

Comparison of the Effects of Miconazole and Propolis in the Treatment of Candida-Associated Denture Stomatitis

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Abstract PURPOSE: This study compared between the efficiency of propolis and miconazole gel as treatment modalities for Candida-associated denture stomatitis. **MATERIALS AND METHODS:** 20 patients suffering from Candida-associated denture stomatitis were divided into two treatment groups: Group I (control group): 10 patients received 20mg/g miconazole oral gel and Group II (study group): 10 patients received Bio-Propolis Capsules 2% (20mg/g). The patients were asked to use the miconazole oral gel or the propolis powder twice a day for 14 days. Examination was done on 1st, 7th and 14th days. Newton's criteria were used to classify the Pre-treatment and post-treatment (CHRO Magar Candida®) and counted through the colony forming unity count (CFU/mL). The intragroup comparison before and after each treatment was done using the Wilcoxon's test while the Kruskal-Wallis's test was used to compare the results of the two treatment groups. **RESULTS:** there was a considerable decrease or total cure of denture stomatitis ($P < 0.05$) and a remarkable reduction of the number of Candida colonies in the two groups. Intergroup comparison revealed that no difference existed between both groups. Newton's score were reduced in the two groups signifying the efficiency of both treatments. **CONCLUSION:** propolis powder has an antifungal activity similar to miconazole, in the treatment of Candida-associated denture stomatitis. Propolis is a safe, inexpensive, natural substance without any known side effects until now. It may therefore be safely to treat Candida-associated denture stomatitis.

Keywords: candida-associated denture stomatitis, miconazole gel, propolis

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1. Introduction

Candidiasis is the most common oral fungal infection [1,2]. *Candida albicans* is the most commonly species found in the infection sites. However, other species such as *C. tropicalis*, *C. dubliniensis*, *C. glabrata*, *C. parapsilosis*, *C. krusei*, and *C. guilliermondii* are found as well [2,3]. Its transformation from commensal into opportunistic pathogen takes place as a result phenotypic changes, production of hydrolytic enzymes, and epithelial adherence, morphogenesis. The fungus pathogenic mechanisms and the development and progress of infection are resisted by the immune defense of the host and local defense responses [3,4]. Corticosteroid therapy, premature birth, diabetes, chemotherapy, HIV infection, prolonged intake of antibiotics, hyposalivation, bad oral hygiene and continuous use of removable dentures are well known predisposing factors of oral candidiasis.

Continuous use of removable dentures and wearing the denture at night can lead to erythematous inflammation of

the mucosa of the palate. Its intensity varies from small red spots to generalized papillary palatal hyperplasia. The prevalence of denture stomatitis among removable denture wearers is about 58–88% [1,2,5]. Porosities or cracks in the denture acrylic resin can exaggerate the condition as it act as a reservoir for fungal colonies [1,2,6,7].

Meticulous denture hygiene, decreasing the general and local factors with antifungal therapy represent an efficient approach in denture stomatitis treatment. Polyenic derivatives (nystatin, fluconazole) and Imidazole related compounds (miconazole) are the most familiar antifungal drugs applied to treat Candida-associated denture stomatitis [8,9,10,11].

Miconazole is a topical oral antifungal with excellent prophylactic and therapeutic effect in the treatment of Candida-associated denture stomatitis, decreasing erythema [2,12] and reducing the *Candida* spp colonies [8,10]. On the other hand, different studies represented rapid recurrence and treatment failure after stopping of the treatment, and absence of appropriate denture hygiene measures [13]. Other draw backs include antifungal toxicity and drugs resistance [6,14,15,16]. So, propolis as a natural product gained special attention.

Propolis is a resinous substance collected from a variety of plants by bees, so its origin area controls its chemical composition [17,18]. Propolis extract includes a broad range of ingredients such as phenolic acids and flavonoids. Flavonoids as pinocembrin, has inhibitory effect on *Candida* [19].

Oral or topic application of propolis extract is a safe, non cytotoxic method without any mutagenic possibility [20,21]. In addition, propolis extract has anti-inflammatory [21,22], antiulcer [23], wound healing, antimicrobial [24,25], and fungicidal activities [16,26,27,28,29].

Denture stomatitis can be cured with the use of alcoholic extract of propolis 20% [28]. But, it has no muco-adhesive qualities and may irritate the oral mucosa. The 1% alcoholic extract of propolis was enough to restrain the *Candida* growth in an Invitro study [27,30,31].

This study aimed to compare propolis powder and miconazole gel (20mg/g), through pre and post treatment (CFUs) No. and Newtons classifications.

2. Materials and Methods

20 complete denture patients suffering from *Candida* associated denture stomatitis, diagnosed through microbiologic cultures from their erythematous palatal mucosa, were included in this study. Patients, who recently used antibiotics and/or antifungals (in the past 2 months) or received any drugs causing xerostomia or hyposalivation or had history of radiotherapy in the head and neck region, were excluded from this study.

Patients were registered at the specialty clinics of Faculty of Dentistry, Taif University between January 2015 and June 2016. This study was approved by Research and Ethics Committee in the Faculty of Dentistry, Taif University. All participants were informed about the objectives of the study and signed the consent form before the start of the study.

On the first day (T0), patients' personal data including past medical and denture histories, habits such as wearing denture during, dentures duration, and denture hygiene were collected. After that all of them were educated and motivated about denture hygiene, the present denture were examined for the presence of *Candida* colonies or other superimposed infection, calculus and acrylic cracks or porosity (Figure 1).



Figure 1. Denture examined for *Candida* or calculus or acrylic cracks.

Intraoral examination was done after removal of the prosthesis through artificial lighting, on the first day (T0), 7 days after the first examination (T7) and 2 weeks after the first examination (T14). The presence of erythematous spots or areas, with or without papillary hyperplasia, was observed in the hard palates. (Figure 2 a, b)



(a) Generalized



(b) Localized

Figure 2. Erythematous spots with or without papillary hyperplasia.



Figure 3. Pre-treatment fungal colonies on Sabouraud dextrose.

Swabs were collected from the palatal mucosa of all patients and aerobically incubated at 28°C on Sabouraud dextrose agar (Difco) containing (100 mg/L) chlo-

ramphenicol. Before isolation the CFUs number and morphological characteristics were detected. After 48 hours, species were isolated and identified in a germ-tube test with positive diagnose of *Candida albicans* (Figure 3).

Newton's classification [32] was used to classify denture stomatitis into Class I (points of hemorrhagic petechiae or localized inflammation of the palatal mucosa); Class II (more diffuse erythema involving part or all of the area covered by the prosthesis); and Type III (erythema associated with papillary hyperplasia in the area covered by the prosthesis).

Patients with identified *Candida* associated denture stomatitis were allocated into 2 groups; (control group) Group I ($n = 10$; mean age 58.8 ± 4.54 years; 7 women and 3 men) treated with topical application of 2% miconazole gel. Group II ($n = 10$; mean age 59.1 ± 5.04 years; 8 women and 2 men) was treated with topical application of propolis Powder. All patients were educated to carry out oral and denture hygiene.

For Group I, the patients were instructed to sprinkle 0.12% chlorhexidine digluconate solution on fitting surface and denture borders, remove excess and apply a thin layer of miconazole oral gel 20mg/g. (Figure 4).

For Group II, the patients were instructed to thoroughly clean the denture and leave it wetted. The Bio-Propolis capsules were opened and the powder was applied very lightly and evenly onto denture fitting surfaces (Figure 5). Any excess powder was thoroughly shaken off. Then the

denture was firmly pressed into place, and bitten down for a few seconds to secure hold (Figure 6). To remove the dentures, the patient was instructed to swish mouth with water, slowly remove dentures using a rocking motion, wipe powder residue from gums and dentures with a soft, moist cloth and apply denture cleanser to thoroughly clean your dentures. The medication applications were applied twice a day for 14 days. Prosthetic maintenance and oral hygiene were followed, and the patients were instructed to remove the prosthesis during the sleep period and put it in a glass of water. After one week all patients were instructed to return to reexamine to validate any treatments intolerance and denture hygiene (T7) (Figure 7). After 14 days of treatment, a second classification for denture stomatitis (T14) was done, new photos were taken, and new swabs of palatal mucosa were collected in the same manner (Figure 8).

The miconazole gel and propolis Powder were weighed before the study (T0), on day 7 (T7) and at the end of the study protocol (T14), to evaluate the adherence to treatment. Patients who consumed more than 5g of the product during treatment were considered as adherents.

Wilcoxon's test was applied to compare the results of clinical classification of the denture stomatitis and the *Candida* spp. colonies number, before and after each treatment while the Kruskal-Wallis's test compared the results of the two treatment groups. The findings were considered significant at $P < 0.05$.



Figure 4. Thin layer of miconazole oral gel 20mg/g. applied to the denture fitting surface.



Figure 5. Propolis capsule opened and sprayed over the wetted denture fitting surface.



Figure 6. Patient instructed to bite down for a few seconds to secure the wetted powder in the denture fitting surface.

3. Results

Denture hygiene measures were followed by all denture wearers in a similar way. Past denture history revealed that the patient used their current dentures for a period ranged from 3 months to 10 years. The age of these patients was 52 -68 years old (mean age 58.95 ± 4.67). There were 15 females (75%) and five males (25%). Newton's classification and the total count of CFUs before and after the treatment with miconazole gel (Group I) and propolis powder (Group II) are summarized in [Table 1](#) and [Table 2](#) respectively. There was significant decreasing or

complete cure of denture stomatitis ([Figure 7](#), [Figure 8](#)) and reduction or elimination of yeast count in the two treatment groups. Comparing the two groups there were no statistical differences either for decrease or disappearance of palatal erythema ($P = 0.12$) or to decrease or elimination of CFUs ($P = 0.89$) ([Figure 9](#)). There were no relation between the severity of erythematous lesion, according to Newton's classification and the number of CFUs. All the patients with persistent denture stomatitis and some CFUs after treatments were instructed to maintain application of their treatment for another 14 days in the same manner.



Figure 7. T7 Results.

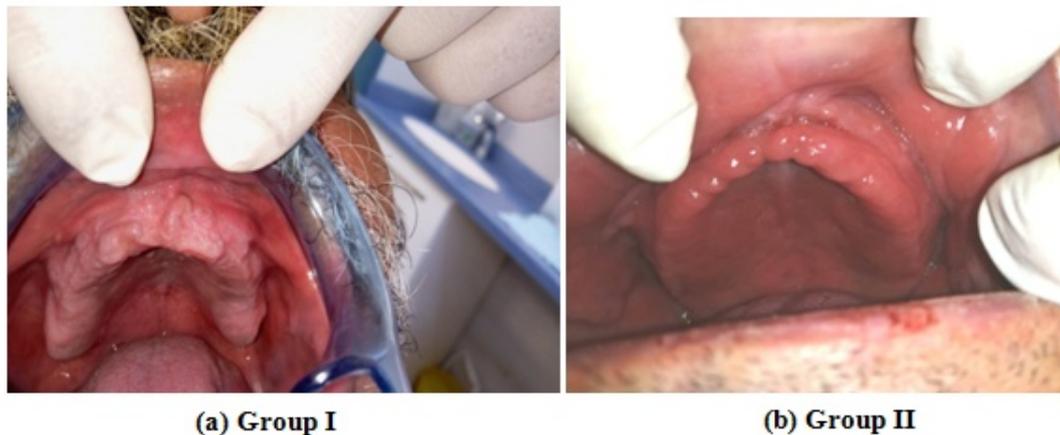


Figure 8. T14 Results.

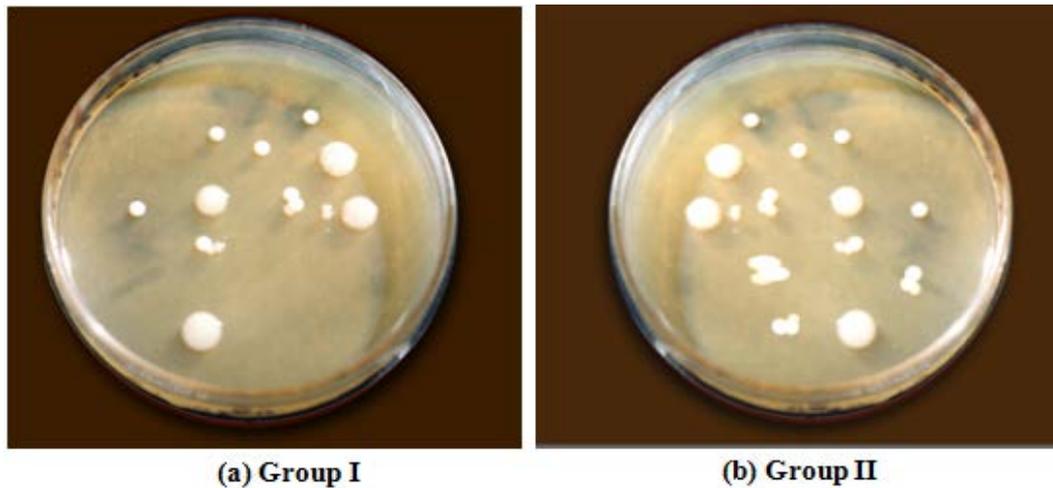


Figure 9. Post-treatment fungal colonies on Sabouraud dextrose.

Table 1. (CFUs) No. and Newtons classification in Group I

Patient	Age	Gender	CFUs No. Before treatment	CFUs NO. After treatment	Newtons classification Before treatment	Newtons classification After treatment
1	58	F	110	0	II	Cure
2	55	M	275	1	III	Cure
3	52	F	20	0	II	I
4	66	F	25	0	I	Cure
5	59	F	16	0	I	Cure
6	62	F	24	0	III	III
7	56	M	235	1	I	Cure
8	60	F	28	1	III	III
9	55	M	24	0	I	I
10	65	F	26	0	III	III

*CFUs: colony-forming units. **Newtons classification (type: I; II; III).

Mean age: (58.8 ± 4.54) Years

Wilcoxon's test (P = 0.0009).

Wilcoxon's test (P = 0.00088).

Table 2. (CFUs) No. and Newton classification in Group II

Patient	Age	Gender	CFUs No. Before treatment	CFUs NO. After treatment	Newtons classification Before treatment	Newtons classification After treatment
1	56	F	75	0	I	Cure
2	68	M	82	2	I	Cure
3	57	F	90	0	II	Cure
4	64	F	150	8	I	I
5	54	F	50	6	II	II
6	52	F	300	91	II	I
7	64	F	200	2	II	I
8	60	F	15	0	III	Cure
9	56	M	565	0	III	I
10	60	F	60	20	II	I

* CFUs: colony-forming units. **Newtons classification (type: I; II; III).

Mean age: 59.1 ± 5.04 Years.

Wilcoxon's test (P = 0.0006).

Wilcoxon's test (P = 0.0032).

4. Discussion

15 female and 5 male patients shared in this study which was in agreement with other studies presenting upper incidence of denture stomatitis among women

[13,29,35], this may be explained that women seek for management or better health care than men and due to hormonal differences [38,39].

The relation between quality of complete dentures and the time limit for the use of the same removable is not

clear; there is a significant relationship between the time of use of prosthesis and oral candidiasis [40]. Cabrini et al 2008 assessed the influences of the time of use and the overall quality of the prostheses, and concluded that it is difficult to generalize the use full life in a period of 1 to 10 years [41].

The presence of irregularities in denture acrylic represent a reservoir for adherence and colonization of *Candida* sp. [2,13,35,42]. Twelve out of the 20 patients included in this study exhibited a history of continuous wearing of the denture during sleeping favoring the reduction of salivary flow and the development of denture stomatitis [2,13,43]. The drug treatment alone is not effective but the denture surface should be disinfected and cleaned using mechanical brushing, and chemical detergents to reduce microorganisms [13,44]. The prosthesis was decontaminated with 0.12% chlorhexidine digluconate spray to remove biofilm and prevent *Candida albicans* colonization [29,45], however the exposure time should be greater than 30 minutes to be effective [45].

Propolis in this study produced an efficient clinical cure, but without decreasing the CFUs; this means that its anti-inflammatory effect overlapped its antifungal action; this was in agreement with the study of Berretta et al [25]. The antifungal effect of propolis was affected by its concentration [46]. In this study, the concentration of propolis was safe and did not induce antifungal action; the treatment time or use of higher concentrations.

There were no clear correlation between CFU reduction and clinical healing or improvement of the lesion; some patients with a higher CFUs number showed clinical curing, while others showed little clinical improvement with a reduction in the CFUs number.

Patient adherence to treatment is essential to clinical improvement; the non-adherent patient may undergo side effects, drug interactions and microorganism resistance [15,16,47].

Miconazole can be considered the ideal topical antifungal for the treatment of oral candidiasis in healthy patients. While, it's long term application may causes resistance [15,48]. While propolis demonstrated antifungal action by at least three mechanisms making it is difficult to develop microbiological resistance [49].

The clinical improvement in this study was similar in both. This was in contrast to Zhang et al 2016 who found that Miconazole has more clinical efficiency than propolis [47].

5. Conclusions

Propolis powder has an antifungal activity similar to miconazole, in the treatment of *Candida*-associated denture stomatitis. Propolis is a safe, inexpensive, natural substance without any side effects until now. So, it can be used to treat *Candida*-associated denture stomatitis.

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