A novel injectable smart piezoelectric hydrogel for periodontal disease treatment with both antibacterial and tissue regeneration effects

Lina Roldan[1,2], Carolina Montoya[1], Santiago Correa[2], Santiago Orrego[1,3]
[1]Department of Oral Health Sciences, Kornberg School of Dentistry, Temple University.
[2]Bioengineering Research Group (GIB), Universidad EAFIT. Medellín, Colombia.
[3]Bioengineering Department, College of Engineering, Temple University. Philadelphia, PA.

Statement of Purpose: Periodontal disease is the most common oral disease globally with 10% of prevalence[1,2]. Periodontitis is caused by a microbial imbalance leading to the destruction of periodontal tissues including gum, bone and failure of teeth[3]. Excessive proliferation of bacteria including *P. gingivalis* results in the evasions of the host immune response[4]. The regeneration of periodontal tissues is limited once damaged[3]. Early-stage treatment for periodontal disease includes mechanical cleaning with adjuvants to remove pathogens. If unsuccessful, regenerative surgery implanting bone grafts is required[4]. There is a lack of a unified treatment with minimally invasive techniques that covers both the removal of pathogens and the regeneration of tissues. Hydrogels have been proposed as a vehicle to deliver drugs in the periodontium to treat periodontitis. However, there is a lack of the unified solution (antimicrobial/regeneration) without the use of antibiotics[5]. The purpose of our study is to develop an injectable, light-curable piezoelectric hydrogel that provide a minimally invasive treatment for periodontitis. Piezoelectric charges will provide antibacterial and regenerative effects and stimulated by vibrations from mastication[6]. The aim of this work is to show the antibacterial and tissue regeneration effects of piezoelectric-hydrogels both in-vitro and in-vivo.

Materials and methods: Piezoelectric hydrogels were fabricated by mixing a GelMA solution (20% (w/v)), 9 mg/mL of silanized barium titanate nanoparticles as piezoelectric filler (BTO) and LAP as photoinitiator 1.5% (w/v). Control hydrogels were prepared without BTO fillers. To characterize the hydrogel performance, biodegradation, voltage and electrical charge generation, injection force and rheology properties were measured. The antibacterial activity of the hydrogel was evaluated using single-specie cultures of *S. mutans*, and *P. gingivalis*. The hydrogel samples were incubated in bacterial liquid cultures under a cyclic mechanical loading (2 N, 10 Hz). After the incubation period, cell viability and metabolism were evaluated using colony-forming units (CFU) and MTT assay respectively. Fluorescence microscopy was used to assess the number of live and dead cells. The experimental murine ligature-induced periodontitis model was used to assess the antibacterial and tissue regeneration effects in-vivo[7]. Hydrogels were implanted in the periodontal pocket for 1 month. Micro-CT and histology between control (periodontal defect treated with Arestin®, without treatment) and treated groups (periodontal defect treated with BTO) was conducted.[7]

Results: Biodegradation tests showed mass reduction of 12% by day 4 and 20% by day 21. The voltage generated by the hydrogel is proportional to the applied mechanical load with an average of 13 mV for a 5 N load. An injection force of 11 N (enough for clinical injectability) was measured. Storage and loss moduli after curing revealed solid-like properties (G'': 10 kPa and G': 11 kPa) showing structural integrity of the hydrogel inside the periodontal pocket. Antibacterial effects were observed for the piezoelectric hydrogel against *S. mutans*, and *P. gingivalis* with a decrease of 30% in the number of viable cells and metabolic activity (Fig. 1A). Regarding the animal model, we induced periodontitis and created defect of 0.5 mm, which was filled by the hydrogel with therapy. At the time of the abstract, regeneration results are pending.

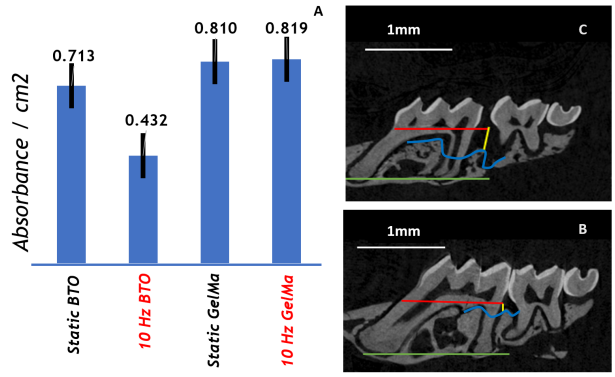

Figure 1. A) Antibacterial (metabolic activity) evaluation for different hydrogels under mechanical stimulation. B) Murine model: Control group without periodontitis. C) experimental group with periodontitis with a pocket size of ~0.7 mm.

Conclusion: According to the results of this study, the piezoelectric hydrogel showed adequate physical and mechanical properties for clinical application. In addition, we showed the antibacterial effects of the piezoelectric hydrogel. Currently, the hydrogel is evaluated in mice to show regeneration and no inflammation. Additional in vitro studies with bone marrow stem cells are underway.

References

1. Peres MA, et al. Oral diseases. *Lancet*. 2019
2. Alemu Abajobir et al. 2017.
3. Gasner NS. *Periodontal Dis*. 2021.
4. Kormas I et al. *Antibiotics (Basel)*. 2020
5. He XT et al. *Acta Biomater*. 2018.
6. M K et al. *J Dent Res*. 2002
7. Marchesan, J et al. *Nature Protocols*. 2018