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CASO CLÍNICO

EFFECT OF ACTIVE OXYGEN-RELEASING AND LACTOFERRIN FOAM ON *Candida* SPECIES ASSOCIATED DENTURE STOMATITIS: A CASE SERIES.

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ABSTRACT

Purpose: To assess the effect of active oxygen-releasing and lactoferrin foam (Blue®m foam) on Denture stomatitis (DS) associated with *Candida* spp., highlighting the interaction of its active ingredients, at slowly releasing therapeutic concentration (<1%) in affected tissues, exerting antifungal, regenerative, and healing effects at the cellular level, and disinfectant action on inert surfaces. **Materials and methods:** observational, descriptive pre-clinical study involving 10 patients. Protocol consisted of two daily applications of 2 pumps of Blue®M foam for 30 days, combined with daily oral hygiene. **Results:** The average age of patients was 64.5 years, with a female preponderance (80%). Poor oral hygiene was observed in 90% of cases. *Candida albican*s was found in 80% of cases, and *Nakaseomyces grabratus* in 20%. Clinical evaluation showed successful healing in 70% of patients. **Conclusions:** This study is groundbreaking in assessing the efficacy of active oxygen and lactoferrin foam, Blue ® M, in treating DS.

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It proved effective in DS associated with *Candida* spp., supporting its use as an alternative treatment. Patients reported satisfaction with the care process and the achieved outcomes.
Keywords: Denture stomatitis, *Candida* spp., lactoferrin, Active oxygen.

INTRODUCTION

Denture stomatitis (DS) is characterized by the presence of erythematous lesions, occasionally accompanied by multiple papules on the mucosa underlying the inner surface of removable dental prostheses[1,2]. This condition predominantly affects the palatal mucosa, with a prevalence of up to 72% in prosthesis-wearing patients[3]. Most commonly, DS is caused by *Candida* species (spp).[4] From a clinical perspective, it is classified according to Newton's[5,6] into three types: Type I, which is a simple localized inflammation; Type II, presenting as a diffuse edematous erythema in the oral mucosa contacting the prosthesis; and Type III, characterized by papular lesions on the palatal mucosa[7]. The treatment is primarily based on clinical-microbiological diagnosis and therapeutic strategies. This includes mechanical and chemical cleaning to address or eliminate causal factors, ranging from the use of topical rinses to the administration of oral antifungal medications[8]. The most common methods are mechanical, using brushes and toothpaste to remove biofilm from the prosthetic surface, and chemical, employing various disinfectant substances[9]. Papadiochou S et al.,[10] divides cleaning systems based on their chemical components and mechanism of action into: alkaline peroxides, alkaline hypochlorites, acids, disinfectants, and enzymes. In the quest for products that do not affect the prosthesis surface, new lines of research are needed to reduce *Candida* aggregation and promote healing of the affected tissue. An example of this is treatment

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with active oxygen. Researchers in the Netherlands have developed a formula of active oxygen and lactoferrin (Blue®m), which has shown promising results. This formula, including sodium perborate, glucose oxidase enzyme derived from honey, xylitol, and lactoferrin, releases oxygen at a therapeutic concentration (<1%) in the affected tissues[11]. In addition to its antimicrobial and anti-inflammatory properties, this product prevents the formation of dysbiotic biofilm and improves wound healing rates in various dental applications, including inflammation, traumatic ulcers, peri-implantitis, and cellular regeneration, among others[12-14, 15]. Similarly, Pawar S et al. demonstrate the protective effect of lactoferrin against oral infection by *Candida albicans*[16]. On the other hand, Guttentag A et al., [17] demonstrated in their study that honey derivatives have potent antifungal activity, inhibiting conidial germination and damaging hyphal structures. Chan A et al., [18] reported that xylitol has an inhibitory effect on the formation of *Candida albicans* biofilms. However, more studies are needed to evaluate patient experience, antifungal effects, and wound healing. The aim of the present study is to assess the effect of active oxygen and lactoferrin foam (Blue®m) on *Candida* spp. associated DS.

MATERIALS AND METHODS

Observational, descriptive, pre-clinical study conducted in collaboration with Prosthesis Clinic I and II of the Faculty of Dentistry at José Antonio Páez University, Valencia, Venezuela and the Mycology Laboratory of the Dr. “Jacinto Convit Biomedicine Institute”, Caracas, Venezuela. Ten patients of both genders with a clinical diagnosis of DS and positive mycological culture were

evaluated. Written informed consent was obtained. Clinical epidemiological information, including age, gender, personal history, and clinical presentation, was collected using a data collection instrument. Patients undergoing chemotherapy and radiotherapy of the head and neck, Sjögren's syndrome, Alzheimer's disease, and those who did not accept informed consent were excluded. This study was approved by the Biomedicine Instituted "Dr. Jacinto Convit" Bioethics Committee.

Clinical procedures for the diagnosis of DS and sample collection

The clinical diagnosis of DS was performed by an oral medicine specialist, following the criteria established by McReynolds DE et al[19]. To document the extent of the lesion, a photographic record was employed using a Canon® EOS Rebel T6 camera. In addition, details related to the denture, such as the type of prosthesis, age, and material used in its fabrication, were recorded. Sample collection was performed using a Culturette applicator (AMIES® Transport Medium), swabbing the surface of the affected palatal mucosa. The collected sample was cultured on selective agar media, such as Sabouraud dextrose agar or Lactrimel agar. There were used both selective agar media in this study to enhance the probability of growth, and there were used 2 to 4 tubes of each.

Mycological Study

A small amount of the sample was taken from the Culturette and placed on a glass slide, stained with a drop of black chlorazol, and observed under a conventional light microscope for the detection of fungal structures. Additionally, the samples were cultured on Sabouraud agar and

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Lactrimel agar, supplemented with chloramphenicol. They were incubated at 37ºC and examined at 48 and 72 hours, assessing the morphology and color of the obtained colonies. The Chromogenic Candida Agar culture medium was used for species identification. Furthermore, conventional tests such as cultivation on Cormeal agar Tween 80 and sugar assimilation were conducted[20,21].

Hygiene Protocol

Patients were provided with a soft-bristle toothbrush (Colgate®) to brush the surface of the dental prosthesis, both on the internal and external parts. Detailed instructions were given on hygiene, including the application of active oxygen and lactoferrin foam (Blue®m) on the internal surface of the prosthesis. Pressing the valve of the Blue®m foam container twice (equivalent to two pump units), allowing it to act for 2 minutes, following the recommendation of Ngeow WC et al[22]. Brush and rinse with tap water; after drying, the foam was reapplied with the same dosage and worn during the day. At night, the same dosage was applied only once; it was left to act for 2 minutes before being soaked in tap water overnight[23]. This procedure was carried out for a period of 30 days.

Clinical Control

On days 4, 7, 15, and 30 of the study, clinical and photographic controls were conducted to assess the healing process using a modified scoring system by Hamzani et al[24] (Table 1).

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Table 1. Characteristics, parameters and scoring in the healing process

Parameters	Score 0	Score 1	Total
Removal of the lesion	Partial: Reduction in the size of the initial lesion	Total: Complete remission of the lesion size	1
Color	More erythematous than healthy tissue	Similar to healthy tissue	1
Healing	Less than 2 mm of the lesion border	More than 2 mm from the lesion border	1
Complete healing			3

This system assigns values to evaluate the lesion's remission (score 0: partial, score 1: total), color (score 0: more erythematous than healthy tissue, score 1: similar to healthy tissue), and healing (score 0: less than 2 mm from the lesion's contour, score 1: more than 2 mm from the lesion's contour). A score of 3 is considered successful healing, a score of 2 reflects acceptable healing, and a score of 0-1 indicates poor healing.

Additionally, mycological cultures were conducted at 30 days to confirm if patients still exhibited candidiasis.

Statistical Analysis

The data were analyzed using descriptive statistics. Quantitative variables were expressed as means ± standard deviation (SD), while qualitative variables were presented in terms of frequency and percentage. To perform the statistical analysis, it was used the SPSS v.15.

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RESULTS

The evaluated patients ranged in age from 28 to 79 years, with a mean ± standard deviation of 64.5 ± 10.9 years, distributed by gender: 2 (20%) male patients and 8 (80%) female patients (Table 2).

Table 2. Initial characteristics of patients evaluated with denture stomatitis

Characteristics	f (%)
Evaluated sample: n	**10**
Age: ȳ ± SD	**(64.5 ± 10.9)**
Gender:	
Male	2 (20.0)
Female	8 (80.0)
Oral Hygiene:	
Good	1 (10.0)
Poor	9 (90.0)
Denture usage time (years): n (%)	
Age: ȳ ± SD	**(15.3 ± 12.0)**
1 to 14	5 (50.0)
15 to 27	3 (30.0)
28 to 40	2 (20.0)
Denture material:	
Polymethylmethacrylate	6 (60.0)
Metal-Acrylic partial denture	4 (40.0)

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Continuing on the topic of oral hygiene, 9 (90%) of the evaluated experimental group had poor oral hygiene, and 1 (10%) had good oral hygiene. Regarding the duration of prosthesis use by the patients: in 5 (50%) cases, the duration of use was between 1 to 14 years; 3 (30%) between 15 to 27 years, and finally, 2 (20%) of the patients had used prostheses for 28 to 40 years, respectively. It is important to note that, on average, the duration of prosthesis use for the patients evaluated was 15.3 ± 12.0 years. Regarding the material used for prosthesis fabrication, 6 (60%) of the cases were made of Polymethylmethacrylate (PMMA), and 4 (40%) of the patients had prostheses made of metal-acrylic partial denture**.**

Regarding the identification of *Candida* spp. in the evaluated patients, it was observed that in 8 cases (80%), the identified species was *Candida albican*s, while in 2 patients (20%), *Nakaseomyces grabratus* was detected (Table 3).

Table 3. Clinical characteristics of the patients evaluated

Characteristics	**f (%)**
***Candida ssp. type* :**	
Nakaseomyces grabrata	2 (20.0)
Candida albicans	8 (80.0)
Classification of denture stomatitis according to Newton:	
Type II	7 (70.0)
Type III	3 (30.0)

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Clinical control of healing process	Deficient	Acceptable	Successful
At 4 days	10 (100.0)	-	-
At 7 days	7 (70.0)	2 (20.0)	1 (10.0)
At 15 days	2 (20.0)	4 (40.0)	4 (40.0)
At 30 days	1 (10.0)	2 (20.0)	7 (70.0)
Patient satisfaction opinion:			
Satisfied			10 (100.0)
Unsatisfied			0 (0.0)

These results indicate the prevalence of *Candida albicans* as the predominant species in the sample studied, with a minority presence of *Nakaseomyces grabratus.* In relation to the clinical control performed to assess the evolution of healing, the following observations were made: At 4 days of treatment, it was observed that all patients (100%) had poor healing; at 7 days, the evaluation resulted in 70% of patients showing poor healing, 20% acceptable healing, and 10% successful healing; at 15 days, healing was determined as follows: 20% poor, 40% acceptable, and 40% successful. Finally, at 30 days, the clinical evaluation showed that 10% of patients had poor healing, 20% had acceptable healing, and 70% had successful healing (Figure 1).

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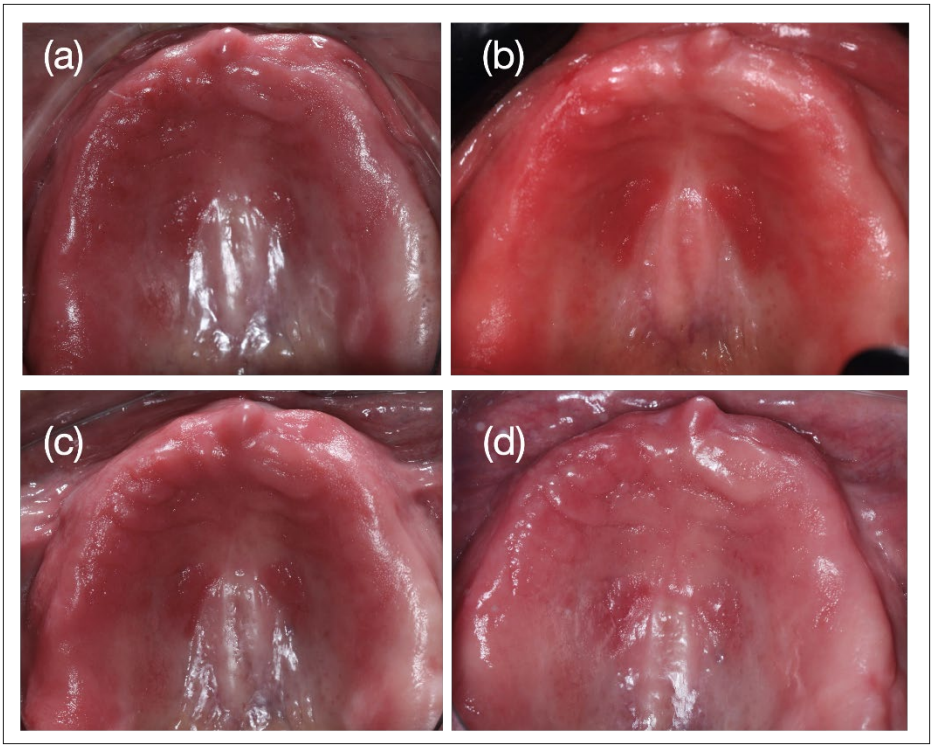

Figure 1. (a): Type II stomatitis according to Newton before treatment with active oxygen and lactoferrin foam. (b): Regression of the lesion at four days of treatment (inadequate healing). (c): Fifteen days of treatment, showing acceptable healing. (d): Thirty days of treatment, demonstrating successful healing.

Additionally, after 30 days, repeat mycological cultures were negative. It is noteworthy that patients expressed a positive opinion regarding the care, treatment, and results obtained. They reported satisfaction with the care process and the achieved outcomes. It is essential to note that two patients (equivalent to 20% of the evaluated sample) did not comply with the nighttime rest of the deteriorated acrylic denture.

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DISCUSSION

This study explores the impact of Oxygen and lactoferrin Foam in the treatment of DS, suggesting that this product could be an innovative addition for denture care and the prevention of *Candida* infections.

Age is a crucial variable, with most studies[1, 6, 7] concurring that this condition is prevalent in older adults, consistent with our findings, where ages ranged from 28 to 79 years with a mean ± standard deviation of 64.5 ± 10.9 years. This information is important as the age of patients can influence the development and severity of DS. Elderly individuals are often more prone to this condition due to factors such as reduced salivary flow and changes in oral mucosa.

This condition more frequently affects the female gender, as reported in several studies[3-7, 25]. In this research, it was observed that 80% of cases affected females, while 20% affected males, aligning with similar findings in previous studies[1, 7, 26]. This contrasts with the study by Sardari F et al. [6], which reported an increase in DS in the male gender. It's important to consider that the female gender often shows more interest in health care, leading to a higher registration of these cases in the literature, which could represent an underreporting of cases in males. Additionally, the current era of implantology is crucial, another factor that may explain the underreporting of male patients with denture stomatitis.

Candida species are oral commensals found in up to 90% of healthy individuals. Several factors contribute to their occurrence, including ill-fitting dentures, prolonged use, poor oral hygiene, and

the type of denture base material. In addition, systemic conditions in the patient, such as xerostomia or diabetes, can play important roles in the pathology[27].

In the present study, oral hygiene was poor in 90% of the group studied, leading to an imbalance in the oral microbiota and facilitating the growth of *Candida* spp[4-7].

The duration of denture use is associated with the presence of DS, as reported in the literature[6-8]. In this study, 50% of the patients used dentures for 1 to 14 years, 30% for 15 to 27 years, and 20% for 28 to 40 years. These results differ from the literature, as DS cases were more frequent in the group with a shorter denture usage time. It is suggested that this prevalence could be linked to poor oral hygiene, facilitated by an unfavorable environment conducive to the transition of *Candida* spp. from commensal to pathogenic. In this study, it was observed that in 60% of cases, PMMA dentures were used. Research has indicated that these PMMA may deteriorate over time due to enzymes and metabolites of the biofilm[22-4,28], resulting in aging of denture materials that increases roughness and susceptibility to *Candida* spp. adhesion[29].

Candida albicans is the most commonly reported species associated with candidiasis[2-4]. The transition from commensal to pathogen depends on the host (immune mechanisms and age), the fungus (adhesion capacity, growth, and virulence factors), and the microenvironment of the oral cavity (hygiene, use of dentures, nutritional deficiencies, systemic diseases, and salivary flow). In this study, 80% of the cases resulted in *Candida albicans*, and 20% in *Nakaseomyces grabratus*, aligning with findings from various authors[1,26,30]. Similarly, Qiu, J et al[31]. found in their study that

Candida albicans was the most commonly identified species, while *Nakaseomyces grabratus* and *Candida tropicalis* were equally prevalent.

Regarding the type of DS present in the evaluated patients, it was determined that 70% of the cases were classified as type II, according to Newton, and 30% as type III. This aligns with reports from López-Labady[7], where types II and III are associated with DS. In contrast, the study by Qiu, J et al[30]. found a higher incidence in types I and II. It is noteworthy that the chronicity of the disease can be explained by the duration of denture use and poor oral hygiene, factors that influence the results found in this study.

Regarding the healing process, after 30 days of treatment, it was observed that 70% of the evaluated patients experienced successful healing. These results align with various authors who emphasize the potential of lactoferrin and oxygen as antifungal agents[15,16]. This effectiveness is attributed, in addition, to proper hygiene and nightly denture rest[1,23].

The individual non-compliance with the hygiene protocol may have affected the progress of healing. The treatment's effectiveness and healing are linked to strict adherence to the prescribed regimen. Variations in compliance could explain differences in the healing process among participants. Personal habits and the individuality of patients may influence the treatment response.

It is important to consider individual factors when interpreting clinical results. The significant reduction in the inflammation area observed after 30 days supports the effectiveness of the evaluated treatment. Oxygen, in combination with lactoferrin, has been shown not only to have an

antifungal effect but also to increase tissue keratinization[11-13], reduce inflammatory infiltrate, enhance fibroblast proliferation and collagen synthesis, and promote angiogenesis by increasing vascular endothelial growth factor. Moreover, the product's components, such as lactoferrin, oxygen, and xylitol, contribute to maintaining proper salivary flow homeostasis[32,33]. Through this treatment, proper hygiene and nighttime rest stimulate mucosal repair and eliminate inflammatory processes caused by candidiasis in DS.

Additionally, the reduction in inflammation contributes to the healing process, which could explain the decrease in *Candida* spp. on dentures, thereby reducing the prevalence of DS. A significant aspect is the notable reduction in halitosis observed in two of the evaluated patients. This observation is supported by other researchers when conducting treatments with active oxygen and lactoferrin to address biofilm accumulation associated with halitosis [33,34].

CONCLUSIONS

This study represents a milestone in evaluating the effectiveness of Blue®m active oxygen and lactoferrin foam in treating DS. The results support the efficacy of Blue®m active oxygen and lactoferrin foam in the treatment of DS associated with *Candida* spp., and offer an easily applicable therapy. However, it emphasizes the importance of strict compliance with the instructions and the hygiene protocol by each patient. Although patients expressed satisfaction, randomized clinical trials with a larger sample are recommended to more robustly validate these promising results.

Conflict of Interest: The authors declare no conflicts of interest.

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REFERENCES

1. Ribeiro AB, Ribeiro AB, de Araújo CB, et al. Effect of a Hygiene Protocol on Denture-Related Stomatitis Remission, Local Inflammatory Factors, and Hemodynamic Responses by Arterial Pressure. Antibiotics (Basel) [Internet]. 2022 [cited 2023 Feb 15];11(10):1320. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9598829/ DOI:10.3390/antibiotics11101320
2. Sterzenbach T, Helbig R, Hannig C, Hannig M. Bioadhesion in the oral cavity and approaches for biofilm management by surface modifications. Clin Oral Investig [Internet]. 2020 [cited 2023 Feb 15];24(12):4237-4260. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7666681/ DOI:10.1007/s00784-020-03646-1
3. Sugio C, Garcia A, Albach T, et al. Candida-Associated Denture Stomatitis and Murine Models: What Is the Importance and Scientific Evidence?. J Fungi (Basel) [Internet]. 2020 [cited 2023 Feb 15];6(2):70. Available from:https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7344758/ DOI:10.3390/jof6020070
4. Le Bars P, Kouadio AA, Bandiaky ON, Le Guéhennec L, de La Cochetière MF. Host's Immunity and Candida Species Associated with Denture Stomatitis: A Narrative Review. Microorganisms [Internet]. 2022 [cited 2023 Feb 15];10(7):1437. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9323190/ DOI:10.3390/microorganisms10071437
5. Bajunaid SO, Baras BH, Weir MD, Xu HHK. Denture Acrylic Resin Material with Antibacterial and Protein-Repelling Properties for the Prevention of Denture Stomatitis.

Polymers (Basel)[Internet]. 2022 [cited 2023 Feb 15];14(2):230. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8777866/ DOI:10.3390/polym14020230

6. Sardari F, Khalili P, Hakimi H, Mahmoudaghaei S, Abedi P. The prevalence of denture stomatitis in cigarette and hookah smokers and opium addicts: findings from Rafsanjan Cohort Study. BMC Oral Health [Internet]. 2021 [cited 2023 Feb 15];21(1):455. Available from:https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8449426/ DOI:10.1186/s12903-021-01807-6
7. López-Labady, J. del V., Gómez, F., Herrera, J., Romaris, M.E., Toro, D.Prevalencia de Estomatitis Subprotésica en un grupo de pacientes venezolanos. Estudio clínico transversal. Acta Odontológica Venezolana [Internet]. 2013 [cited 2023 Feb 15]; 51(4). Available from: https://www.actaodontologica.com/ediciones/2013/4/art-8/
8. Sartawi SY, Abu-Hammad S, A Salim N, Al-Omoush S. Denture Stomatitis Revisited: A Summary of Systematic Reviews in the Past Decade and Two Case Reports of Papillary Hyperplasia of Unusual Locations. Int J Dent [Internet]. 2021 [cited 2023 Feb 15];2021:7338143. Available from:https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8528609/ DOI:10.1155/2021/7338143
9. Ucar B, Rojas G, Lelis An. Acción de agentes químicos en la eliminación de cándida albicans sobre prótesis dentales. Acta Odontológica Venezolana [Internet]. 2007 [cited 2023 Feb 17]; 45(2). Available from: https://www.actaodontologica.com/ediciones/2007/2/art-7/
10. Papadiochou S, Polyzois G. Hygiene practices in removable prosthodontics: A systematic review. Int J Dent Hyg [Internet]. 2018 [cited 2023 Feb 17];16(2):179-201. Available from:https://onlinelibrary.wiley.com/doi/10.1111/idh.12323 DOI:10.1111/idh.12323
11. Eisenbud DE. Oxygen in wound healing: nutrient, antibiotic, signaling molecule, and therapeutic agent. Clin Plast Surg [Internet]. 2012 [cited 2023 Feb 19];39(3):293-310. Available from:https://www.plasticsurgery.theclinics.com/article/S0094-1298(12)00043-0/fulltext DOI:10.1016/j.cps.2012.05.001
12. Mattei B, Imanishi S, de Oliveira R, de Campos P, Weiss S, Deliberador T. Mouthwash with Active Oxygen (blue®m) Induces Keratinocytes Proliferation. Journal of Stomatology [Internet]. 2020 [cited 2023 Feb 19];10(1):107-114. Available from:https://www.scirp.org/journal/paperinformation?paperid=100593 DOI:10.4236/ojst.2020.106012
13. Mattei B, Imanishi S, de Oliveira R, de Campos P, Weiss SG, Deliberador T. Mouthwash with Active Oxygen (blue®m) Reduces Postoperative Inflammation and Pain. Case Rep Dent [Internet]. 2021 [cited 2023 Feb 19];2021:5535807. Available from:https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8187063/ DOI:10.1155/2021/5535807

14. Juliana H, Tarek S. Comparative study of the effect of BlueM active oxygen gel and coe-pack dressing on postoperative surgical depigmentation healing. Saudi Dent J [Internet]. 2022 [cited 2023 Feb 26];34(4):328-334. Available from:https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9177883/ DOI:10.1016/j.sdentj.2022.04.005
15. Nakano M, Suzuki M, Wakabayashi H, et al. Synergistic anti-candida activities of lactoferrin and the lactoperoxidase system. Drug Discov Ther [Internet]. 2019 [cited 2023 Feb 26];13(1):28-33. Available from:https://www.jstage.jst.go.jp/article/ddt/13/1/13_2019.01010/_article DOI:10.5582/ddt.2019.01010
16. Pawar S, Markowitz K, Velliyagounder K. Effect of human lactoferrin on Candida albicans infection and host response interactions in experimental oral candidiasis in mice. Arch Oral Biol [Internet]. 2022 [cited 2023 Feb 26];137. Available https://pubmed.ncbi.nlm.nih.gov/35286948/ DOI: 10.1016/j.archoralbio.2022.105399.
17. Guttentag A, Krishnakumar K, Cokcetin N, Hainsworth S, Harry E, Carter D. Inhibition of Dermatophyte Fungi by Australian Jarrah Honey. Pathogens [Internet]. 2021 [cited 2023 Mar 15];10(2):194.Available from:https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7918412/ DOI:10.3390/pathogens10020194 DOI:10.3390/pathogens10020194
18. Chan A, Ellepola K, Truong T, Balan P, Koo H, Seneviratne CJ. Inhibitory effects of xylitol and sorbitol on Streptococcus mutans and Candida albicans biofilms are repressed by the presence of sucrose. Arch Oral Biol [Internet]. 2020 [cited 2023 Mar 15];119. Available from:https://pubmed.ncbi.nlm.nih.gov/32932149/ DOI:10.1016/j.archoralbio.2020.104886
19. McReynolds DE, Moorthy A, Moneley JO, Jabra-Rizk MA, Sultan AS. Denture stomatitis-An interdisciplinary clinical review. J Prosthodont [Internet]. 2023 [cited 2023 Apr 20];32(7):560-570. Available from:https://onlinelibrary.wiley.com/doi/10.1111/jopr.13687 DOI:10.1111/jopr.13687
20. Ebru E, Jülide SG, Elvan Hİ, Şükran Y, Alper T, Yasemin Y, et al. Medically important Candida spp. identification: an era beyond traditional methods. Turk.J.Med Sci [Internet]. 2022 [cited 2023 April 20];52(3):834-840. Available from:https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10390122/ DOI: 10.55730/1300-0144.5380.
21. Liguori G, Di Onofrio V, Lucariello A, Galle´ F, Signoriello G, Colella G, D'Amora M, Rossano F. Oral candidiasis: a comparison between conventional methods and multiplex polymerase chain reaction for species identification. Oral Microbiology Immunology [Internet]. 2009 [cited 2023 April 19]; 24: 76–78. Available from:https://onlinelibrary.wiley.com/doi/10.1111/j.1399-302X.2008.00447.x DOI:10.1111/j.1399-302x.2008.00447.x

22. Ngeow W, Tan C, Goh Y, Deliberador T, Cheah C. A Narrative Review on Means to Promote Oxygenation and Angiogenesis in Oral Wound Healing. Bioengineering (Basel) [Internet]. 2022 [cited 2023 April 20];9(11):636. Available from:https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9688034/ DOI:10.3390/bioengineering9110636
23. Lim SR, Lee JS. Three dimensional deformation of dry-stored complete denture base at room temperature. J Adv Prosthodont [Internet]. 2016 [cited 2023 Feb 19];8(4):296-303. Available from:https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4993843/ DOI:10.4047/jap.2016.8.4.296
24. Hamzani Y, Chaushu G. Evaluation of early wound healing scales/indexes in oral surgery: A literature review. Clinical Implant Dentistry and Related Research [Internet]. 2016 [cited 2023 April 20];20(6):1030-1035. Available from:https://onlinelibrary.wiley.com/doi/10.1111/cid.12680 DOIi:10.1111/cid.12680
25. Singh HP, Bansal P, Sh T. Denture Stomatitis and Candida albicans in the Indian Population: A Systematic Review and Meta-Analysis. Cureus [Internet]. 2023 [cited 2023 Oct 5];15(9):e45182. Available from:https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10575763/ DOI:10.7759/cureus.45182
26. Moosazadeh M, Akbari M, Tabrizi R, et al. Denture Stomatitis and Candida Albicans in Iranian Population: A Systematic Review and Meta-Analysis. J Dent (Shiraz) [Internet]. 2016 [cited 2023 Oct 5];17(3):283-292. Available from:https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5103476/
27. Gad MM, Fouda SM. Current perspectives and the future of Candida albicans-associated denture stomatitis treatment. Dent Med Probl. [Internet]. 2020 [cited 2023 Oct 5]; 57(1):95-102 Available from:https://pubmed.ncbi.nlm.nih.gov/32307934/ DOI:10.17219/dmp/112861
28. Matsuo H, Suenaga H, Takahashi M, Suzuki O, Sasaki K, Takahashi N. Deterio- ration of polymethyl methacrylate dentures in the oral cavity. Dent Mater J [Internet]. 2015 [cited 2023 Oct 8];34:234–9. Available from:https://www.jstage.jst.go.jp/article/dmj/34/2/34_2014-089/_article DOI:10.4012/dmj.2014-089
29. De Souza R, Chaves C, Rohani K, et al. Palatal brushing for the treatment of denture stomatitis: A multicentre randomized controlled trial. J Prosthodont Res [Internet]. 2023 [cited 2023 Oct 8];67(1):93-102. Available from:https://www.jstage.jst.go.jp/article/jpr/67/1/67_JPR_D_21_00258/_article DOI:10.2186/jpr.JPR_D_21_00258
30. Budtz-Jörgensen E, Stenderup A, Grabowski M. An epidemiologic study of yeasts in elderly denture wearers. Community Dent Oral Epidemiol [Internet]. 1975 [cited 2023 Oct

9];3(3):115-119. Available from:https://pubmed.ncbi.nlm.nih.gov/1056815/ DOI:10.1111/j.1600-0528.1975.tb00291.

31. Qiu J, Roza M, Colli K. et al. Candida-associated denture stomatitis: clinical, epidemiological, and microbiological features. Braz J Microbiol [Internet]. 2023 [cited 2023 Oct 9];54, 841–848.Available from:https://link.springer.com/article/10.1007/s42770-023-00952-0 DOI:10.1007/s42770-023-00952-0
32. Rafeek R, Carrington CVF, Gomez A, et al. Xylitol and sorbitol effects on the microbiome of saliva and plaque. J Oral Microbiol [Internet]. 2018 [cited 2023 Oct 15];11(1):1536181. Available from:https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6225370/ DOI:10.1080/20002297.2018.1536181
33. Rosa L, Lepanto MS, Cutone A, et al. Lactoferrin and oral pathologies: a therapeutic treatment. Biochem Cell Biol [Internet]. 2021 [cited 2023 Oct 19];99(1):81-90. Available from:https://pubmed.ncbi.nlm.nih.gov/32213143/ DOI:10.1139/bcb-2020-0052
34. Wyszyńska M, Nitsze-Wierzba M, Białożyt-Bujak E, Kasperski J, Skucha-Nowak M. The Problem of Halitosis in Prosthetic Dentistry, and New Approaches to Its Treatment: A Literature Review. J Clin Med [Internet]. 2021 [cited 2023 Oct 19];10(23):5560. Available from:https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8658399/ DOI:10.3390/jcm10235560