Effect of Oleuropein on Fungal Infection for Denture Wearers

Ibrahim H. Alfahdawi (ibrahimhm7@yahoo.com)
Al Maaref University College

Wasan Mohammed Alsewuidi
Al Maaref University College

Research Article

Keywords: Oral Infection, Denture stomatitis, Fungal infection, Oleuropein

Posted Date: February 3rd, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1310278/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License
Abstract

**Background:** Oleuropein, the main phenolic element of extra virgin olive oil, is rising in popularity as well as relevance among scientists and the general public.

**Purpose:** Therefore, in this study, the activity of oleuropein, a complicated phenol present in significant levels in olive tree products, against the common fungal pathogen Candida albicans was investigated.

**Procedures:** Oleuropein is administered twice a day for two weeks to the tissue surfaces of dentures.

**Results:** After using oleuropein, the signs and symptoms of stomatitis, such as discomfort, redness, and inflammation, progressively faded. After two days to two weeks, the denture stomatitis healed by using an oleuropein. Patients with denture stomatitis underwent inspection and assessment of the mucosa, Candidal quantification culture, and verification of the disease using three methods: Germ tube, Gram stain, and ChromAgar media after therapy.

**Conclusions:** The use of oleuropein in dentistry is possibly the most methodologically substantiated. Periodontology, mucous membrane pathology, and oral surgery all use oleuropein, orthodontics, and prosthodontics, among other dental professions. It was proven to be significantly high efficient when applied twice a day on the fitting inside surface of the denture base for two weeks.

Introduction

Olive oil contains active substances such as oleic acid, phenolic components, and squalene. Principal phenole components, Extravirgin olive oil's bitterness and pungent flavor come from hydroxytyrosol as well as oleuropein (1). Researchers discovered antioxidant and anti-inflammatory capabilities, as well as hepatoprotection, neuroprotection, hypoglycemic and hypolipidemic effects, and cardiovascular protection. Antiproliferative activities in cell lines, anticancer effects in animals, and antibacterial and antiviral properties have all been reported (2). Oleuropein increases the functional activity of immunocompetent macrophages by triggering the inducible shape for enzyme (nitric oxide synthase), which enhances production of 'nitric oxide' (NO) in macrophage challenge in addition to lipopolysaccharides. Oleuropein has long been recognized to reduce lypoxygenase activity and leukotriene production, making it an anti-inflammatory (3).

Oleuropein inhibits the growth of G⁻ and G⁺ bacteria, and mycoplasma. Oleuropein-like structure of phenol appear for have antibacterial properties via damaging bacterial membranes and/or changing peptidoglycans in cells (4). In vitro, oleuropein showed activities against fungus with a minimum inhibiting concentrations (MIC) for 12.5 mg/mL. Following labeling with fluorescent DNA-binding dyes, morphological changes inside nucleus for investigated treatment of experimental tests with subinhibiting concentration for oleuropein revealed which apoptosis is the major cause for cells dead (5). Oleuropein is discovered for inhibiting Staphylococcus aureus, Bacillus subtilis, as well as Pseudomonas
solanecearum (6). It also inhibits Bacillus megaterium (7) germination and sporulation, as well as the expansion of sprouting Bacillus cereus spores (8).

Mycoplasma hominis, Mycoplasma fermentas, Mycoplasma pneumoniae, and Mycoplasma pirum were all investigated in vitro. Oleuropein suppressed mycoplasmas at dosages ranging from 20 to 320 mg/L (9). Invitro experiments were used for investigate the effectiveness for the phenolic compounds upon Candida albicans, Considering the wide frequency of opportunistic fungal diseases as well as its potential potency, chemical products have considerable antimicrobial effects and might be a potential source of new anti-candidal medicines (10). Although Candida albicans is the most prevalent Candida species to cause invasive. throughout latest years, fungal pathogens effects of non-organisms are now more common (11). A rise in serious human infections caused by fungus in immunocompromised people, as well as a tendency for medication resistance to conventional treatments, necessitated the development of more effective therapy (12). The oil extract of sage was the most effective in inhibiting the studied microorganism, whose effect exceeded the use of chemical gargling lotion Chlorhexidine gluconate and alcoholic extract, which showed a lower rate of inhibition, while the aqueous extract did not show any inhibition of bacterial growth. (13).

Controlling these fungi, which cause pre-and post-harvest diseases in agricultural goods, as well as the detrimental environmental consequences of pesticides used to battle the problem, is a problem that has yet to be solved. The current focus is on creating new microbial control strategies and feasible alternatives, as well as minimizing the overuse of synthetic fungicides, which have a negative impact on the environment as well as human and animal health (14, 15, 16).

*Candida albicans* is a parasitic microbe in the environment which live on healthy people's mucosal surfaces and can cause opportunistic infections if the host is vulnerable. Candida albicans has to be a wide common Candida organism that causes advanced pathogens, but infections caused by non-albican species have become more widespread in recent years (17). A spike in serious human infections caused by fungus in immunocompromised people, as well as a tendency for medication resistance to conventional therapies, triggered that requirement for further successful treatment. Numerous studies have shown that olive leaf extract and its constituents, primarily oleuropein with hydroxytyrosol, have health benefits, including antibacterial and antioxidant properties. The genus, species, strain, and isolation source, as well as the active components in the leaf extracts, may influence antifungal resistance (18, 19, 20, 21). This study looked at on the potential effective for oleuropein, a complex phenol found in high concentrations in olive tree derivatives, on an opportunist fungus *Candida albicans*.

**Procedures**

Oleuropein is an antifungal that is used to prevent contamination of denture stomatitis. Before starting therapy, fungal samples are taken from each patient's palatal mucosa and prosthesis tissue surfaces (30 denture wearers with denture stomatitis). Oleuropein has previously been used for the following purposes: For fourteen days, it was applied twice daily to the tissue surface of the denture. Denture
stomatitis patients are urged following 5 days, then cease therapy as well as waiting for 48 hours prior starting again being evaluated and having their dentures swapped for culture.

After a 48-hour gap from therapy, repeat the culture after seven days. To remove any residue from the previous treatment, the internal of the dental prosthesis surface was thoroughly cleaned by a toothbrush, soap, as well as water before adding Oleuropein. Following treatment, all patients would have a mucous membranes of the palate analysis and evaluation, as well as a candidal quantified culture was taken from the palatal mucosal and the denture’s tissue surface, but were diagnosed to use the three techniques below:

1. Germ Tube (22, 23, 24) (figure 1).
2. Gram Stain (25, 26) (figure 2).
3. ChromAgar media (24) (figure 3).

Results And Discussion

When applied as a topical on the skin, oleuropein is a considerably safer, non-toxic, and non-irritating chemical. Denture stomatitis is a chronic illness affecting denture wearers in the denture-bearing area, particularly under the maxillary prosthesis. To refute the fact that several antifungals fail to cure stomatitis, the results revealed that over the course of 2–14 days, the oleuropein treatment gradually eliminated most stomatitis symptoms, such as redness, bleeding, discomfort, tenderness, and inflammatory till no signs or symptoms were visible (figure 4). Because the causes of denture stomatitis differ, a variety of treatment approaches should be considered, improperly fitted prosthesis, hygienic care, and antimicrobial medication applied topically or systemically are all factors to consider. In the dental laboratory, rough sections of denture tissue surfaces had to be smoothed. The evidence backs up the following statements: Nystatin tablets containing for 2 weeks, 500,000 unit is permitted to dissolve 3 times every day.

Alfahdawi, 2017 (21) discovered similar findings while propolis paste was placed on the inner surface of the denture 3 times a day for 2 weeks to manage prosthesis stomatitis. Nystatin is developed as a pastille or oral solution. To treat denture-related stomatitis, upon the inner surface, miconazole varnishes or gels were administered externally. One application of miconazole varnish or two applications of miconazole gel is effective for two weeks (25, 26). Martins et al., 2002 (27) and Shahin Nejat et al., 2015 (28) investigated an effectiveness of a propolis paste formulation in denture stomatitis patients. Oleuropein was utilized in the clinic to prevent the use of systemic antifungal drugs in nystatin-resistant patients. Itching, as well as concerns Allergic contact dermatitis, for example, must be emphasized like a negative impact. Denture stomatitis is an inflammatory disorder that affects a large number of dental patients as a result of candida infections caused by filthy dentures in addition to trauma.
Although *Candida albicans* was the normal part for the oral microflora, it can become a pathogen due to a variety of local or systemic causes. Once a thorough history is taken, a good diagnosis is made, and predisposing factors are eliminated, denture stomatitis is treated with antifungal medications. In many situations, topical applications of nystatin, amphotericin, miconazole, and other antifungals are beneficial. Systemic ketoconazole, fluconazole, or itraconazole can be used to treat candidiasis since the biofilms are much more susceptible to antifungal drugs. Moreover, several medication interactions are explored in candida-related denture stomatitis to avoid the use of systemic antifungal medications in clinical practice; oleuropein was used. When applied twice a day for 14 days to the fitting inside surface of the denture base, oleuropein was found to be significantly more efficient (figure 4). Juven and Henis in 1970 (29) tested oleuropein, which is abundant in olive leaves, for antifungal activity against Rhodotorula sp., Candida albicans, and Saccharomyces cerevisiae; however, no inhibition effect was observed against such yeasts (29, 30).

**Conclusion**

1. Treated oral disorders such as Rhodotorula ssp., Candida albicans, and S. cerevisiae using the antibacterial action of oleuropein.

2. The use of oleuropein in dentistry is arguably the most well-documented and is presently being used in a variety of studies. Oleuropein is commonly used in Periodontology, oral mucosa pathology, oral surgery, orthodontics, and prosthetics are some of the specialties in dentistry, among other dental disciplines.

3. Oleuropein has been shown to be substantially more effective when applied twice a day for 14 days to the fitting inside surface of the denture base.

**Declarations**

**Ethics Approval and Consent to Participate**

The ethical clearance of verbal informed consent and assent was accepted by the Al-Maaref University College of Dentistry Department, and oral informed consent was received from the study subjects.

**Consent for publication**

Not applicable

**Availability of data and materials**

At this time, the data for this research region cannot be made public. On reasonable request, it will be made available by the respective author.

**Disclosure**
For this paper, the author declares that they have no competing interests.

Funding

None

Author Contributions

The author contributed significantly to the study's conception, design, data, and methodology. The author participated in the writing, rewriting, or critical evaluation of the article; provided final approval of the version to be published; agreed on the journal to which the article was submitted; and agreed to be responsible for all parts of the work.

Acknowledgements

Al-Maaref University College in Anbar, Iraq, is funding the study.

References

1. Fangxue Xu, Yujuan Li, Mengmeng Zheng, Xiaozhi Xi, Xuelan Zhang and Chunchao Han, Structure Properties, Acquisition Protocols, and Biological Activities of Oleuropein Aglycone, Front. Chem., 13 August 2018.

2. Syed Haris Omar, Oleuropein in Olive and its Pharmacological Effects, Sci Pharm. 2010 Apr-Jun; 78(2): 133–154.

3. Carla Marchetti,1 Marco Clericuzio,2 Barbara Borghesi,3 Laura Cornara,3 Stefania Ribulla,2 Fabio Gosetti,2 Emilio Marengo,2 and Bruno Burlando, Oleuropein-Enriched Olive Leaf Extract Affects Calcium Dynamics and Impairs Viability of Malignant Mesothelioma Cells, Evidence-Based Complementary and Alternative Medicine / 2015.

4. Nataša Zorić, Nevenka Kopjar, Ivan Bobnjarić, Igor Horvat, Siniša Tomić, Ivan Kosalec, Antifungal Activity of Oleuropein against Candida albicans-The In Vitro Study, Molecules, 2016 Nov 28;21(12):1631.

5. Semra Topuz, Mustafa Bayram, Oleuropein extraction from leaves of three olive varieties (Olea europaea L.): Antioxidant and antimicrobial properties of purified oleuropein and oleuropein extracts, Journal of food processing and preservation, 07 June 2021.

6. Fleming H.P., Walter W.M., Etchells J.L. Antimicrobial properties of oleuropein and products of its hydrolysis. J. Appl. Microbiol. 1973;26:777–782.

7. Rodriguez M.M., Perez J., Ramos-Cormenzana A., Martinez J., Effect of extracts obtained from olive oil mill waste waters on Bacillus megaterium ATCC, 33085. J. Appl. Bacteriol. 1988;64:219–225.

8. Tassou C.C., Nychas G.J.E., Board R.G., Effect of phenolic compounds and oleuropein on the germination of Bacillus cereus T spores, Biotechnol. Appl. Biochem. 1991;13:231–237.
9. Furneri P.M., Marino A., Saija A., Uccella N., Bisignano G., In vitro antimycoplasmal activity of oleuropein, Int. J. Antimicrob. Agents. 2002;20:293–296.

10. Teodoro G., Ellepola K., Senevirante C.J., Koga-Ito C.Y. Potential use of phenolic acids as anti-candida agents: A review. Front. Microbiol. 2015;6:1420.

11. Sardi J.C.O., Scorzon L., Bernardi T., Fusco-Almeida A.M., Mendes Giannini M.J.S., Candida species: Current epidemiology, pathogenicity, biofilm formation, natural antifungal products and new therapeutic options, J. Med. Microbiol. 2013;62:10–24. 12.

12. Nataša Zorić, Nevenka Kopjar, Ivan Bobnjarić, Igor Horvat, Siniša Tomić, and Ivan Kosalec, Antifungal Activity of Oleuropein against Candida albicans, The In Vitro Study, Molecules. 2016 Dec; 21(12): 1631

13. Ibrahim H. ALFAHDAWI, Wasan Mohammed ALSEWIDI, Sura A. JABER, Comparing the Inhibitory Effectiveness of Salvia Officinalis Extracts and Chlorhexidine (CHX) Mouthwash on Some Oral Bacterial Species, Lat. Am. J. Pharm. 40 (special issue): 210-5 (April 2021)

14. Innocenzo Muzzalupo1,2*, Giuliana Badolati1, Adriana Chiappetta3*, Nevio Picci1 and Rita Muzzalupo,1n vitro Antifungal Activity of Olive (Olea europaea) Leaf Extracts Loaded in Chitosan Nanoparticles, Front. Bioeng. Biotechnol., 03 March 2020

15. Cota-Arriola, O., Cortez-Rocha, M., Burgos-Hernandez, A., Ezquerra-Brauer, J., and Plascencia-Jatomea, M. (2013). Controlled release matrices and micro/nanoparticles of chitosan with antimicrobial potential: development of new strategies for microbial control in agriculture. J. Sci. Food Agric. 93, 1525–1536.

16. Rodriguez-Maturino, A., Troncoso-Rojas, R., Sánchez-Estrada, A., González-Mendoza, D., Ruiz-Sanchez, E., Zamora-Bustillos, R., et al. (2015). Antifungal effect of phenolic and carotenoids extracts from chiltepin (Capsicum annum var. glabriusculum) on Alternaria alternata and Fusarium oxysporum. Rev. Argent. Microbiol. 47, 72–77.

17. Kosenco S.V. and Kosorich Tiu. The Treatment of periodontitis with research. Stomatologia-MOSK,1990;69:27-29.

18. Mathivanan V., et al, A review on Propolis – as Folk Medicine, Indian J. of Scie.2013; Vol. 2 No. 3 Jan.

19. Vijay D. Wagh*and Rameshwar D. Borkar, Indian propolis: a potential natural antimicrobial and antifungal agent. International Journal of Pharmacy and Pharmaceutical Sciences,2012; Vol 4, Issue 4.

20. Seidel V, Peyfoon E, Watson DG, Fearley J. Comparative study of the antibacterial activity of propolis from different geographical and climatic zones. Phytother. Res.2008; 22(9):1256-1263. doi: 10.1002/ ptr. 2480. 7-Velazquez C., Nava

21. Ibrahim Alfahdawi, Effect of Propolis on Fungal Infection for Denture Wearers and Dry Socket, Tikrit Journal for Dental Sciences 5 (2017) 33-39 33

22. Evans E. G. and Richardarson, Medical Mycology a practical a proach. IRL Press ,U.K. 1989;

23. Ron J. Doyle. Biofilms, Methoda in Enzymology, 1999;310: 644- 656.
24. James DB. Biofilms II: Process Analysis and Applications. New York, USA: Wiley-liss. 2000.
25. Odds F.C. Candida and Candidiosis. Leicester University, U.K. 1979.
26. Lucio Milillo, Lo. Muzio L, Carlino P., Serpico R., Coccia E., Scully CCandida related Denture Stomatitis
A pilot study of the efficacy of an amorolfine antifungal varnish, Int. J. Prosthodont . . 2005; 18(1): 55-59.
27. Martins RS., Pêreira ES. Jr., Lima SM., Senna MI., Mesquita RA., Santos VR. Effect of commercial
ethanol propolis extract on the in vitro growth of Candida albicans collected from HIV-seropositive
and HIV-seronegative Brazilian patients with oral candidiasis. J. Oral Sci. 2002; 44(1): 41-48.
28. Shahin Nejat, Abdollah Ghasemi Pirbaluti, Masoud Yazdani and Maryam Foroughi, In Vivo
Antifungal Activity of Some Medical Herbs and Propolis against Fungal pathogens Associated with
Ringworm, International Conference on Chemical, Environmental and Biological Sciences (CEBS-
2015) 2015;March 18-19, Dubai (UAE).
29. Juven B., Henis Y. (1970). Studies on antimicrobial activity of olive phenolic compounds. J. Appl.
Bacteriol., 33: 721-732.
30. Zorić N., Kopjar N., Oršolić N., Tomic S., Kosalec I. Olive leaf extract activity against Candida
Albicans and C. dublieniensis—The in vitro viability study. Acta Pharm. 2016;66:411–421.

Figures

Figure 1

Germ tube
Figure 2
Gram stain

Figure 3
ChromAgar media

Figure 4
Sensitive of *Candida Albicans* to oleuropein