

The effect of dental cleanser from plant extracts inhibiting the growth of *Candida albicans* on acrylic resin plates: a systematic review

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ABSTRACT

Background: Sodium hypochlorite is a denture cleaning solution that is widely used as an efficient cleaning method. However, it has disadvantages of uncomfortable taste and smell. Therefore, therapeutic plant extracts are safer for the human body, they are used as an alternative for denture cleaning agents. **Objective:** To analyze the effect of active compounds extracted from therapeutic plants in inhibiting the growth of *Candida albicans*. **Methods:** Ten selected articles were obtained from five search engines with due observance of PICO and specified inclusion criteria, then an assessment was carried out on ten selected articles which were assessed based on the assessment criteria of The Joanna Briggs Institute Critical Appraisal Tools checklist and deserved to be included in writing a systematic review.

Results: The plant extracts from ten articles were lemongrass extract and cinnamon extract, which were fungistatic and fungicidal; while the extracts of black cumin, mangrove leaf, rosella flower, ketapang leaf, mexican tea, and grape seed were fungistatic only. **Conclusion:** The active compounds of the terpenoid and phenolic groups from had adequate antifungal activity, but the active compounds in the phenolic group had lower antifungal activity due to the withdrawal of chlorophyll and carotenoid pigments which are known to have antioxidant and antifungal properties.

Keywords: denture cleanser, plant extract, *Candida albicans*, minimum inhibitory

INTRODUCTION

Edentulism is still considered as one of the main oral health problems since it affects a large part of the world population because for decades the public oral health policy in underdeveloped or developing countries was based on tooth extraction for treating pain, caries, and infection, among other oral problems. This curative practice is reflected in the contemporary population, in which it was found a high number of partially or completely edentulous individuals.¹ This population is generally rehabilitated with removable prostheses, which are fabricated of polymethyl methacrylate, due to the good esthetic qualities and excellent cost benefit ratio.²

Oral candidosis is an opportunistic infection caused by overgrowth and penetration of the oral tissues by pathogenic forms, hyphae and pseudohyphae, of *Candida spp.*, mainly *Candida albicans*. *Candida-associated denture stomatitis* (CADS), the most frequent type of oral candidosis and the most common mucosal alteration in the elderly, affects approximately 65% of removable denture wearers and has been associated with multiple etiologic factors. Despite its etiology involving systemic and local factors, CADS is mainly associated with an overgrowth of *Candida* in pathogenic form on the denture surface as a biofilm. The first crucial step of denture biofilm formation is adherence of yeast-form cells to the acrylic surfaces.¹

Maintenance of denture hygiene plays an important role in the denture care process because

it can help maintain the strength, stability and retention of the denture, as well as maintain the health of the surrounding tissue in the oral cavity.³

The most common method of controlling biofilm on dentures is brushing with toothpaste, because it is easy to reach and low cost. Mechanical brushing is a simple and widely used cleaning method to control biofilm on dentures. However, there are pores in acrylic resin, and in some situations, toothbrush bristles do not properly clean the pores.⁴ In addition, many denture users are geriatric patients, who have had decreased visual acuity or even loss of motor skills, thereby impairing cleaning and performance. Although immersion in chemical solutions has been recommended as a complementary method for mechanical cleaning, it has been observed that this treatment also fails to remove the biofilm *C. albicans*. In cases where *C. albicans* is a persistent infection, the use of antifungal agents has become a daily routine, e.g. fluconazole and nystatin. *C. albicans* drug resistance is one of the major problems in fighting the survival and spread of biofilms and can ultimately lead to treatment failure.⁴

This article reviews the effect of dental cleanser from plant extracts inhibiting the growth of *C. albicans* on acrylic resin plates.

METHODS

This systematic review is written according to the guidelines of preferred reporting items for systematic reviews and meta-analyses (PRISMA)

for reporting studies evaluating health care interventions. Population, intervention, control, and outcome (PICO) questions of the present systematic review were *C. albicans* on acrylic resin plates, active compounds of therapeutic plant extracts, the effect of active compounds on the growth of *C. albicans*, and minimal inhibitory concentration of therapeutic plant extracts on the growth of *C. albicans*.

The Wiley Online Library, Science Direct, Pubmed Online Library, Cochrane Library, and Google Scholar were the searching engine of to get articles in English. The searchings were conducted to identify articles published in dental journals from January 2016 to December 2020 focusing on effect of dental cleanser from plant extracts inhibiting the growth of *C. albicans*. The MeSH key-words used were *denture cleanser*, *plant extract*, *C. albicans*, and *minimum inhibitory*. The electronic search is limited to articles in English, the search period, and the type of text availability. A manual search of published full-text articles and related reviews was carried out afterwards. There are 825 studies describing this topic but only 10 articles meeting the inclusion criteria. Specific keywords were used to identify appropriate study needs, and followed the characteristics of the PICO questions.

For the eligibility criteria, inclusion criteria were articles in English, published in the year 2016 to 2020, fulltext of laboratory experimental research and clinical reports, research using plant extracts, using the *minimum inhibitory concentration* (MIC) and *colony forming unit* (CFU) tests.

Meanwhile, the exclusion criteria were research that discusses denture cleaners that do not use plant extracts as the main ingredient, and research that is in abstract or in a report.

The special keywords were used by the three authors to select the articles being analyzed in the abstract and the full text. Independently, researchers selected papers based on predefined inclusion criteria. After that, all abstracts and full texts were downloaded and evaluated one by one. Eligibility criteria were used to identify the articles to be used for this systematic review.

The data were retrieved by three reviewers that regarding following parameters: year of publication; effect of denture cleanser from plants extract; and objective. All of the full-texts which met the inclusion criteria were read independently by the three reviewers, and evaluated to formulate this systematic review.

RESULTS

The database search yielded 825 references,

including 43 from Wiley Online Library, 78 from Science Direct, 669 from Pubmed Online Library, 10 from Cochrane Library, and 26 from Google Scholar. After removing duplicate references, there were 799 studies remained. The titles and abstracts were reviewed afterward, and 19 studies were eligible for further analysis. The full-texts then be reviewed by the authors and yielded 10 articles which met the inclusion criteria. The flowchart of article selection is shown in Fig. 1 with total 10 selected articles from initial yield of 825 studies by electronic literature search. After 825 titles reviewed, 10 articles were declared eligible for this systematic review inclusions, whereas the other 815 articles were excluded for some different reasons.

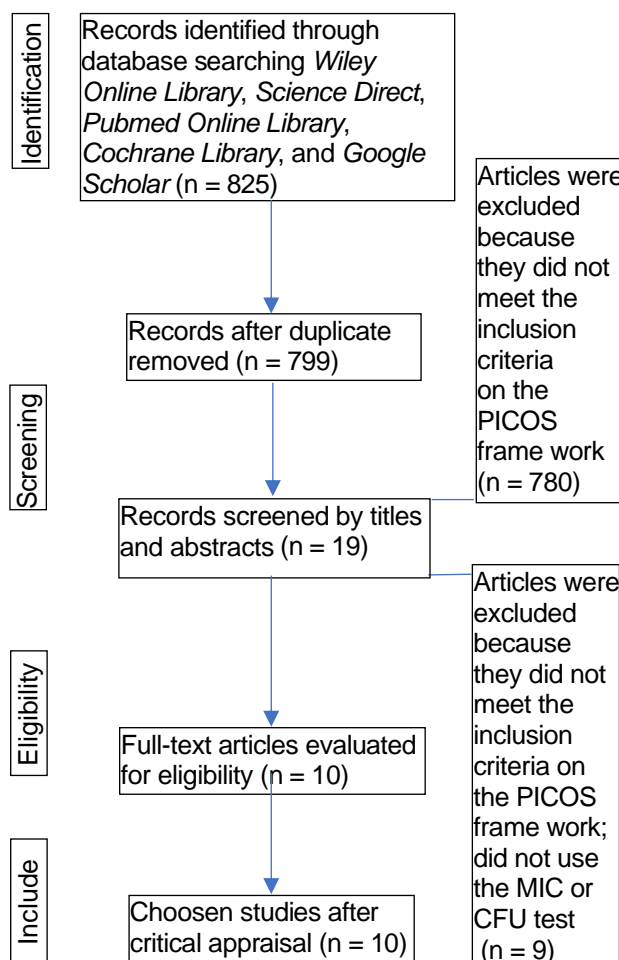


Figure 1 PRISMA flow chart of article selection

DISCUSSION

Cell walls and membranes play an important role in cell viability, morphogenesis, response to environmental influences, and pathogenesis; thus, these morphological changes are thought to reflect damage to cell homeostasis, resulting in cell death. So, this systematic review of effective therapeutic plant extracts inhibits the growth of *C. al-*

Table 1

No	Author (Year)	Plant Extract	Concentration	Active compound	Secunder metabolit	Sample	Group control	Test	Type	Result
1	de Fátima LD, et al (2016)	Essential oil from citronella & cinnamon	citronella 250 µg/mL; Cinnamon 65.5 µg/mL	Citronella & cinnamaldehyde	Terpenoid	9	Phosphat Buffer Saline	MIC & CFU	Fungistatic & fungicidal	Inhibitory effect from citronella 250 µg/mL & cinnamon on MIC 65.5 µg/mL, both essential oil significantly (p<0,05) reduce microorganism and biofilm
2	Madeira PLB, et al (2016)	Lemongrass extract	0.625 mg/mL	Citronelal & linalool	Terpenoid	9	Distilled water	MIC	Fungistatic & fungicidal	Minimum concentration of lemongrass extract needed to inhibit growth <i>C.albicans</i> 0.625 mg/mL. The presence of lemongrass extract during biofilm development resulted in a decrease in the number of cells (p<0.05) which makes MIC enough to reduce approx 90% cell (p<0.0001). Lemongrass extract has significant antifungal effects at all concentrations (p<0,05).
3	Khan MA, et al, (2016)	<i>Nigella sativa</i> / black seeds (Thymoquinone) Essential oil from thyme (p-Cymene & timol)	0.25 mg/mL	Thymoquinone p-Cymene timol	Terpenoid	60	Distilled water	CFU	Fungistatic	Essential oil from thyme and black seeds has almost equal effectiveness against <i>C.albicans</i> but the difference was not statistically significant (p = 0,79)
4	Al-Thobity AM, et al (2017)	<i>Nigella sativa</i> / black seeds (essential oil, alcaloid, fix oil, protein & saponin)	0.5%	Thymoquinone (TQ)	Terpenoid	80	PMMA 0%	MIC	Fungistatic	The inhibitory effect of TQ on MIC significantly reduced the number of <i>C.albicans</i> . The addition of 0.5% TQ to PMMA caused a significant decrease in <i>C.albicans</i> . Increasing the of TQ (0.5-5%), the number of <i>C.albicans</i> decreased drastically to zero using the slide count evaluation method
5	Ariamanesh H, et al (2019)	<i>Nigella sativa</i> / black seeds	0.2 mg/mL	Alcoholic extract from <i>Nigella sativa</i> /black seeds	Terpenoid	30	+positive control: nistatin 100.000 unit -control: distilled water	CFU	Fungistatic	Black seeds at low concentrations (0.2 and 0.4 mg/mL) has a low antifungal effect against <i>C.albicans</i> . However, with increasing concentrations of black cumin, the number of <i>Candida</i> colonies decreased significantly
6	Utama MD, et al (2017)	Mangrove leaves extract (<i>Avicennia marina</i>)	10%	Flavonoid & saponin	Fenolic	10	Denture cleanser commersil	MIC	Fungistatic	7.5% mangrove leaves extract had optimal inhibition against the growth of <i>S.mutans</i> (p <0.05). Mangrove leaf extract at a concentration of 10% had not shown an inhibitory effect against <i>C.albicans</i>

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No	Author (Year)	Plant Extract	Concentration	Active compound	Secunder metabolit	Sample	Group control	Test	Type	Result
7	Utama MD, et al (2017)	Rosella flower extract (<i>Hibiscus sabdarifa L</i>)	10%	anthocyanin, riboflavin, β-caroten, polisakarida, & flavonid	Fenolic	90	Denture cleanser commersil	CFU	Fungistatic	There was no significant difference in effectiveness between the immersion time of 5, 10, and 15 minutes in the 10% rosella
8	Gonçalves LM, et al (2019)	Ketapang leaves extract (<i>Terminalia catappa Linn.</i>)	0.25 mg/mL	Tanin, fraksi n-butanol Terminalia catappa Linn	Fenolic	108	Fluconazole solution	MIC	Fungistatic	MIC value is 0.25 mg/mL of the n-butanol fraction of <i>Terminalia catappa Linn.</i> (FBuTC) was observed for the planktonic cells of <i>C.albicans</i> and <i>C.glabrata</i> . FBuTC exposure at 10xMIC had a significant effect on the biofilm <i>C.albicans</i> , indicating a decrease in cell count
9	Maria P, et al (2019)	<i>Chenopodium ambrosioides</i> extract / Mexican tea extract	0.25 mg/mL	Quercetin & kaempferol	Fenolic	72	+control: sodium hypochlorite (SH 1%) -control: Phosphat	MIC	Fungistatic	The observed effect of mexican tea extract on MIC for planktonic <i>C.albicans</i> cells obtained a value of 0.25 mg/mL, indicating antifungicidal activity. The effect of mexican
10	Chiaki Tsutsumi-Ara et al (2019)	Grape fruit seeds extract	0,1 %	Polifenol	Fenolic	250	Distilled water	CFU	Fungistatic	The treatment with 1% grape seed extract for 5 minutes almost completely removed the biofilm formed on the resin. Treatment with 0.1% grape seed extract, Polident, & 0.1% G + P for 5 minutes showed a statistically significant inhibitory effect on the biofilm. The 0.1% GSE and 0.1% G + P treatment gave a persistent inhibitory effect on the biofilm.

bicans consists of two groups of metabolites secondary, namely terpenoids and phenolic.

For secondary metabolites of the terpenoid group, among others, are obtained from essential oils of the cinnamon plant with the active compound in the form of cinnamaldehyde,⁵ essential oil of lemongrass with active compounds such as citronellal, geraniol, and citronellol,⁶ black seeds with the content of essential oils obtained from the compound *Nigella sativa* seeds active in the form of thymoquinone, p-Cymene, and thymol.^{7,8}

Secondary metabolites of the phenolic group are obtained from mangrove leaves with active compounds in the form of flavonoid and saponin,⁹ rosella flower with active compounds in the form of anthocyanin, riboflavin, beta-carotene, polysaccharide, and flavonoid,¹⁰ ketapang leaves with active compounds in the form of tannins and n-butanol (*Terminalia catappa* Linn). Fraction,¹¹ Mexican tea extract with the active compound form quercetin and kaempferol, grape seed extract with active compounds in the form of polyphenols.¹²

The terpenoid compounds are lipophilic; the antifungal activity in the secondary metabolites of the terpenoid group can cause the membrane to be blocked from dissolving lipids found on the cell membrane. The antifungal activity of phenolic compounds can damage cell walls and cell membranes, precipitate proteins, and inactivate enzymes.

This systematic review concludes that two groups of secondary metabolites namely terpenoids and phenolic, have adequate antifungal activity, but from several articles found that phenolic compounds have antifungal activity not as good as the antifungal activity of the terpenoids due to withdrawal some pigment content. Pigments contained in both plants therapeutic namely chlorophyll and choratenoids pigments which are known to be a high antioxidant and antifungal properties activities. None of the plant extracts from the selected ten articles are toxic, from the article it is concluded that because the plant extract is not toxic, it is used as an alternative ingredient for denture cleanser.

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