EAS Journal of Dentistry and Oral Medicine
Abbreviated Key Title: EAS J Dent Oral Med
ISSN: 2663-1849 (Print) & ISSN: 2663-7324 (Online)
Published By East African Scholars Publisher, Kenya

OPEN ACCESS

Volume-6 | Issue-6 | Nov-Dec-2024 | DOI: https://doi.org/10.36349/easjdom.2024.v06i06.001

Original Research Article

Efficacy and Safety of EPX® Biomolecule Mouthwash for Treating Chronic Gingivitis

Citlali Martínez-Morales[1*], Mara Gómez-Flores[2], Maikel Hermida-Rojas[3], Roberto Ibarra-Wiley[4], Marco Arturo Moreno-Solorio[5]

[1]Candidate for a Doctorate in Dental Sciences, Master's Degree in Health Sciences, School of Dentistry, Mexicali, Autonomous University of Baja California, Mexico
[2]Doctor in Dental Sciences, Master's Degree in Educational Sciences, Specialist in Periodontics, Full-time Professor, School of Dentistry, Mexicali, Autonomous University of Baja California, Mexico
[3]Doctor in Medical, Dental and Health Sciences, Master's Degree in Oral Health, Specialist in Oral and Maxillofacial Surgery, Full-time Professor, School of Dentistry, Mexicali, Autonomous University of Baja California, Mexico
[4]Doctor of Science in Chemical Engineering, Master's Degree in Industrial Administration, C. E. O. Medical Tech Laboratories S.A. de C.V
[5]Master's Degree in Dental Clinical Sciences, Subject Professor, School of Dentistry, Mexicali, Autonomous University of Baja California, Mexico

Article History
Received: 26.09.2024
Accepted: 05.11.2024
Published: 08.11.2024

Journal homepage:
https://www.easpublisher.com

Quick Response Code

Abstract: ***Introduction*:** Chronic gingival diseases are primarily caused by microorganisms present in dentobacterial plaque, which can be controlled through mechanical methods like brushing or chemically using mouthwashes. The Autonomous University of Baja California has developed a chitosan-based molecule enriched with colloidal silver nanoparticles (EPX® Biomolecule), which acts as an antiseptic and is administered topically. ***Objective***: This study aims to evaluate the efficacy and safety of EPX® Biomolecule mouthwash in the treatment of chronic gingivitis. ***Methods***: An experimental study, phase I clinical trial, was conducted involving a randomized sample of 50 adult patients diagnosed with chronic gingivitis, treated at the Santé Dental Clinic from January to December 2022, following the acquisition of informed consent. The study comprised a case group of 25 patients treated with EPX® Biomolecule mouthwash, compared against a control group of 25 patients receiving 2% chlorhexidine oral rinse. Statistical analysis was performed using Student's t-test, with a significance level set at $p<0.05$. ***Results***: The majority of participants were women (54%), under 30 years of age (92%), students (58%), and had completed high school (82%). At 15 days, both treatments exhibited similar effects; however, chlorhexidine showed a marginally better response at 30 days, which was statistically significant for the Gingival Index ($p = 0.01$) and the Hemorrhagic Index ($p = 0.01$). No significant differences were observed in dentobacterial plaque levels, although adverse reactions were noted with chlorhexidine. ***Conclusions***: Both treatments effectively reduced bleeding and gingival edema, with chlorhexidine demonstrating improved outcomes at 30 days. There were no differences in plaque control, and an isolated adverse reaction was associated with chlorhexidine.

Keywords: Gingivitis, Nanotechnology, Mouthwashes, Chlorhexidine, Oral Hygiene Index, Clinical Trial, Phase I.

INTRODUCTION

Gingivitis is a common and mild form of periodontal disease characterized by irritation, redness, swelling and bleeding of the gum tissue. It is crucial to take gingivitis seriously and treat it promptly, as while it does not cause bone loss, untreated gingivitis can progress to more severe gum disease, known as periodontitis, potentially leading to tooth loss. Epidemiological studies indicate that gingivitis is nearly universal, affecting both children and adults, and ranks

***Corresponding Author:** Citlali Martínez-Morales
Candidate for a Doctorate in Dental Sciences, Master's Degree in Health Sciences, School of Dentistry, Mexicali, Autonomous University of Baja California, Mexico

as the second most prevalent oral disease worldwide, with its prevalence and severity increasing with age [1, 2].

The primary cause of gingivitis is poor oral hygiene. Good oral health practices, including regular tooth brushing, flossing, dental checkups, and the use of antiseptic mouthwashes, are essential for preventing and reversing this condition. Gingivitis is initiated by a dental biofilm of bacteria that inflames the gingiva, making plaque control critical for both preventive and therapeutic success. While brushing is emphasized, mouthwashes can effectively complement mechanical cleaning methods [3-7].

Mouthwashes should possess several key characteristics: the ability to eliminate plaque in hard-to-reach areas, rapid action, safety, efficacy against both gram-positive and gram-negative bacteria, be user-friendly, pleasant taste and penetrate the bacterial biofilm. Throughout history, various substances have been used as mouthwashes, with chlorhexidine gluconate emerging as the most widely used in the past decade. This synthetic compound has multiple antibacterial properties and is utilized in a range of medical, surgical, and dental procedures. In dentistry, it serves as an antimicrobial agent that controls bacterial biofilm and inhibits the adhesion of plaque. However, chlorhexidine is not without drawbacks, as it can cause brown pigmentation on teeth, produce a metallic taste, and alter taste sensations, prompting the search for alternative oral rinses [8-10].

In exploring new agents for plaque control, mouthwashes containing chitosan— a natural cationic biopolymer derived from chitin—have gained attention due to their diverse biomedical applications. As one of the most abundant polysaccharides in nature, chitosan offers significant benefits in medicine, including hemostatic, antifungal, antibacterial, antioxidant, and antitumor effects, while also promoting defense mechanisms. It also promotes bioadhesion to oral surfaces and accelerates bone formation by enhancing osteoblast activity in bone tissue. Importantly, chitosan is non-toxic and biocompatible, offering an economical option for oral health [9-13].

The primary biological activities of chitosan in dentistry include osteoconduction, stimulation of soft tissue repair, drug release, and its use in oral hygiene products such as mouthwashes. Chitosan facilitates bone formation by promoting the migration of polymorphonuclear and progenitor cells, thereby accelerating wound healing [14].

Consequently, chitosan effectively addresses the needs associated with inflammatory processes in gingivitis, ensuring safety while minimizing the risks associated with other mouthwashes [15]. While the oral cavity is never completely sterile, mouthwashes can help reduce the microbial load on the oral mucosa. When selecting an antiseptic, it is essential to assess the benefits against the potential for undesirable side effects [16, 17].

Dentists play a crucial role in educating patients on proper brushing techniques, but achieving optimal gingival health free from bacterial plaque often requires additional strategies, such as the incorporation of chemical agents (oral rinses) to reduce and delay plaque formation [18].

Chlorhexidine remains the leading adjunct for maintaining periodontal health, but it does carry adverse reactions. Consequently, there is a growing interest in exploring alternative agents that mitigate these side effects. Mouthwashes containing biomaterials such as chitosan offer promising therapeutic solutions for periodontal conditions due to their broad-spectrum antimicrobial and antifungal properties, as well as adhesion, analgesic, and hemostatic capabilities that inhibit bacterial cell function [8-24].

Over the past decade, the Autonomous University of Baja California in Mexico has developed innovative medications utilizing nanotechnology, expanding its applications to dentistry for the diagnosis, treatment, and prevention of periodontal diseases. This research has led to the creation of a chitosan-derived nanomolecule enriched with silver nanoparticles, which has demonstrated in vitro bactericidal activity, low cytotoxicity, and minimal adverse effects in animal models. This molecule, named EPX® Biomolecule, shows considerable potential against pathogenic microorganisms found in periodontal disease biofilms.

With patients diagnosed with gingivitis daily in both our country and globally, there is a pressing need for research and development of alternative techniques based on chitosan enriched with nanoparticles. It is critical to evaluate the absence of complications or adverse effects associated with the application of chitosan as an oral mouthwash. This research aims to assess the pharmacological properties of EPX® Biomolecule, providing a pertinent approach to addressing the prevalent health issue of gingivitis and offering a promising alternative for maintaining periodontal health in affected patients.

Objectives

General Objective

To evaluate the efficacy and safety of EPX® Biomolecule, in its pharmaceutical form as a mouthwash, for the treatment of gingivitis in adult patients.

Specific Objectives

1. Determine the periodontal clinical characteristics of the studied population.
2. Describe the changes in periodontal indices following the application of both mouthwashes.

3. Analyze the clinical periodontal results after the use of the mouthwashes under investigation.
4. Identify any adverse reactions associated with the application of both mouthwashes.

MATERIALS AND METHODS

Study design

An experimental phase I clinical trial was conducted to evaluate the efficacy and safety of EPX® Biomolecule in its pharmaceutical form of as a mouthwash for the treatment of gingivitis in adult patients. From a population of 116 patients clinically diagnosed with gingivitis, a random sample of 50 patients was selected from the Santé Clinic, located in downtown Mexicali, Baja California, Mexico. All treatments were administered between January and December 2022, with comprehensive medical records maintained for each participant. Diagnoses were performed by a Master in Health Sciences, and the treatment plan involving antiseptics was confirmed by two specialists in the dental surgical field, both holding Doctorates in Dental Sciences.

During the controlled clinical trial, the sample of 50 patients represented 43.1% of the overall study population. Throughout the investigation, two parallel randomized groups were established: one case group of 25 patients treated with EPX® Biomolecule and one control group of 25 patients.

Inclusion Criteria

1. Adult patients diagnosed with gingivitis who attended the dental office at the Santé Clinic, with no significant personal and pathological medical history impacting the progression of the disease.
2. Patients exhibiting probing depths of less than 3 mm, without attachment loss, possessing a minimum of 20 teeth, and who have not received periodontal therapy within the six months preceding the consultation.
3. Patients demonstrating suitable mental and emotional conditions for participation in an experimental study of this nature.
4. Patients who provided valid informed consent and agreed to participate in the clinical trial.

Exclusion Criteria

1. Adult patients diagnosed with gingivitis who attended the dental office at the Santé Clinic, but have significant personal and pathological medical history impacting the disease progression, or pregnant women.
2. Patients with pocket depths greater than 3 mm, with attachment loss, having fewer than 20 teeth, and/or who have received periodontal therapy within the six months prior to consultation.
3. Patients currently undergoing orthodontic treatment with fixed or removable appliances.
4. Patients lacking the mental and emotional conditions necessary for participation in an experimental study of this nature.
5. Patients who declined to participate in the clinical trial.

Exit Criteria

1. Patients who expressed a decision to withdraw from the experimental study.
2. Patients who opted to use antiseptics other than those specified in the study.
3. Patients who failed to attend follow-up visits for monitoring their periodontal condition.

Data Collection

Objectivity of Observation

The independent variable in this study was the type of mouthwash used for treatment. The case group comprised 25 patients treated with EPX® Biomolecule mouthwash, while the control group consisted of 25 patients receiving chlorhexidine rinse. The dependent variables were measured before treatment and at 15 and 30 days post-application, using standardized periodontal indices. Measurements were consistent in terms of method, location, and timing.

Concurrent Comparison:

Clinical observations were conducted to assess the changes induced by the antiseptics during treatment. This was supplemented with clinical examinations and systematic comparisons of gingival health at the 15-day and 30-day intervals.

Random Assignment of Treatments:

Patients with gingivitis were randomly assigned to either the case or control group to balance known and unknown confounding factors. This randomization ensured that the groups were comparable across all characteristics throughout the study's progression.

Masking:

The level of masking adhered to the trial's design, aimed at minimizing subjectivity in the evaluation of results. Both antiseptics were presented with coherent explanations, ensuring that neither patients nor operators could make comparisons between the treatments.

Use of Epidemiological Indices:

Several indices were employed to measure gingival health and hygiene status before, during, and after treatment with both mouth rinses:

1. **Löe and Silness Gingival Index**:

This tool was utilized to assess the severity of gingival inflammation by observing the gingiva around the teeth for signs of gingivitis, including redness, swelling, and bleeding upon probing.

2. **Löe and Silness Bleeding Index**:

This clinical tool evaluated the presence of gingival bleeding, a key indicator of inflammation and an early sign of periodontal disease. The index measured the tendency for gingival bleeding when pressure was applied with a WHO-type periodontal probe in the gingival sulcus, noting the absence or presence of bleeding 30 seconds post-probing, classified into four grades.

3. **Löe and Silness Plaque Index**:

This important tool assessed the amount of bacterial plaque present on the tooth surfaces, as plaque accumulation is a critical factor in the development of gingivitis.

Biostatistical Data Analysis

Data analysis was performed using SPSS for Windows version 29.0, with all data also backed up in Microsoft Excel 2016. Descriptive statistics were initially employed to summarize the data collected at baseline and during patient follow-up. Subsequently, post hoc tests were conducted to identify differences between the treatment groups. The Student's t-test was utilized as a parametric statistical tool to determine whether significant differences existed between the means of the two groups, with a significance threshold set at $p<0.05$.

Bioethics Considerations

The study protocol was conducted in accordance with the principles outlined in the Declaration of Helsinki by the World Medical Association, the CIOMS Guidelines, and Resolution 008430 of October 4, 1993. Compliance was also ensured with the Mexican Official Standard NOM-059-SSA1-2013 regarding good manufacturing practices for medicines, as well as the legal frameworks established by National Health Sector agencies and the General Health Law. The protocol was reviewed and approved by the Research and Postgraduate Ethics and Evaluation Committee of the School of Dentistry, Mexicali, UABC. Ethical compliance was maintained throughout the study, considering the objectives, procedures, associated risks, and benefits. Confidentiality was preserved through the use of codes, ensuring that personal identities were not disclosed during data analysis.

RESULTS AND DISCUSSION

In the initial stage of the study, key social, demographic, and clinical variables of the participating patients were analyzed, including sex, age, marital status, and level of education, as well as clinical indicators of initial gingivitis and oral hygiene prior to the use of mouth rinses. **Table 1** presents the distribution of patients according to these social and demographic variables, along with their initial clinical status.

These data provide insight into the sample's social determinants of health, indicating that this population had access to healthcare services and education. However, despite this access, their perception of oral health risk appeared inadequate, as evidenced by the prevalence of suboptimal oral hygiene practices.

Table 1: Distribution of Patients According to Social and Demographic Variables and Initial Clinical Status.

Variable	Number of Patients (n=50)	Percentage (%)
Age groups		
30 years old or younger	46	92
31 years old or older	4	8
Sex		
Female	27	54
Male	23	46
Marital status		
Single	41	82
Married	9	18
Education level		
Pre-university	41	82
University	9	18
Occupation		
Student	29	58
Employee	11	22
Professional	8	16
Housewife	2	4
Clinical aspects of gingivitis		
Bleeding	42	84
Pain	1	2
Edema	42	84
Initial oral hygiene		
Good	2	4

Regular	27	54
Poor	21	42

Source: Study database

In this study, female patients predominated, comprising 54% of the total number of participants, while male patients accounted for 46%. The majority of patients (92%) were 30 years of age or younger, with only 8% being 31 years old or older. Single patients represented 82% of the sample, compared to 18% who were married. Most patients had completed their pre-university education, aligning with their occupations: 58% were students, 22% were employees, and 16% were professionals.

Regarding the initial clinical characteristics of the patients, all were diagnosed with chronic gingivitis. Bleeding was observed in 84% of the patients, and chronic edema affected 84% as well, with only 2% reporting any type of pain. An assessment of oral hygiene revealed that regular oral hygiene practices predominated in 54% of patients, followed by poor oral hygiene in 42%, while only 4% demonstrated good oral hygiene.

In the second stage of the research, the effectiveness of daily use of the mouthwash containing EPX® Biomolecule was evaluated in comparison to the daily application of chlorhexidine rinse. Following the initial evaluation, patients were monitored at 15-day and 30-day intervals, allowing for a comparison of clinical parameters between both groups based on the observed variables.

Table 2 presents the differences in the Löe and Silness Gingival Index corresponding to the progression of patients undergoing the studied treatments. The analysis revealed that, at the conclusion of the 15-day treatment period, no significant differences were observed in the gingival index between the two groups. This finding suggests that both treatments effectively contribute to the reduction of the gingival index. However, at the 15-day follow-up after the treatment concluded, the group receiving chlorhexidine treatment exhibited a lower gingival index compared to the group using the EPX® Biomolecule.

Table 2: Differences in the Löe and Silness Gingival Index According to Treatment Evolution.

Mouthwash Type	Löe and Silness Gingival Index		
	Prior to treatment **Severe gingivitis**	15 days **Mild gingivitis**	30 days **Moderate gingivitis**
Chlorhexidine	2.2775(.3890)	.8375(.2393)	1.0550(.2475)
EPX® Biomolecule	2.4675(.2254)	.9575(.3022)	1.2650(.2927)
Difference	-.19	-.12	-.21
p	**.040**	.126	**.009**
Note: Student's t-test for difference of two independent groups.			

Source: Identification Card/ Medical History of Sante Dental Clinic, Mexicali, BC

Table 3 presents the differences in the Löe and Silness Bleeding Index reflecting the progression of patients under the studied treatments. At the conclusion of the treatment, no significant differences were identified; both treatments demonstrated effectiveness in reducing the bleeding index. However, at the 15-day follow-up, the group treated with EPX® Biomolecule exhibited a greater increase in the hemorrhagic index. This suggests that the chlorhexidine group had a more pronounced effect on controlling the hemorrhagic index in a statistically significant manner.

Table 3: Differences in the Löe and Silness Bleeding Index According to Treatment Evolution.

Mouthwash Type	Löe and Silness Bleeding Index		
	Prior to treatment **Bleeding and swelling**	15 days **Bleeding and swelling**	30 days **Bleeding and swelling**
Chlorhexidine	1.76(.43)	.12(.33)	.12(.33)
EPX® Biomolecule	2.00(.28)	.08(.27)	.48(.51)
Difference	-.24	.04	-.36
p	**.026**	.646	**.005**
Note: Student's t-test for difference of two independent groups.			

Source: Identification Card/ Medical History of Sante Dental Clinic, Mexicali, BC

Table 4 illustrates the changes observed in the plaque index. Both treatments proved effective in reducing the plaque index by the end of the treatment period and at the 15-day follow-up. Notably, no significant differences were found between the two treatment groups.

Table 4: Löe and Silness plaque index differences according to Treatment Evolution

Mouthwash Type	Löe and Silness Plaque Index		
	Prior to treatment **Regular**	15 días **Excelente control**	30 días después **Excelente control**
Chlorhexidine	1.76(.52)	.48(.51)	.64(.49)
EPX® Biomolecule	1.92(.57)	.64(.49)	.64(.49)
Difference	-.16	-.16	.000
p	.307	.264	1.0
Note: Student's t-test for difference of two independent groups.			

Source: Identification Card/ Medical History of Sante Dental Clinic, Mexicali, BC

Rinses formulated with chitosan, such as EPX® Biomolecule, exhibited therapeutic effectiveness comparable to that of chlorhexidine, indicating that both rinses possess a strong antimicrobial effect against periodontal diseases. However, chlorhexidine demonstrated a longer-lasting effect than the chitosan rinses, maintaining favorable results even 15 days after discontinuation. Conversely, chlorhexidine was associated with a minimal percentage of adverse reactions, while no patients treated with chitosan reported any allergic reactions, highlighting its potential for treating and preventing gingivitis.

This research evaluated the efficacy of EPX® Biomolecule in the treatment of gingivitis, comparing it with the conventional treatment of chlorhexidine. The findings suggest that EPX® Biomolecule is an effective alternative for reducing the clinical signs of gingivitis, presenting therapeutic effectiveness similar to chlorhexidine, with both rinses maintaining a sustained antimicrobial effect throughout the study.

In conclusion, while chlorhexidine showed greater reductions in inflammation and bacterial plaque, the EPX® Biomolecule—comprised of chitosan enriched with nanoparticles—emerges as a viable alternative with a superior safety profile. This may enhance patient adherence to treatment and minimize unwanted side effects. Long-term studies are recommended to further assess its prolonged clinical effectiveness and its impact on overall oral health.

CONCLUSION

1. The studied population exhibited a predominance of poor periodontal health, with all cases showing signs of gingival inflammation, hemorrhage, and bacterial plaque in the majority of patients.
2. Significant improvements were noted with the application of the mouthwash containing EPX® Biomolecule, indicating its effectiveness in reducing gingival inflammation, gingival bleeding, and bacterial plaque, particularly in comparison to the conventional chlorhexidine mouthwash.
3. In terms of adverse reactions associated with both mouthwashes, no adverse reactions were reported in patients using EPX® Biomolecule. In contrast, adverse reactions were observed in some patients treated with chlorhexidine.

Acknowledgements:

We extend our gratitude to Dr. Roberto Ibarra-Wiley, Director of Medicaltech Laboratories S.A. de C.V., for their invaluable support during the completion of this research.

Funding: No funding sources were provided for this study.

Conflict of Interest: None declared.

REFERENCES

1. Revilla-León, M., Gómez-Polo, M., Barmak, A. B., Inam, W., Kan, J. Y., Kois, J. C., & Akal, O. (2023). Artificial intelligence models for diagnosing gingivitis and periodontal disease: A systematic review. *The Journal of Prosthetic Dentistry*, *130*(6), 816-824.
2. Lee, Y. H., Shin, S. I., & Hong, J. Y. (2023). Investigation of volatile sulfur compound level and halitosis in patients with gingivitis and periodontitis. *Scientific Reports*, *13*(1), 13175.
3. Abdullaeva, N. I., & Akhmedov, A. A. (2023). Immunological Aspects of the Pathogenesis of Gingivitis and Periodontitis. *Central Asian Journal of Medical and Natural Science*, *4*(5), 17-21.
4. Parlak, H. M., Buber, E., Gur, A. T., Karabulut, E., & Akalin, F. A. (2023). Statherin and alpha-amylase levels in saliva from patients with gingivitis and periodontitis. *Archives of Oral Biology*, *145*, 105574.
5. Chang, L. U., Yi, C. H. U., Jian Ru, L. I. U., & Wen Yi, L. I. U. (2021). Subgingival microbial profiles of young Chinese adults with stage I/II periodontitis, gingivitis and periodontal health status. *Chin J Dent Res*, *24*(3), 167-175.
6. Iniesta, M., Chamorro, C., Ambrosio, N., Marín, M. J., Sanz, M., & Herrera, D. (2023). Subgingival microbiome in periodontal health, gingivitis and different stages of periodontitis. *Journal of Clinical Periodontology*, *50*(7), 905-920.
7. Artigas, R. S., Sánchez, R. J. S., Romero, C. R. S., & Lara, A. E. (2021). Factores de riesgo de enfermedad periodontal. *Correo Científico Médico de Holguín*, *25*(1).

8. Cárdenas, J. E. G., Hernández, D., López, M., González-Pérez, B., & Salas-Flores, R. (2022). Estudio clínico comparativo de la efectividad de la clorhexidina con quitosano al 0.1% vs clorhexidina convencional al 0.12% para el control de placa bacteriana y gingivitis en pacientes embarazadas. *Archivos de Medicina, Salud y Educación Médica*, 83-88.
9. Cruz-Rodríguez, T. E., Rylander-Yamada, J., de la Paz Martínez-Nuño, M., Morales-González, Y., del Carmen Roa-González, S., & de Jesús Méndez-Quevedo, T. (2021). Efecto del aloe vera con aceites esenciales sobre la placa bacteriana en comparación a la clorhexidina. *Revista Mexicana de Medicina Forense y Ciencias de la Salud*, *5*(S3), 149-152.
10. Bustamante, O. C., Troncos, L. G. P., de Zebrauskas, A. P. P., Leandro, K. C. R., & Sime, C. L. D. C. H. (2020). Antisépticos Orales: Clorhexidina, flúor y triclosán. *Salud & Vida Sipanense*, *7*(1), 4-16.
11. de Queiroz, B. B., & Tomaz, A. F. (2021). Eficácia do Curativo de Quitosana na Cicatrização: Uma Revisão Integrativa. *TEMA-Revista Eletrônica de Ciências*, *21*(34).
12. Vilasan, A., Venkatesh, P. M., Varadhan, K. B., George, J. P., & Dubey, A. (2020). Comparative evaluation of chitosan chlorhexidine mouthwash in plaque control: A preliminary randomized controlled clinical trial. *J Int Acad Periodontol*, *22*(3), 166-173.
13. Sharma, K., Madan, E., Nirwal, A., & Fatima, Z. (2024). Comparative Evaluation of Efficacy of Chitosan and Chlorhexidine Mouthwash in Plaque Control and Gingivitis: An Observational Study. *Cureus*, *16*(10).
14. Leo, M., Martínez, L., Rincón, F., & Ramos, R. L. O. (2021). Propiedades químicas y microbiológicas de membranas de quitosano/propóleo con utilidad para regeneración tisular en cavidad bucal. *Acta bioclínica*, *11*(22), 7-29.
15. Narvaez-Flores, J. J., Vilar-Pineda, G., Acosta-Torres, L. S., & Garcia-Contreras, R. (2021). Efectos citotóxicos y antiinflamatorios del quitosano y la gelatina hemostática en cultivo celular oral. *Acta Odontológica Latinoamericana*, *34*(2), 98-103.
16. Mira, J., Vivancos, F., Porcar, M., & Pascual, J. (2022). Estudio de prueba de concepto sobre la eficacia de una pasta dental y un colutorio para hacer frente simultáneamente a gingivitis e hiperestesia dental. *RCOE*, *27*(2), 235-42.
17. Apaza Quispe, L. E., & Quilla Quispe, L. (2024). Nivel de conocimientos sobre colutorios bucales y técnicas de cepillado en estudiantes de odontología de una universidad privada, *Puno* 2023.
18. Vaca, W. V., & Conde, M. M. C. (2022). Higiene bucodental base de prevención odontológica. *Revista Científica de Odontología UNITEPC*, *1*(2), 28-32.
19. Jafernik, K., Ładniak, A., Blicharska, E., Czarnek, K., Ekiert, H., Wiącek, A. E., & Szopa, A. (2023). Chitosan-based nanoparticles as effective drug delivery systems—a review. *Molecules*, *28*(4), 1963.
20. Collado-Gonzalez, M., & Esteban, M. Á. (2022). Chitosan-nanoparticles effects on mucosal immunity: A systematic review. *Fish & Shellfish Immunology*, *130*, 1-8.
21. Wathoni, N., Herdiana, Y., Suhandi, C., Mohammed, A. F. A., El-Rayyes, A., & Narsa, A. C. (2024). Chitosan/Alginate-Based Nanoparticles for Antibacterial Agents Delivery. *International Journal of Nanomedicine*, 5021-5044.
22. Mikušová, V., & Mikuš, P. (2021). Advances in chitosan-based nanoparticles for drug delivery. *International Journal of Molecular Sciences*, *22*(17), 9652.
23. Guardiola, S. H., & Zapata, M. E. V. (2021). Andamios de quitosano con L-Arginina para su aplicación en salud dental. *Revista Nacional de Odontología*, *17*(2), 1-21.
24. Guadarrama-Escobar, O. R., Serrano-Castañeda, P., Anguiano-Almazán, E., Vázquez-Durán, A., Peña-Juárez, M. C., Vera-Graziano, R., Morales-Florido M.I., Rodríguez-Pérez B., Rodríguez-Cruz I.M., Miranda-Calderón J.E., & Escobar-Chávez, J. J. (2023). Chitosan nanoparticles as oral drug carriers. *International Journal of Molecular Sciences*, *24*(5), 4289.

Cite This Article: Citlali Martínez-Morales, Mara Gómez-Flores, Maikel Hermida-Rojas, Roberto Ibarra-Wiley, Marco Arturo Moreno-Solorio (2024). Efficacy and Safety of EPX® Biomolecule Mouthwash for Treating Chronic Gingivitis. *EAS J Dent Oral Med, 6*(6), 96-102.