy

Introduction

Oral candidiasis in adults with partial or total prostheses, also known as denture stomatitis, is a common fungal infection of the oral cavity primarily caused by *Candida albicans*. Patients using partial or total prostheses tend to have a higher risk of plaque accumulation and food debris under the prosthesis, favoring an environment conducive to the growth of *C. albicans*.[1–7] Other risk factors include age, pre-existing immunosuppressive diseases, impaired salivary gland function, drug interactions, high-carbohydrate diets, and extreme living conditions.[1,6,8–14]

This study is of great interest in the dental field[15,16] because the imbalance generated between this commensal fungus and its host (human) allows the development of opportunistic infections.[17–20] In healthy populations, the presence of the microorganism *C. albicans* is between 2 and 7% and in hospitalized individuals between 13 and 76%. These data are alarming and represent health problems that must be addressed in a timely manner. Various therapeutic options exist as a solution to this pathology;[21,22] in this study, we reviewed treatment using a phytotherapeutic approach, since the use of plant species with medicinal properties could have potential advantages over conventional pharmacological therapies[23,24] Bioactive components of plant species act by damaging the cell walls of microorganisms, destabilizing the cell membrane and inhibiting ergosterol synthesis, modulation of the immune system and inhibition of adhesion and biofilm formation. The combination of these mechanisms may make plant-based therapies an effective and natural option for the treatment of *Candida albicans* infections.[25,26]

Experimental studies on the development and formulation of new oral phytotherapeutic treatments are still limited; hence, there is a need for therapeutic options aimed at reducing and eradicating pathogenic microorganisms such as *C. albicans*.[24,27] Several studies have demonstrated the antifungal efficacy of *C. citratus* in the treatment of oral candidiasis;[27–30] however, the evidence is inconsistent, highlighting the need for a systematic review that comprehensively evaluates these findings.[31] This

Received: 14 May 2024
Accepted: 2 August 2024
Published: 10 September 2024

study aimed to systematically review the literature in order to critically and exhaustively evaluate the efficacy of *C. citratus* as an antifungal therapy for oral candidiasis.

Materials and Methods

This systematic review was conducted according to the PRISMA 2020 guidelines[31,32] to determine whether the phytochemical components of *C. citratus* exhibit effective antifungal characteristics and thus provide evidence for new therapeutic options applicable to the dental field. The study protocol was registered in the PROSPERO database (CRD42023437844).

Search Strategy

A comprehensive literature search was conducted in MEDLINE (via PubMed), Scopus, Web of Science (WOS), and SciELO databases for articles published up to December 31, 2023, using variations of keywords such as "patients with oral candidiasis", "anticandidal activity", "lemon verbena", "*Cymbopogon citratus*", and "oral candidiasis"[33] (see Table 1).

Table 1 Search Strategy

Database	Search Strategy	Results
PubMed	(((candidiasis oral) AND (prosthetic patients)) OR (lemon verbena)) OR (Cymbopogon citratus) AND "Cymbopogon"[Mesh]	5
	(((((oral candid*) AND ("candidiasis"[Mesh])) OR (oral thrush)) AND (sick person)) AND (lemon verbena)) OR (Cymbopogon citratus)	8
	(((((oral candidiasis) AND ("Patients"[Mesh])) AND (experimental)) AND (Cymbopogon citratus)) OR (lemon grass)) OR (lemon citratus)	21
	(((((oral thrush) OR (oral candidiasis)) AND ("Patients"[Mesh])) AND (oral prosthesis)) OR (lemon grass)) OR (lemon verbena) AND "Cymbopogon"[Mesh]	13
	(("Candidiasis"[Mesh]) AND "Mouth"[Mesh]) AND "Antifungal Agents"[Mesh]) AND "Cymbopogon"[Mesh]	1
	((((((antifungal activity) OR (oral candidiasis)) AND (Cymbopogon citratus)) OR (lemon grasses)) AND (antifungal drugs)) OR (antifungals)) AND "Patients"[Mesh]	5
	Total	53
Web of Science	ALL=((((candidiasis oral) AND (prosthetic patients)) OR (lemon verbena)) OR (Cymbopogon citratus) AND "Cymbopogon"[Mesh])	212
	ALL=(((((oral candid*) AND ("candidiasis"[Mesh])) OR (oral thrush)) AND (sick person)) AND (lemon verbena)) OR (Cymbopogon citratus)	408
	ALL=((((((oral candidiasis) AND ("Patients"[Mesh])) AND (experimental)) AND (Cymbopogon citratus)) OR (lemon grass)) OR (lemon citratus))	141
	ALL=(((((oral thrush) OR (oral candidiasis)) AND ("Patients"[Mesh])) AND (oral prosthesis)) OR (lemon grass)) OR (lemon verbena) AND "Cymbopogon"[Mesh]	132
	ALL=(((((prosthetic materials) AND (anti-candid*)) AND (lemon verbena)) OR (Cymbopogon citratus)) AND "Patients")	7
	(((((((ALL=(antifungal activity)) OR ALL=(oral candidiasis)) AND ALL=(Cymbopogon citratus)) OR ALL=(lemon grasses)) AND ALL=(antifungal drugs)) OR ALL=(antifungals)) AND ALL=(Patients)) AND ALL=(Stomatitis)	46
	Total	946

(*Continued*)

Table 1 (Continued).

Database	Search Strategy	Results
Scopus	(TITLE-ABS-KEY (candidiasis AND oral AND prosthetic AND patients OR lemon AND verbena) OR ALL (Cymbopogon AND citratus) AND ALL ("Cymbopogon"[mesh])) AND (LIMIT-TO (DOCTYPE, "ar")) AND (LIMIT-TO (EXACTKEYWORD, "Article"))	6
	TITLE-ABS-KEY ((((((oral AND candid*) AND ("candidiasis"mesh])) OR (oral AND thrush)) AND (sick AND person)) AND (lemon AND verbena)) OR (Cymbopogon AND citratus)) AND (LIMIT-TO (DOCTYPE, "ar")) AND (LIMIT-TO (LANGUAGE, "Chinese"))	12
	TITLE-ABS-KEY ((((candidiasis AND oral) AND (prosthetic AND patients)) OR (lemon AND verbena)) OR (Cymbopogon AND citratus) AND "Cymbopogon"[mesh]) AND (LIMIT-TO (DOCTYPE, "ar"))	1
	TITLE-ABS-KEY ((((candidiasis AND oral) AND (prosthetic AND patients)) OR (lemon AND verbena)) OR (Cymbopogon AND citratus) AND "Cymbopogon"[mesh])	2
	TITLE-ABS-KEY (((((prosthetic AND materials) AND (anti-candid*)) AND (lemon AND verbena)) OR (Cymbopogon AND citratus)) AND "Patients") AND (LIMIT-TO (DOCTYPE, "ar")) AND (LIMIT-TO (EXACTKEYWORD, "Article"))	73
	TITLE-ABS-KEY ((((("Candidiasis") AND "Mouth") AND "Antifungal Agents") AND "Cymbopogon") AND (LIMIT-TO (DOCTYPE, "ar")) AND (LIMIT-TO (EXACTKEYWORD, "Article"))	3
	TITLE-ABS-KEY (((((((antifungal AND activity) OR (oral AND candidiasis)) AND (Cymbopogon AND citratus)) OR (lemon AND grasses)) AND (antifungal AND drugs)) OR (antifungals)) AND "Patients")) AND (LIMIT-TO (DOCTYPE, "ar")) AND (LIMIT-TO (EXACTKEYWORD, "Article")) AND (LIMIT-TO (LANGUAGE, "Chinese") OR LIMIT-TO (LANGUAGE, "Japanese"))	694
	TITLE-ABS-KEY (((((((antifungal AND activity) OR (oral AND candidiasis)) AND (Cymbopogon AND citratus)) OR ("lemon grasses")) AND (antifungal AND drugs)) OR (antifungals)) AND "Patients" AND "Stomatitis")) AND (LIMIT-TO (DOCTYPE, "ar")) AND (LIMIT-TO (EXACTKEYWORD, "Article") OR (LIMIT-TO (EXACTKEYWORD, "Antifungal Agent")) OR (LIMIT-TO (EXACTKEYWORD, "Humans")) AND (LIMIT-TO (LANGUAGE, "Chinese")) OR (LIMIT-TO (LANGUAGE, "Japanese"))	1
	Total	792
SciELO	(((candidiasis oral) AND (prosthetic patients)) OR (lemon verbena)) OR (Cymbopogon citratus) AND "Cymbopogon"	133
	Total	133
	Total number of articles	1924

Inclusion Criteria

Articles in English and Spanish that reported in vivo and in vitro studies involving the presence of *C. albicans*, antimycotic efficacy of *C. citratus*, oral candidiasis, patients of any sex and age and patients using or not using oral prostheses were included.

Exclusion Criteria

Non-relevant studies and reviews, clinical case reports, studies with low-quality scientific evidence, studies in Chinese and Russian languages, studies without full text available, conferences, surveys, studies of other active components, letters, and editorial opinions were excluded.

Study Selection, Data Extraction, and Analysis

Study selection was performed by two independent reviewers who initially assessed the titles and abstracts of the identified articles and excluded those that did not meet the eligibility criteria. After the initial evaluation, all studies were imported into Mendeley Reference Manager software (version 2.72.0) to eliminate duplicates. Potentially eligible full-

text articles were independently analyzed by the reviewers based on the inclusion/exclusion criteria, and any disagreement was resolved through consultation with a third author. The PRISMA flow diagram (Figure 1) shows the included and excluded studies. The information from each selected article was compiled into an evidence table (Tables 2 and 3) using Microsoft Office Excel, reporting data on in vivo and in vitro studies, year of publication, first author, study type, study unit, population characteristics, application, effects of *C. citratus* on oral health, control group, main findings, database, and journal names.

Quality Assessment

The "Risk of Bias in Non-randomized Studies – of Interventions" (ROBINS I) tool was used to determine the methodological quality and risk of bias of the studies identified. This tool has been used in non-randomized interventional studies. The response options of this tool allow for the assessment of low, moderate, serious, and critical risks based on the individual evaluation of each article, resulting in a color-coded graphical representation. The quality assessment was conducted by the reviewers (K.C.-L. and M.L.-I). In cases of disagreement, a third reviewer (E.P.-Q.) assessed the articles, and consensus was reached through discussion.

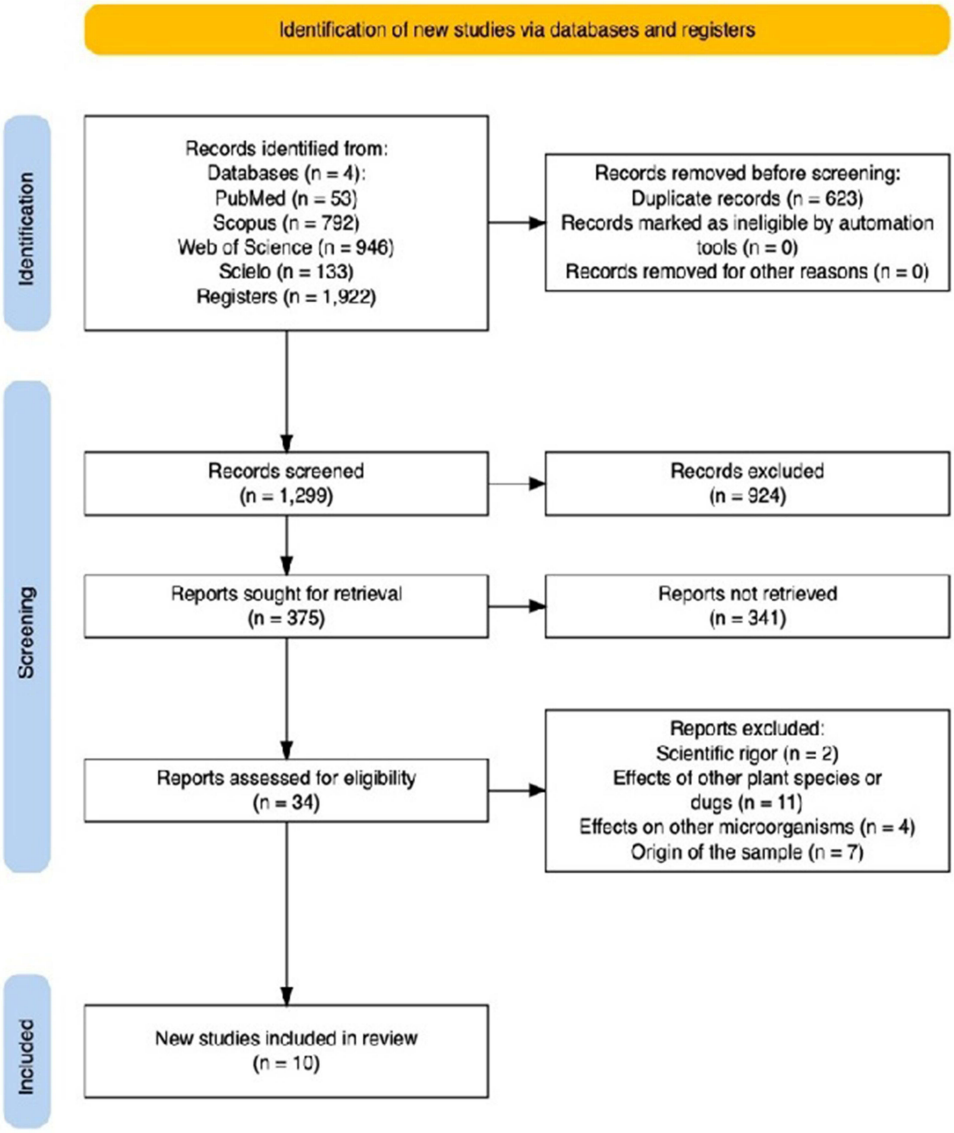

Figure 1 The PRISMA flow diagram.

Table 2 Characteristics of the Studies in Chronological Order, Describing the Main Author, Type of Design, Study Unit, Outcome, and Control

Year	First Author	Type of Study	Unit of Study	Outcome	Control	Reference
2009	Wright	Clinical trial	82 patients	Positive antifungal effect	Not reported	[34]
2010	Tyagi	In vitro	ATCC 10231 *(C. albicans)*	Positive antifungal effect	Not reported	[35]
2010	Taguchi Yuuki	In vitro	TIMM 1768 and TIMM 2640 (*C. albicans*)	Positive antifungal effect	Not reported	[36]
2013	Almeida	In vitro	*C. albicans* ATCC 18804 isolated from the oral cavity of healthy individuals	Positive antifungal effect	Sterile distilled water	[28]
2014	Amornvit	In vitro	ATCC 10231 (*C. albicans*)	Positive antifungal effect	Nystatin	[37]
2014	Boukhatem	Clinical trial/ in vitro	60 male and female Swiss albino mice	Positive antifungal effect	Not reported	[24]
2014	Bersan	In vitro	CBS 562 (*C. albicans*)	Positive antifungal effect	Nystatin	[38]
2019	Pedroso	Clinical trial/ in vitro	SC 5314 (*C. albicans*) and 20 worms	Positive antifungal effect	Amphotericin	[39]
2022	Paiva	In vitro	292 pre-identified Candida strains from the oral cavity of oncologic patients (*C. albicans* ATCC 90028, *C. dubliniensis* CBS 7987, *C. parapsilosis* ATCC 22019, *C. glabrata* MYA 2950, *C. krusei* ATCC 6258, and *C. utilis* ATCC 9950)	Positive antifungal effect	Not reported	[27]
2023	Revelo Motta	In vitro	ATCC 10231 (*C. albicans*)	Positive antifungal effect	Nystatin (+) Saline solution (–)	[31]

Table 3 Study Characteristics According to Article Title, Study Location, Database, and Journal and Database

Article Title	Study Location	Database	Journal	Reference
Treatment of oral thrush in HIV/AIDS patients with lemon juice and lemon grass (*Cymbopogon citratus*) and gentian violet.	South Africa	WOS, PubMed, Scopus	*Phytomedicine Journal*	[34]
Liquid and vapour-phase antifungal activities of selected essential oils against *Candida albicans*: Microscopic observations and chemical characterization of *Cymbopogon citratus*.	Unspecified	PubMed, Scopus, Web of Science, Embase	*BMC Complementary and Alternative Medicine*	[35]
Therapeutic Effects on Murine Oral Candidiasis by Oral Administration of Cassia (*Cinnamomum cassia*) Preparation	Japan	PubMed	*Japanese Society for Medical Mycology*	[36]
Antimicrobial activity of the essential oil of *Cymbopogon citratus* (DC) Stapf. on *Staphylococcus spp., Streptococcus mutans* and *Candida spp*	Brazil	SciELO	*Rev. Bras. Pl. Med., Campinas*	[28]

(*Continued*)

Table 3 (Continued).

Article Title	Study Location	Database	Journal	Reference
Lemongrass-incorporated tissue conditioner against *Candida albicans* culture	Unspecified	Scopus	*Journal of Clinical and Diagnostic Research*	[37]
Lemon grass (*Cymbopogon citratus*) essential oil as a potent anti-inflammatory and antifungal drugs	Unspecified	Scopus-WOS-PubMed Central	*Evidence-Based Complementary and Alternative Medicine*	[24]
Action of essential oils from Brazilian native and exotic medicinal species on oral biofilms.	Brazil	PubMed Central, Scopus	*BMC Complementary and Alternative Medicine*	[38]
In vitro and in vivo Anti-*Candida spp*. Activity of plant-derived products	Unspecified	Scopus, PubMed, WOS	*Plants*	[39]
Association of the essential oil of *Cymbopogon citratus* (DC) Stapf with nystatin against oral cavity yeasts	Brazil	SciELO	*Anais da Academia Brasileira de Ciencias*	[27]
Evaluation of Ecuadorian lemongrass oil as an inhibitor of some oral pathogens.	Ecuador	Scopus, SciELO	*Revista Cubana de Estomatología*	[31]

Results

The total number of publications initially identified was 1,922, of which 53 were from PubMed, 792 from Scopus, 946 from the Web of Science, and 133 from SciELO. After removing duplicates, 1,299 articles were reviewed, and 1,289 were excluded based on the eligibility criteria. Ten articles were evaluated based on the full-text inclusion criteria, including in vitro studies and/or clinical trials (see Table 2).

Characteristics of the Included Studies in Chronological Order

In a randomized controlled trial, Wright investigated the use of lemon juice and *C. citratus* for the treatment of oral candidiasis in patients with HIV.[34]

In 2010, Tyagi reported that the minimum inhibitory concentration (MIC) of *C. citratus* essential oil in the liquid phase was higher than that in the vapor phase, and a 4-hour exposure to the vapor phase was sufficient to cause a 100% loss in the viability of *C. albicans* cells. Chemical analysis revealed that *C. citratus* essential oil is dominated by oxygenated monoterpenes, particularly α-citral or geranial and β-citral or neral. This study suggests that the use of *C. citratus* essential oil in the vapor phase may be an effective method for controlling *C. albicans* growth.[35]

In an in vitro study, Taguchi et al reported that *C. citratus* has antifungal activity against *C. albicans* strains TIMM 1768 and TIMM 2640.[36]

In 2013, Almeida et al showed that the essential oil of *C. citratus* reduced the colony-forming units (CFU/mL) of *S. aureus, S. mutans*, and *C. albicans*, both individually and in combination, thereby demonstrating the efficacy of the active components of *C. citratus*.[28]

In an in vitro study, Amornvit et al demonstrated that *C. citratus* has potent antifungal activity against *C. albicans* ATCC 10231, with a minimum inhibitory concentration (MIC) of 0.06% (v/v).[37]

Boukhatem et al reported significant results and stated that *C. citratus* essential oil (LGEO) has potent antifungal effects. LGEO was administered orally and topically and showed promising antifungal activity against *C. albicans, C. tropicalis*, and *Aspergillus niger*, with *C. albicans* being the most important species. This study had a mixed design (both in vitro and clinical trials).[24]

In 2014, Bersan et al evaluated the antifungal activity of essential oils from various medicinal plants, including *C. citratus*, against oral pathogens (*C. albicans*) and their effects on biofilm formation.[38]

The efficacy of several essential oils obtained from different plants, including *C. citratus*, was demonstrated by Pedroso in an in vitro/clinical test study on worms contaminated with *C. albicans*, showing the antifungal efficacy of this plant.[39]

In 2020, Paiva reported that *C. citratus* essential oils inhibit and eradicate yeast from the oral cavity, including *Candida spp*., which are the main causative agents of oral candidiasis and thrush. The use of *C. citratus* essential oil in combination with nystatin may constitute a possible alternative to conventional pharmacological treatments for oral fungal infections, particularly in cases where microorganisms are resistant to commonly used drugs.[27]

An in vitro study conducted by Revelo aimed to define the possible preventive and therapeutic effects of essential oils in the treatment of oral diseases, resulting in the selection of *C. citratus* for its antibacterial, antifungal, antioxidant, antiproliferative, antiviral, and anti-inflammatory properties and reported significant antifungal activity.[30]

Methodological Quality and Risk of Bias

Most studies have reported a reduction in fungal burden after treatment with *C. citratus*. However, the methodological quality of the studies varied and some showed limitations in terms of design and execution. Therefore, each study was evaluated in seven domains (D): D1: Bias due to confounding; D2: Bias in the selection of participants; D3: Bias in the classification of interventions; D4: Bias due to deviations from intended interventions; D5: Bias due to missing data; D6: Bias in the measurement of outcomes; and D7: Bias in the selection of reported results. Based on these domains, judgment was made regarding the quality and risk of bias of each study. In general, most studies had a moderate risk, with one showing a serious risk owing to significant design problems (Figure 2).

The results of these domains are presented here. D1: Most studies showed moderate risk, except for one that showed critical risk; the latter had multiple issues to be used as evidence. D2: All studies presented a moderate risk because of the absence of randomization. D3: Most studies presented a moderate risk, with only one publication classified as having serious risk. D4: Almost all studies presented low risk, one had moderate risk, and one had critical risk. D5: All studies had moderate risk, except for one that presented serious risk. D6: All studies presented a moderate risk. D7: All studies presented low risk, as they were comparable to randomized trials.

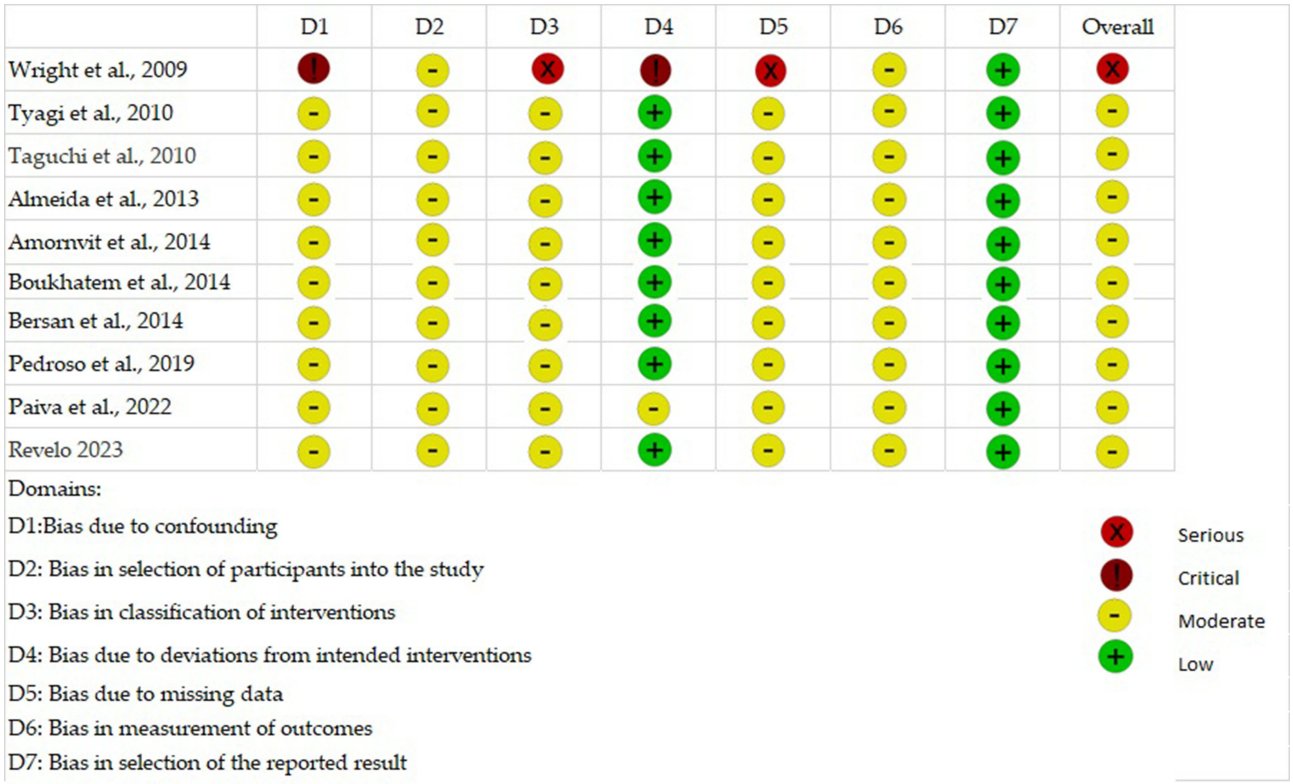

Figure 2 Risk of bias domains.

Discussion

Over the past few decades, increased antimicrobial resistance has become a significant threat to the global public health. This phenomenon diminishes the effectiveness of conventional treatments, elevates the morbidity and mortality associated with common infections, and complicates routine medical procedures, such as surgeries or organ transplants. The escalation of antimicrobial resistance is correlated with increased healthcare expenses, prolonged illness duration, and elevated mortality rates.[40–42] Factors contributing to this phenomenon often stem from the inappropriate and indiscriminate use of antimicrobials, inaccurate diagnoses, inappropriate treatments, therapeutic non-adherence, or adverse effects of conventional medications.[41–43] For example, prosthetic stomatitis is often managed with systemic or local medications, which may not be consistently effective because of inadequate therapeutic strategies or treatment discontinuation owing to adverse effects, potentially fostering antimicrobial resistance. Hence, several studies have explored the use of active components derived from medicinal plants (phytotherapeutics) for the treatment of oral diseases such as stomatitis induced by *C. albicans*.[44–46]

This systematic review aimed to evaluate scientific evidence regarding the efficacy of the active components of *C. citratus* as an antifungal therapy for oral candidiasis. Ten studies, including both in vitro and clinical trials, were reviewed, which revealed a limited number of studies, particularly clinical trials.[47,48]

Clinical Trial

All studies have reported the antifungal efficacy of the active components of *C. citratus*. Of these, six studies were exclusively in vitro trials, three were hybrid in vitro and clinical trials, and one was solely a clinical trial. Exclusive in vitro studies have investigated the essential oil of *C. citratus* against *C. albicans* strains, exhibiting promising antifungal effects that are comparable to those of conventional therapies. Despite the variability in quantitative results and units of measurement, all cases underscored the effectiveness of phytotherapy, as corroborated by previous studies.[21,22,46,49] Additionally, these studies have reported efficacy against other microbial species and demonstrated bacteriostatic and microbicidal effects against *Staphylococcus spp*. and *S. mutans* strains.[28] The bioactive efficacy of lemongrass was elucidated through chemical analysis, highlighting its high oxygenated monoterpene content, notably α-citral, geranial, and β-citral, which confer antimicrobial properties.[35] However, the reviewed in vitro studies often yield heterogeneous results, focusing only on *C. albicans* or assessing the antimicrobial, anti-inflammatory, and antiproliferative effects of diverse bacterial strains.

Mixed Trials (in vitro / Clinical)

Two hybrid in vitro and clinical trials have been conducted. Both studies conducted microbiological evaluations of *Candida spp*. strains, followed by an assessment of the antifungal and anti-inflammatory properties of lemongrass in mice and demonstrated its effectiveness against *C. albicans, C. tropicalis*, and *Aspergillus niger*. In another study, the antifungal efficacy was assessed in worms. Notwithstanding the reported effectiveness, these findings warrant additional studies on the toxicity and adverse effects.

A mixed study was conducted to evaluate various plant species, including lemon balm (Melissa officinalis), thyme (*Thymus vulgaris*), rosemary (*Rosmarinus officinalis*), roselle (*Hibiscus sabdariffa*), green tea (*Camellia sinensis*), and cassia (*Cinnamomum cassia*). This study revealed that the anti-Candida activities of *C. citratus*, green tea, and cassia surpassed those of the other herbs tested, with cassia exhibiting the most favorable results, which is consistent with previous studies.[50,51]

Randomized Clinical Trial

The last included study was a randomized clinical trial that assessed the safety and efficacy of lemon juice and *C. citratus* in the treatment of oral candidiasis in HIV/AIDS patients. Lemon juice and *C. citratus* exhibited superior efficacy compared with the control (gentian violet) in the treatment of oral candidiasis. Notably, adverse effects were more frequent in the control group than in the lemon juice and *C. citratus* groups, suggesting that phytotherapy might mitigate

the adverse effects associated with conventional treatments. However, this study was limited by its small sample size (90), which underscores the necessity for future studies to strengthen the existing evidence.[22]

The findings of this systematic review are expected to have a significant impact on clinical dental practice, particularly in settings with restricted access to conventional antifungals. Despite the absence of comprehensive pharmacological studies verifying its safety, toxicity, and adverse effects, these findings are promising for clinical application. If the efficacy and safety of *C. citratus* in the treatment of oral candidiasis are substantiated, it could emerge as an alternative or adjunct therapeutic option. Nonetheless, potential limitations such as variability in plant quality, product preparation based on active components, and study heterogeneity must be addressed. Further studies, particularly clinical trials, are required to validate the initial findings of this review and to establish clear clinical guidelines for *C. citratus* in oral candidiasis treatment with the aim of mitigating adverse effects and combating antimicrobial resistance.[21,22,48,52,53]

Lastly, we mention that this study used ROBINS I, a powerful tool that helped to evaluate the risk of bias in the estimation of harm or benefit of interventional studies that did not use randomization, obtaining objective results, as expected, and according to this study, its use is recommended in medical areas, justifying it due to the scarcity of ECCAS.[53]

Study Limitations

Owing to limited information and limited clinical trials, the review of the effects of *C. citratus* needs to be expanded to include in vitro studies involving both healthy and diseased individuals. The dearth of clinical trials that could provide more insights into the efficacy of *C. citratus* against *C. albicans* in vivo means that a precise definition of its therapeutic role requires further research.

Conclusion

This systematic review of the antifungal efficacy of *C. citratus* against oral candidiasis revealed a promising set of studies supporting its potential as an alternative or complementary therapy. Despite the variability in methodological quality and study design among the analyzed studies, the findings consistently suggested a significant antifungal effect of *C. citratus* against *C. albicans*. These results are encouraging and highlight the need for further research, particularly well-designed clinical trials, to validate and expand our understanding of the therapeutic benefits of *C. citratus* in the treatment of oral candidiasis, thereby contributing to improved clinical care and patient quality-of-life.

Acknowledgments

The authors thank the Universidad Católica de Cuenca for their constant and timely support.

Funding

Universidad Católica de Cuenca. Project: DISEÑO Y ELABORACIÓN DE UN ENJUAGUE BUCAL CON INGREDIENTES ACTIVOS NATURALES, PARA NEUTRALIZAR Y ELIMINAR HONGOS ORALES EN PACIENTES QUE PORTAN PRÓTESIS PARCIAL Y/O TOTAL, with code PICODS21- 21.

Disclosure

The authors have declared that there are no conflicts of interest in this work.

References

1. Hellstein JW, Marek CL. Candidiasis: red and White Manifestations in the Oral Cavity. *Head Neck Pathol*. 2019;13(1):25–32. doi:10.1007/s12105-019-01004-6
2. Imbert C, Willems HME, Krom BP. Advances in Experimental Medicine and Biology Advances in Microbiology, Infectious Diseases and Public Health, 931, 2016, 13–17.
3. O'Donnell LE, Robertson D, Nile CJ, et al. The oral microbiome of denture wearers is influenced by levels of natural dentition. *PLoS One*. 2015;10 (9). doi:10.1371/journal.pone.0137717.
4. Scully C, El-Kabir M, Samaranayake LP. Candida and Oral Candidosis: a Review. *Crit Rev Oral Biol Med*. 1994;5(2):125–157. doi:10.1177/10454411940050020101
5. Webb BC, Thomas CJ, Willcox MDP, Harty DWS, Knox KW. Candida-associated denture stomatitis. Aetiology and management: a review. Part 1. Factors influencing distribution of candida species in the oral cavity. *Aust Dent J*. 1998;43(1):45–50. doi:10.1111/j.1834-7819.1998.tb00152.x

6. Abe S, Sato Y, Inoue S, et al. Aceites esenciales de plantas, especialmente aceite esencial de hierba limón, y Actividad anti-Candida albicans del citral, un terpenoide. *Jpn J Med Mycol*. 2003;44(4):285–291. doi:10.3314/jjmm.44.285
7. Sawadogo I, Paré A, Kaboré D, et al. Antifungal and Antiaflatoxinogenic Effects of Cymbopogon citratus, Cymbopogon nardus, and Cymbopogon schoenanthus Essential Oils Alone and in Combination. *J Fungi*. 2022;8(2):117. doi:10.3390/jof8020117
8. Bortoluci F, Milanezi J, Galvao S. Natural medicaments in endodontics – a comparative study of the anti-inflammatory action. *Endodontics*. 2004;18(2):174–179.
9. De Clerck C, Maso SD, Parisi O, Dresen F, Zhiri A, Haissam Jijakli M. Screening of antifungal and antibacterial activity of 90 commercial essential oils against 10 pathogens of agronomical importance. *Foods*. 2020;9(10):1418. doi:10.3390/foods9101418
10. Hato H, Kichiro S, Sato J, Hasebe A, Yamazaki Y, Kitagawa Y. Factor associated with oral candidiasis caused by co-infection of Candida albicans and Candida glabrata: a retrospective study. *J Dent Sci*. 2022;17(3):1458–1461. doi:10.1016/j.jds.2021.10.020
11. Mayer FL, Wilson D, Hube B. Candida albicans pathogenicity mechanisms. *Virulence*. 2013;4(2):119–128. doi:10.4161/viru.22913
12. Millsop JW, Fazel N. Oral candidiasis. *Clin Dermatol*. 2016;34(4):487–494. doi:10.1016/j.clindermatol.2016.02.022
13. Vélez-León EM, Albaladejo-Martínez A, Cuenca-León K, Encalada-Verdugo L, Armas-Vega A, Melo M. Caries Experience and Treatment Needs in Urban and Rural Environments in School-Age Children from Three Provinces of Ecuador: a Cross-Sectional Study. *Dent J*. 2022;10(10):185
14. Venzon L, Mariano LNB, Somensi LB, et al. Essential oil of Cymbopogon citratus (lemongrass) and geraniol, but not citral, promote gastric healing activity in mice. *Biomed Pharmacother*. 2018;98:118–124. doi:10.1016/j.biopha.2017.12.020
15. Carlos Groppo F, De Cássia Bergamaschi C, Cogo K, et al. Use of Phytotherapy in Dentistry. *Phytother Res*. 2008;22(8):993–998.
16. Shui Y, Li J, Lyu X, Wang Y. Phytotherapy in the management of denture stomatitis: a systematic review and meta-analysis of randomized controlled trials. *Phytother Res*. 2021;35(8):4111–4126. doi:10.1002/ptr.7073
17. Butzge JC, Pivotto C, Mezzomo L, et al. Antifungal Properties of Essential Oils Derived from the Genus Cymbopogon: a Systematic Review. *Chem Biodivers*. 2023;20(10). doi:10.1002/cbdv.202300663.
18. Mosquera Cardenas HJ. Identificación de candida en cavidad bucal de pacientes con diabétes yvih/sida. *Revis Estomatol*. 2022;30(1). doi:10.25100/re.v30i1.9305
19. Polaquini SRB, Svidzinski TIE, Kemmelmeier C, Gasparetto A. Effect of aqueous extract from Neem (Azadirachta indica A. Juss) on hydrophobicity, biofilm formation and adhesion in composite resin by Candida albicans. *Arch Oral Biol*. 2006;51(6):482–490. doi:10.1016/j.archoralbio.2005.11.007
20. Ponde NO, Lortal L, Ramage G, Naglik JR, Richardson JP. Candida albicans biofilms and polymicrobial interactions. *Crit Rev Microbiol*. 2021;47(1):91–111. doi:10.1080/1040841X.2020.1843400
21. Contaldo M, Di Stasio D, Romano A, et al. Oral Candidiasis and Novel Therapeutic Strategies: antifungals, Phytotherapy, Probiotics, and Photodynamic Therapy. *Curr Drug Deliv*. 2023;20(5):441–456. doi:10.2174/1567201819666220418104042
22. Cuenca-León K, Pacheco-Quito EM, Granda-Granda Y, Vélez-León E, Zarzuelo-Castañeda A. Phytotherapy: a Solution to Decrease Antifungal Resistance in the Dental Field. *Biomolecules*. 2022;12(6):789. doi:10.3390/biom12060789
23. Sharma S, Mohler J, Mahajan SD, Schwartz SA, Bruggemann L, Aalinkeel R. Microbial Biofilm: a Review on Formation, Infection, Antibiotic Resistance, Control Measures, and Innovative Treatment. *Microorganisms*. 2023;11(6):1614. doi:10.3390/microorganisms11061614
24. Boukhatem MN, Ferhat MA, Kameli A, Saidi F, Kebir HT. Lemon grass (Cymbopogon citratus) essential oil as a potent anti-inflammatory and antifungal drugs. *Libyan J Med*. 2014;9(1). doi:10.3402/ljm.v9.25431
25. Gutierrez J, Barry-Ryan C, Bourke P. Antimicrobial activity of plant essential oils using food model media: efficacy, synergistic potential and interactions with food components. *Food Microbiol*. 2009;26(2):142–150. doi:10.1016/j.fm.2008.10.008
26. de Buriti BMA, Figueiredo PLB, Passos MF, da Silva JKR. Polymer-Based Wound Dressings Loaded with Essential Oil for the Treatment of Wounds: a Review. *Pharmaceuticals*. 2024;17(7):897.
27. De Paiva LF, Teixeira-Loyola ABA, Schnaider TB, De Souza AC, Zacaroni Lima LM, Dias DR. Association of the essential oil of Cymbopogon citratus (DC) Stapf with nystatin against oral cavity yeasts. *An Acad Bras Cienc*. 2022;94(1). doi:10.1590/0001-3765202220200681
28. Almeida, Akisue, Cardoso, et al. Antimicrobial activity of the essential oil of Cymbopogon citratus (DC) Stapf. on Staphylococcus spp. Streptococcus mutans and Candida spp. *Rev Bras Pl Med*. 2013;15(4):474–482. doi:10.1590/S1516-05722013000400002
29. Konsberg R, Axéll T, Sweden M, Olso N. Treatment of Candida-infected denture stomatitis with a miconazole lacquer. *Oral Med*. 1994;78(3):306–311.
30. Revelo Motta G. Evaluación del aceite de hierbaluisa ecuatoriana como inhibidor de algunos patógenos orales. *Rev Cubana Estomatol*. 2023;60(1):4125.
31. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:1.
32. Haddaway NR, Page MJ, Pritchard CC, McGuinness LA. PRISMA2020: an R package and Shiny app for producing PRISMA 2020-compliant flow diagrams, with interactivity for optimised digital transparency and Open Synthesis. *Campbell Syst Rev*. 2022;18(2). doi:10.1002/cl2.1230
33. Ebingen VC, María AC, Katherine CL, Mirella CC, Diego PV, Alberto AC. CLINICAL STUDIES DESIGN IN DENTISTRY. *Revista OACTIVA UC Cuenca Mayo-Agosto*. 2016;1:1.
34. Wright SC, Maree JE, Sibanyoni M. Treatment of oral thrush in HIV/AIDS patients with lemon juice and lemon grass (Cymbopogon citratus) and gentian violet. *Phytomedicine*. 2009;16(2–3):118–124. doi:10.1016/j.phymed.2008.07.015
35. Tyagi AK, Malik A. Liquid and vapour-phase antifungal activities of selected essential oils against candida albicans: microscopic observations and chemical characterization of Cymbopogon citratus. *BMC Complement Altern Med*. 2010;10(1). doi:10.1186/1472-6882-10-65
36. Taguchi Y, Takizawa T, Ishibashi H, et al. Therapeutic Effects on Murine Oral Candidiasis by Oral Administration of Cassia (Cinnamomum cassia) Preparation. *Nippon Ishinkin Gakkai Zasshi*. 2009;2009:1.
37. Amornvit P, Choonharuangdej S, Srithavaj T. Lemongrass-incorporated tissue conditioner against Candida albicans culture. *J Clin Diagn Res*. 2014;8(7):50–52.
38. Bersan SMF, Galvão LCC, Goes VFF, et al. Action of essential oils from Brazilian native and exotic medicinal species on oral biofilms. *BMC Complement Altern Med*. 2014;14(1). doi:10.1186/1472-6882-14-451.
39. Pedroso RDS, Balbino BL, Andrade G, et al. In vitro and in vivo Anti-Candida spp. Activity of plant-derived products. *Plants*. 2019;8(11):494. doi:10.3390/plants8110494

40. Christaki E, Marcou M, Tofarides A. Antimicrobial Resistance in Bacteria: mechanisms, Evolution, and Persistence. *J Mol Evol*. 2020;88(1):26–40. doi:10.1007/s00239-019-09914-3
41. McEwen SA, Collignon PJ. Antimicrobial Resistance: a One Health Perspective. *Microbiol Spectr*. 2018;6(2). doi:10.1128/microbiolspec.ARBA-0009-2017
42. Scott HM, Acuff G, Bergeron G, Bourassa MW, Simjee S, Singer RS. Antimicrobial resistance in a One Health context: exploring complexities, seeking solutions, and communicating risks. *Ann NY Acad Sci*. 2019;1441(1):3–7. doi:10.1111/nyas.14057
43. Rusic D, Bozic J, Bukic J, et al. Antimicrobial Resistance: physicians' and Pharmacists' Perspective. *Microb Drug Resist*. 2021;27(5):670–677. doi:10.1089/mdr.2020.0272
44. Casaroto AR, Lara VS. Phytomedicines for Candida-associated denture stomatitis. *Fitoterapia*. 2010;81(5):323–328. doi:10.1016/j.fitote.2009.12.003
45. De Souza Vasconcelos LC, Correia Sampaio MC, Correia Sampaio F, Higino JS. Use of Punica granatum as an antifungal agent against candidosis associated with denture stomatitis. *Mycoses*. 2003;46(5–6):192–196. doi:10.1046/j.1439-0507.2003.00884.x
46. Ghorbani A, Sadrzadeh A, Habibi E, et al. Efficacy of Camellia sinensis extract against Candida species in patients with denture stomatitis. *Curr Med Mycol*. 2018;4(3):15–18. doi:10.18502/cmm.4.3.174
47. Jamshidi-Kia F, Lorigooini Z, Amini-Khoei H. Medicinal plants: past history and future perspective. *J Herbmed Pharmacol*. 2018;7(1):1–7. doi:10.15171/jhp.2018.01
48. Enioutina EY, Teng L, V. FT, et al. Phytotherapy as an alternative to conventional antimicrobials: combating microbial resistance. *Expert Rev Clin Pharmacol*. 2017;10(11):1203–1214. doi:10.1080/17512433.2017.1371591
49. Caruso S, Valenti C, Marinucci L, et al. Systematic Review of Zinc's Benefits and Biological Effects on Oral Health. *Materials*. 2024;17(4):800. doi:10.3390/ma17040800
50. Karadağlıoğlu Öİ, Ulusoy N, Başer KHC, Hanoğlu A, Şık İ. Antibacterial activities of herbal toothpastes combined with essential oils against streptococcus mutans. *Pathogens*. 2019;8(1):20. doi:10.3390/pathogens8010020
51. Ferreira EDS, Rosalen PL, Benso B, et al. The Use of Essential Oils and Their Isolated Compounds for the Treatment of Oral Candidiasis: a Literature Review. *Evid Based Complement Alternat Med*. 2021;2021:1–16. doi:10.1155/2021/1059274
52. Madeira PLB, Carvalho LT, Paschoal MAB, et al. In vitro effects of lemongrass extract on Candida albicans biofilms, human cells viability, and denture surface. *Front Cell Infect Microbiol*. 2016;6(JUN). doi:10.3389/fcimb.2016.00071.
53. Lalla RV, Dongari-Bagtzoglou A. Antifungal medications or disinfectants for denture stomatitis: commentary. *Evid Based Dentist*. 2014;15(2):61–62. doi:10.1038/sj.ebd.6401032