CAN DENTURE STOMATITIS BE TREATED WITH ORGANIC INGREDIENTS ?-mini review

Dana Gabriela Budală[1], Maria Bolat[1†], Roxana Ionela Vasluianu[1*], Dan Nicolae Bosînceanu[1], Carina Balcoș[2], Zinovia Surlari[3], Monica Mihaela Scutariu[1†], Florinel Cosmin Bida[1], Dragoș Ioan Virvescu[3*], Elena Raluca Baciu [1]

[1]"Gr. T. Popa" U.M.Ph. - Iași, Romania, Faculty of Dentistry, Implantology, Removable Dentures, Dental Technology

2-"Gr. T. Popa" U.M.Ph. - Iași, România, Faculty of Dentistry, Department of Surgery

3-"Gr. T. Popa" U.M.Ph. - Iași, România, Faculty of Dentistry, Department of Odontology-Periodontology, Fixed Protheses

[*] Corresponding author: Roxana Vasluianu e-mail: roxana30200@yahoo.com

Dragoș Virvescu e-mail: dragosvirvescu@yahoo.com

[†] Authors with the same contribution as first author

ABSTRACT

Introduction: Behavioral management approaches are employed with youngsters who are scared or unwilling to cooperate. Podiatric patients' discomfort and anxiety can be alleviated by the use of pharmacologic sedation, anesthesia, and analgesia. Oral sedative midazolam is frequently prescribed for children because of its safety, rapid onset, and mild amnesia, all of which make it a popular choice among pediatricians. Midazolam/ketamine and its combinations are discussed in this review article, covering the advantages of using oral route of sedation, pharmacokinetics and range of oral dosages, and the use of antagonists for clinical dentistry treatment procedures.

Keywords: pediatric patients, anesthesia, midazolam, ketamine, etc.

INTRODUCTION.

Denture stomatitis (DS) is an inflammatory disease of the tissues that support the denture and is frequently found in denture wearers [1].

Symptoms of denture stomatitis include an inflamed mucosa, a burning feeling under the top denture, as well as an altered sense of taste. 36.7 % who wear dentures are at risk of having DS [2].

Dental trauma, reduced salivation, denture cleanliness, denture base material, age of dentures, the wearer's cellular immune system, and changes in oral microbiota are all risk factors [3].

DS can be triggered by the presence of biofilms on the denture's surface. It is made up of desquamated epithelial cells and the biofilm matrix, which is a combination of pathogenic and opportunistic bacteria and fungi [3,4].

Oral bacteria like Candida albicans, the key etiological agent in the pathophysiology of DS, are protected by this biofilm matrix, which operated as a physical barrier. [5].

Another factor that helps Candida thrive is the anaerobic microenvironment created between dentures and oral tissues [6,7].

S. aureus, which is also known as bacterial-yeast interaction, is another key element in Candida's colonization of the denture and oral mucosa. Candida and S. aureus were often found in the dental prosthesis of patients with DS. C.albicans and S.aureus will not only attach to the denture material's fissures and defects, but they will also colonize the surfaces that come into touch with the oral mucosa [7-9].

When C. albicans and S. aureus have a mutualistic connection, it has been shown to modify the microbes' phenotypic characteristics, promote drug resistance, and create a distinctive biofilm architecture, all of which contribute to the severity of illness. Antifungal miconazole's sensitivity was decreased by the C. albicans-S.aureus biofilm, which showed synergistic pathogenicity [10,11].

The existence of DS has been known for a long time, but no therapies have been proposed as the best course of action due to the high rate of relapse. Because of the disease's complicated etiology, therapy focuses on removing risk factors.

Brushing, washing with commercial cleanser products, and employing disinfectants such as chlorhexidine and sodium hypochlorite are indicated for denture cleaning techniques for DS caused by Candida infection. Commercial denture cleaners, on the other hand, may be ineffective in the fight against fungus. [12,13].

Failure in ensuring denture hygiene contributes to DS recurrent case even following the treatment regimen. The specific antifungal agents such as amphotericin B, nystatin, miconazole or clotrimazole also used locally or systemically to cease candida from developing [14,15].

REVIEW

Plant extracts and phytocompounds are among the medicinal medicines under investigation by scientists for the management and treatment of DS.

Patients' safety and fewer side effects are the primary considerations when evaluating natural products to replace commercial medications.

Plant extracts have been used for a wide variety of purposes for many thousands of years [5], and essential oils are potential sources of novel antimicrobial compounds [6]. They are now attracting attention as useful antimicrobials to be incorporated into mouth rinses.

For example, Australian tea tree oil, peppermint, and sage oil were shown to be the most potent against anaerobic oral bacteria [7], and manuka, tea tree, eucalyptus, lavandula, and rosmarinus (rose-mary) oils to inhibit the growth of cariogenic and periodontopathic bacteria [8].

Yeast and C. albicans were able to securely adhere to the surfaces of resin, glass, ceramics, and metal in in vitro studies by Edgerton [12]. When it comes to cleaning a denture, chlorhexidine and formalin are two of the most regularly utilized disinfectants. Side effects include staining and bleaching [14], and an unpleasant smell [15] may accompany them.

Plants contain a vast variety of aromatic molecules, or phytochemicals, many of which have antibacterial properties. It has been shown by Sokovié and van Griensven [16] that the essential oil of thyme, which contains the active ingredients pcymene and thymol, has potent antifungal and antipathogenic properties [19].

►*Medicinal plants*

Propolis

Tree exudates, flower sap, bee salivary secretions, wax, and pollen combine to form the resinous material known as propolis. Bees employ it for a variety of purposes, including thermal insulation, sealing, and microbial protection [17].

Due to the complexities of its chemical makeup, its source plant and the nearby vegetation are key factors [18,19]. Volatile oils (5–10 percent), waxes (30–40 percent), resins, balsams, and pollen grains are all components of propolis, which are rich in vital elements such as magnesium, nickel, calcium, iron, and zinc. Propolis is also composed of a variety of other substances.

Flavonoids and phenolic acids, esters, phenolic aldehydes, and ketones are among the polyphenols found in propolis, making up the majority of its organic contents [20].

Even while propolis samples from diverse sources have varying compositions, they all show comparable antimicrobial activities [21] because this effect is of paramount relevance to the survival of the honeycomb. As an antibacterial agent, propolis is a powerful choice.

Biological activity of propolis has been studied in dental research primarily with regard to the healing process, the suppression of dental plaque development, and the prevention of dental caries [29,30].

Propolis' beneficial characteristics

are mostly due to phenolic chemicals, such as flavonoids [19,21].

A decrease in phenolic component concentration does not always mean a decrease in activity. lowering of dose plays an important role in decreasing the unpleasant effects [21-23]

In this scenario, it is clear that there are additional substances that have a role in the biological action. Even the process of extracting propolis might have an effect on its efficacy, since various solvents solubilize and extract different components [18,20].

Ethanol, methanol, and water are the most often utilized extracts in biological experiments [18]. It's unlikely that bees alter the chemical makeup of propolis throughout the course of a season, and this is because they visit the same plant sources year-round [24].

C. albicans has been the subject of several studies looking into the antifungal properties of propolis [13–32], with the greatest results coming from the ethanol extract [13–20,31].

Although flavonoid molecules were thought to be responsible for the inhibitory action on yeast, this effect might possibly be attributed to a distinct class of chemicals [25].

It is possible that propolis' antibacterial effect occurs both directly against microbes and indirectly by stimulating the immune system and destroying other microorganisms.

Propolis' antifungal action may be a result of alterations in the cell wall that cause the cell membrane to rupture, as revealed by scanning electron micrography [33].

Macrophages' microbicidal activity can be boosted by propolis, according to Sforcin [26].

Propolis has been shown to have antifungal and anti-inflammatory properties, which might be useful in the treatment of DS at the local level [9,34]. Although propolis is widely used across the world, only a few studies have been done to assess the therapeutic effects of propolis on this oral ailment.

All of the patients evaluated by Santos et al. [34] were treated with an ethanol extract of propolis to treat oral candidiasis induced by dentures, and all of the lesions disappeared.

►*Pomegranate*

Anthocyanins and other phenolic compounds found in pomegranate (P. granatum) have high antioxidant properties. Pomegranate fruit contains 80% juice and 20% seed as edible components (approximately 80% of total fruit weight).

Pomegranate fruit extract contains anthocyanins, which give the fruit and juice its red color, as well as hydrolysable tannins, which account for 92 % of the fruit's anti-oxidant action [35].

Several of the biological effects of pomegranate juice have the potential to be significant in the field of medicine. P. granatum has been shown to have anti-atherogenic, anti-oxidant, anti-tumor, and virucidal properties.

Additionally, this fruit's antibacterial properties have been extensively studied. Oral bacteria and Candida albicans appear to be susceptible to the P. granatum extract, according to a number of investigations, including those looking at suppression of adhesion[39–41].

► *essential oils (EOs)*

EOs are chemically complex, natural compounds produced by aromatic plants with promising biological properties.

Mint, eucalyptus, lemon, thyme, and tea plant essential oils have been shown to be antifungal, notably against Candida spp. There are occasions when using essential oils (EOs) near the skin might result in an undesired reaction, such as irritation or contact sensitivity.

A variety of testing procedures and cell line sources and samples have resulted in inconsistencies in the toxicity statistics for EOs. A 50% decrease in cell survival at 20–2700 g/ml has been seen during studies on M. alternifolia toxicity.

Cancer cells are cytotoxic to C. limon at a concentration of 25.57 g/ml, while the IC50 range for T vulgaris is 76.02–180.4 ng/ml.

Studies on the antifungal potential of EOs against Candida spp. are sparse, in part because the antifungal actions of EOs do not correspond to a particular pathway exclusively.

Since plant extracts as antifungal medicines have not yet been fully accepted, optimizing and validating antifungal activity is the first stage in the acceptance process.

RSM and ANN have recently been offered as effective methods for the creation, enhancement, and optimization of many biochemical processes, including as the synthesis of enzymes.

We know that medicinal plants' biological activity is dependent on their chemical composition and that this activity is correlated with the existence of one or more secondary metabolite categories.

According to these findings, the most effective EO would have the highest terpene concentration. However, the study found that EOs containing the most terpenes did not have the greatest antifungal effectiveness.

It is possible that EO and Candida spp. have complicated chemical interactions, and that synergism and antagonism might occur amongst EO components. This conclusion is surprising.

Only 300 of the more than 3000 EOs that have been investigated are currently available for sale in different forms. Essential oils (EOs) are made up of a wide range of chemicals, such as sesquiterpenes, monoterpenes and their oxygenated derivatives such oxides, phenols, ketones, esters, aldehydes and nitrogen- or sulfur-containing molecules.

In fennel and anise EO, anethole has been identified as one of the active principles and displayed various biological actives including, anti-inflammatory activity.

There are several phytochemical components, such as terpenoids, that are responsible for the EO's potent effect. Recently, the antioxidant potential of Origanum majorana L. EO was studied by Olfa et al.

Due to the presence of monoterpenes such as oxygenated monoterpenes linalool and alpha-terpineol, this medicinal herb has an anti-oxidant effect. These oxygenated monoterpenes outperformed sesquiterpene hydrocarbons in terms of activity.

The EO of medicinal plants showed antibacterial activity against food borne bacteria and also has antioxidant activities.

P. aeruginosa was suppressed by 0.5 percent (v/v) of cinnamon bark oil and cinnamaldehyde essential oil.

Cinnamon bark oil and eugenol also suppressed the production of pyocyanin and 2-heptyl-3-hydroxy-4 (1H)-quinolone, as well as the swarming motility and hemolytic activity of P. aeruginosa. Enterohemorrhagic E. coli 0157: H7 biofilm development was also suppressed at 0.01 percent (v/v) of cinnamon bark oils and active components (cinnamaldehyde and eugenol).

Almeida et al. demonstrated the anti-Candida and antibiofilm efficacy of two essential oils from Cymbopohon winterianus (citronella) and Cinnamon cassia (cinnamon).

A substantial reduction in viable bacteria and biofilm buildup was seen at 0 hours with both oils. However, by 48 hours, there was no difference between the biofilms that had been treated and those that hadn't.

It has been shown that the essential oil of Origanum vulgare possesses bactericidal and fungicidal properties, which may be linked to the chemicals carvacrol and thymol, which are the phenolic components present in large quantities in some essential oils, such as the Origanum vulgare.

Some essential oils have been shown to inhibit the growth of Candida species, including C. albicans, but with a significant degree of susceptibility, which suggests that fungicides may have disadvantages over anti-enzymatic compounds, especially antiphospholipathics, which would reduce the virulence of the strains, allowing a smaller number of infections of this type.

When working with plant-based goods, it's important to keep an eye out for changes in the chemical makeup of the essential oil, which might influence its pharmacological qualities and antibacterial activity [17]. Because of the wide variety of species, pests, soil conditions, harvest time, geographic location, climate, and growing circumstances, the composition and concentration of Origanum essential oil components can vary widely.

It is also important to note that the drying process of oregano, extraction methodology, and anatomical portion of the plant utilized for extraction all have an impact on the essential oil output and composition.

However, our knowledge on oral bioavailability of oregano phytochemicals and products as well as on their safety, side and adverse effects, toxicological risks and interactions with pharmaceuticals is still scanty [32].

This suggests that natural oils don't block proteinase and phospholipase inhibition by expression since they don't appear to target fungal metabolic or biosynthetic activities. Protease inhibitors were observed to have no effect on Candida growth on complex medium (e.g. Sabouraud and YPD) where Sap synthesis is not necessary for nitrogen supply and growth.

CONCLUSIONS

Against this background, some phytomedicines can be suggested for the treatment of the candidal infection and consequently for DS.

Nevertheless, further research is needed in order to clarify the antifungal mechanism of these extracts under different conditions. In addition, further clinical studies are required before they are used.

Current opinion is that for their safe use, it is important to have standardized preparations of medicinal plant medications, which may be less toxic than many synthetic medicines.

REFERENCES

1. Shivraj HN, Arti SN, Young-Soo K. Total phenolics, antioxidant, antitumor, and enzyme inhibitory activity of Indian medicinal and aromatic plants extracted with different extraction methods. Biotech 2017;7:76—86.
2. Carvalho PHA, Duval AR, Leite FM, Nedel F, Cunico W, Lund RG. (7-Chloroquinolin-4-yl)arylhydrazones: Candida albicans enzymatic repression and cytotoxicity evaluation. Part 2. J Enz Inhib and Med Chem (Online) 2016;31:126—31.
3. Frohner IE, Bourgeois C, Yatsyk K, Majer O, Kuchler K. Candida albicans cell surface superoxide dismutases degrade host-derived reactive oxygen species to escape innate immune surveillance. Mol Microbiol 2009;71:240—52.
4. Enfert CD, Hube B. Candida: comparative and functional genomics. Norfolk, U.K: Caister Academic Press; 2007.
5. Felk A, Kretschmar M, Albrecht A, Schaller M, Beinhauer S, Nichterlein T, Sanglard D, Korting

HC, Schäfer W, Hube B. Candida albicans hyphal formation and the expression of the Efg1-regulated proteinases Sap4 to Sap6 are required for the invasion of parenchymal organs. Infect Immun 2002;70: 3689—700.

6. Phan QT, Myers CL, Fu Y, Sheppard DC, Yeaman MR, Welch WH, Ibrahim AS, Edwards JE, Filler SG. Als3 is a Candida albicans invasin that binds to cadherins and induces endocytosis by host cells. PLoS Biol 2007;5:64.
7. Schaller MA, Lundy SK, Huffnagle GB, Lukacs NW. CD8+ T cell contributions to allergen induced pulmonary inflammation and airway hyperreactivity. Eur J Immunol 2005;35:2061—70.
8. Oliveira SGD, Lund RG, Pereira CMP, Piva E. Anti-candida and anti-enzyme activity and cytotoxicity of 2-phenyl-4H-chromen4-one. Afr J Microbiol Res 2016;10:219—24.
9. Barros LM, Boriollo MF, Alves AC, Klein MI, Gonçalves RB, Höfling JF. Genetic diversity and exoenzyme activities of Candida albicans and Candida dubliniensis isolated from the oral cavity of Brazilian periodontal patients. Arch Oral Biol 2008;53:1172-8.
10. Kadir T, Gümrü B, Uygun-Can B. Phospholipase activity of Candida albicans isolates from patients with denture stomatitis: the influence of chlorhexidine gluconate on phospholipase production. Arch Oral Biol 2007;52:691-6.
11. Budala DG , Baciu ER , Surlari Z, Balcos, C , Virvescu DI . Interim Crowns Of Pmma And Bis-Acryl Resin And Their Colour Change In Various Conditions-A Comparative Study, Romanian Journal of Oral Rehab., 2021;13(2):231.
12. Wu T, Samaranayake LP, Cao YB, Wang J. In-vitro proteinase production by oral Candida albicans isolates from individuals with and without HIV infection and its attenuation by antymycotic agents. Jour Med Microbiol 1996;44:311-6.
13. Lyon JP, dos Santos FV, de Moraes PC, Moreira LM. Inhibition of virulence factors of Candida spp. by different surfactants. Mycopath 2011;171:93-101.
14. Price MF, Wilkinson LD, Gentry LO. Plate method for detection of phospholipase activity in Candida albicans. Sabour 1982;20: 7-14.
15. Koga-Ito CY, Lyon JP, Vidotto V, de Resende MA. Virulence factors and antifungal susceptibility of Candida albicans isolates from oral candidosis patients and control individuals. Mycopathology 2006;161:219—23.
16. Bosinceanu DN , Bosinceanu, DG , Bolat, M , Baciu, R , Forna N . Flexible Acrylate Versus Classic-Viable Therapeutical Solution, Romanian Journal of Oral Rehab., 2017;8(1):7-11.
17. Lima IO, Oliveira RAG, Lima EO, Farias NMP, de Souza EL. Antifungal activity from essential oils on Candida species. Braz J Pharmac 2006;16:197—201.
18. Cleff MB, Meinerz AR, Faria RO, Xavier MO, Santin R, Nascente PS, Rodrigues MR, Meireles MCA. Inhibitory activity of origanum essential oil against important fungus in veterinary. Arq Bras Med Vet Zootec 2010;62:1291—4.
19. Leyva-López N, Gutiérrez-Grijalva EP, Vazquez-Olivo G, Heredia JB. Essential Oils of Oregano: Biological activity beyond their antimicrobial properties. Molecules 2017;22:989.
20. Uygun-Can B, Kadir T, Gumru B. Effect of oral antiseptic agents on phospholipase and proteinase enzymes of Candida albicans. Arch Oral Biol 2016;62:20—7.
21. Bobichan H, Bouchet P. Action of chlorhexidine on budding Candida albicans: scanning and transmission electron microscopic study. Mycopathol 1987;100:27—35.
22. Hiom SJ, Furr JR, Russell AD, Dickinson JR. Effects of chlorhexidine diacetate and cetylpyridinium chloride on whole cells and protoplasts of Saccharomyces cerevisiae. Microbios 1993;74: 111—20.
23. Hiom SJ, Russell AD. Uptake of 14C-chlorhexidine gluconate by Saccharomyces cerevisiae, Candida albicans and Candida glabrata. Lett Appl Microbiol 1995;21:20—2.

24. D'Arcangelo G, Barile M, Passarella S, Quagliariello E. Uncoupling of mitochondrial oxidative phosphorylation by hexetidine. Biochem Biophys Res Commun 1987;147:801—8.
25. Guillen J, Bernabeu A, Shapiro S, Villalain J. Location and orientation of triclosan in phospholipid model membranes. Eur Biophys J 2004;33:448—53.
26. Thomas S, Tsang CSP, Mathew A, Bhaskar S, Priya SP. A study on exoenzyme activities of Candida albicans isolated from oral cavities of HIV-infected patients on HAART. J Hum Virol Retrovirol 2015;2:1—5.
27. Bosinceanu DN, Sandu IG , Bisinceanu DG, Forna NC. Study of Candida albicans Colonies on a New Polymer used to Create Complete Dentures. I Rev Chimie, 2014;65(4): 466-469.
28. Samaranayake YH, Dassanayake RS, Cheung BP, Jayatilake JA, Yeung KW. Differential phospholipase gene expression by Candida albicans in artificial media and cultured human oral epithelium. APMIS 2006;114:857—66.
29. Spagnoletti A, Guerrini A, Tacchini M, Vinciguerra V, Leone C, Maresca I, Simonetti G, Sacchetti G, Angiolella L. Chemical composition and bio-efficacy of essential oils from italian aromatic plants: Mentha suaveolens, Coridothymus capitatus, Origanum hirtum and Rosmarinus officinalis. Nat Prod Commun 2016;11:1517—20.
30. Bolat M , Bosinceanu DG , Sandu IG , Bosinceanu DN , Surlari Z , Balcos C , Solomon O , Vitalariu A . Comparative Study on the Degree of Bacterial Biofilm Formation of Dental Bridges Made from Three Types of Materials, Mater.Plastice, 2019;56(1):144-147.
31. Hussain AI, Anwar F, Rasheed S, Nigam PS, Janneh O, Sarker SD. Composition, antioxidant and chemotherapeutic properties of the essential oils from two Origanum species growing in Pakistan. Braz J Pharmacogn 2011;21:943—52.
32. Begnini KR, Nedel F, Lund RG, Carvalho PHD, Rodrigues MRA, Beira FTA, Del-Pino FAB. Composition and antiproliferative effect of essential oil of Origanum vulgare against tumor cell lines. J Med Food 2014;17:1129—33.
33. Pina G, Lia EN, Berretta AA, Nascimento AP, Torres EC, Buszinski AFM, et al. Efficacy of propolis on the denture stomatitis treatment in older adults: a multicentric randomized trial. Innov Aging 2017;1(Suppl.1):398.
34. Pinelli LA, Montandon AA, Corbi SC, Moraes TA, Fais LM. Ricinus communis treatment of denture stomatitis in institutionalised elderly. J Oral Rehabil 2013;40:375-80
35. Santos VR, Pimenta FJ, Aguiar MC, do Carmo MA, Naves MD, Mesquita RA. Oral candidiasis treatment with Brazilian ethanol propolis extract. Phytother Res 2005;19:652-4.
36. Santos VR, Gomes RT, de Mesquita RA, de Moura MD, Franca EC, de Aguiar EG, et al. Efficacy of Brazilian propolis gel for the management of denture stomatitis: a pilot study. Phytother Res 2008;22:1544-7.
37. Sefidgar SAA, Moghadamnia A, Tafti AA, Sahebjami M, Heydari M, Motallebnejad M. Evaluation of the effect of Artemisia sieberi mouthwash 1% on denture stomatitis (a preliminary study). Casp J Intern Med 2010;1:47-9.
38. Bosinceanu DG ,Sandu IG ,Bosinceanu DN, Martu I, Surlari Z ,Forna NC . Clinical Use of a New Polymer in Complete Dentures Fabrication (I), Mater.Plastice, 2018;55(3):423-425.
39. Soares DGS, de Oliveira CB, Paulo MQ, Carvalho MFFP, Padilha WWN. Clinical and microbiological evaluation of the treatment of denture stomatitis with Schinus terebinthifolius Raddi (Aroeira) tincture. Pesqui Bras Odontoped Clin Integr 2010;10:365-70.
40. Suarez MCP, Carballo MMR, Cruz EG, Banqueris RF, Núnez IB, Hechavarria LA. Gel de propóleos en el tratamiento de la estomatitis subprotesis con candidiasis asociada. Multimed 2006;10.
41. Tay LY, Jorge JH, Herrera DR, Campanha NH, Gomes BP, Andre Dos Santos F. Evaluation of

different treatment methods against denture stomatitis: a randomized clinical study. Oral Surg Oral Med Oral Pathol Oral Radiol 2014;118:72-7.
42. Vasconcelos LC, Sampaio MC, Sampaio FC, Higino JS. Use of Punica granatum as an antifungal agent against candidosis associated with denture stomatitis. Mycoses 2003;46:192-6.
43. Corona Carpio MH, López Verdecia CA, Duharte Escalante A, Ramón Jimenez R, Tamayo Hernández Y. Efectividad de la tintura de propóleos al 10 % en pacientes con estomatitis subprótesis. MEDISAN 2018;22:863-74.