



## HYDROGEL SCAFFOLD IN TREATMENT OF PERIODONTAL INTRABONY DEFECT (REVIEW ARTICLE)

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### Abstract

A promising method for treating periodontal problems is hydrogel, a substance made of functional polymers. With excellent biocompatibility, hydration retention, and sustained release, it has the potential to mimic the extracellular matrix and offer periodontal cells with adequate attachment sites and growth conditions. In order to serve as a guide for future work, we have outlined the key elements of hydrogel in this paper's discussion of periodontal tissue regeneration and major hydrogel production techniques. Hydrogels are crucial in the engineering of periodontal tissue because they offer cells the perfect habitat. Future research must focus on the creation of intelligent, multipurpose hydrogels for periodontal reconstruction.

**Keywords:** periodontal regeneration, hydrogel, infrabony defect, periodontitis

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## 1. INTRODUCTION

Periodontium is the structures surrounding teeth and it is composed of both hard and soft tissue collectively. Periodontal ligament (PDL) and alveolar bone around the teeth, as well as cementum, are rebuilt during periodontal reconstruction (1). A successful regeneration of the injured periodontal tissue is the desirable outcome of periodontal therapy. In order to stop the spread of inflammation and the subsequent deterioration of periodontal tissue, the primary goal of conventional periodontal therapies such mechanical debridement and flap surgery is to remove plaque and pathological granulation tissue (2).

The ideal goal of periodontal regeneration therapy is to restore the morphology and function of the distracted periodontium, although this is still a difficult task. The current clinical treatments to periodontal regeneration use guided tissue regeneration and bone grafts, although these methods have limitations in indications including intraosseous defects and class II fissure defects. Their ability to regenerate is further constrained by their high technical sensitivity (3).

One of the effective methods for repairing periodontal tissue that has been harmed by dental pathogen is to use a wide variety of scaffold materials that have been developed in recent years to encourage alveolar bone development inflammation. The creation of new periodontal tissues can be aided

by the use of ideal biomaterials, which can attract regeneration-related functional cells, encourage their proliferation, and differentiate them. The simultaneous or sequential restoration of the morphology and functionality of the PDL, alveolar bone, and cementum, however, poses the primary problem in periodontal regeneration therapy at the moment (4).

Hydrogels are three-dimensional water-swollen polymeric materials that have been extensively employed in biomedical applications such cell culture, drug administration, and tissue engineering. They offer excellent biocompatibility, mechanical strength, and accessibility. Biomaterials offer a three-dimensional framework for cell adhesion, proliferation, and differentiation in tissue engineering. The scaffold should be a three-dimensional, porous, network-like structure that gives cells the room they need to deposit extracellular matrix and exchange cellular compounds with their surroundings. Hydrogels can imitate the milieu of the extracellular matrix, which is advantageous for cell attachment, proliferation, and differentiation. This is possible because of their unusual three-dimensional mesh structure, high porosity, superior hydrophilicity and viscoelasticity, and tunable compositions. Hydrogels have acquired popularity because they exhibit substantial potential for periodontal regeneration whether combined with medication, stem cells, or growth hormones (5), (6), (7).

## **2. Hydrogel Components in Periodontal Regeneration**

The fundamental elements of hydrogels determine the substance's characteristics and use. Additionally, bioactive chemicals can be encapsulated within hydrogels to provide them antibacterial, anti-inflammatory, osteogenetic, and osteoimmunology properties, as well as to enhance the regeneration of periodontal tissue as required. Hydrogel classified into two parts natural and synthetic hydrogel.

### **2.1. Natural hydrogel**

Natural polymers are polymers that derived from natural sources, as collagen, glycoproteins and proteoglycan. ECM consists of the same structures of natural polymers so they are highly biocompatible and biodegradable, and don't produce harmful products during degradation. Also, natural hydrogels are water soluble so they facilitate cell migration, adhesion and proliferation due to hydrophilic properties. However, these properties natural polymers have low mechanical strength and stability. The most common natural polymers that are widely used are collagen, alginate, hyaluronic acid and Chitosan (8).

#### **2.1.1. Collagen**

Collagen is a crucial part of the extracellular matrix, has a wide range of cell signaling binding sites, and has great biocompatibility. It is frequently utilized to create periodontal tissue engineering scaffolds. Collagen can help functional cells involved in periodontal regeneration adhere, develop, proliferate, and differentiate in a specific direction (9), (10). Collagen membranes used as barriers to protect epithelial migration/ingrowth to allow regenerative ability of pluripotent cells at area of lesion to repopulate in periodontal and implant treatments are examples of resorbable collagens that are used in oral wound dressing, accelerating wound healing, and closure for graft and extraction sites (11).

#### **2.1.2. Chitosan**

Is a natural polysaccharide that resembling glycosaminoglycan in biological and chemical structure. Enzymatically solidified chitosan hydrogels with or without cell loading demonstrated excellent potential in periodontal regeneration in terms of functional ligament length, according to Yan, X. Z. et al. (12). After four weeks of implantation, chitosan hydrogels were largely destroyed, according to histological research, without having any negative effects on the tissues around them (12).

#### **2.1.3. Hyaluronic acid**

Hyaluronic acid (HA) is a naturally occurring polysaccharide that has been widely used in various

biomedical applications, including tissue engineering and regenerative medicine. HA-based hydrogels have shown great potential for periodontal regeneration due to their ability to mimic the native extracellular matrix (ECM) of periodontal tissues. One study published in the Journal of Clinical Periodontology evaluated the use of an HA-based hydrogel for periodontal regeneration in dogs. The results showed significant improvement in new bone formation and periodontal regeneration compared to a control group without the hydrogel treatment (13). Another study published in Materials Science and Engineering: C investigated the use of a composite hydrogel containing both HA and chitosan for periodontal regeneration. The study found that the composite hydrogel showed better cell proliferation and migration as well as improved osteogenic differentiation compared to a hydrogel containing only HA or chitosan (14). Overall, these studies suggest that HA-based hydrogels have great potential for periodontal regeneration and warrant further investigation in clinical trials.

### **2.2. Synthetic hydrogel**

Synthetic hydrogels have shown promising results in periodontal regeneration. These hydrogels are typically made from biocompatible polymers and can be designed to mimic the natural extracellular matrix (ECM) found in tissues. One approach involves using hydrogels as a delivery vehicle for growth factors, which are critical for stimulating cell proliferation and differentiation. The hydrogel can be loaded with growth factors such as bone morphogenetic proteins (BMPs), platelet-derived growth factor (PDGF), or transforming growth factor-beta (TGF- $\beta$ ), among others. These growth factors can then be released slowly over time, providing a sustained stimulus for tissue regeneration. Another approach involves using hydrogels as a scaffold for cell growth. In this method, the hydrogel is seeded with cells such as mesenchymal stem cells (MSCs) or periodontal ligament cells (PDLs). The cells can then attach to the hydrogel and proliferate, forming new tissue (15). Overall, synthetic hydrogels show great promise in the field of periodontal regeneration, as they can be tailored to meet specific needs and provide a platform for both growth factor delivery and cell growth. However, more research is needed to fully understand their potential and optimize their use in clinical settings. Some of the types of synthetic hydrogels that have been studied for periodontal regeneration include: Polyethylene glycol (PEG), Polyvinyl alcohol (PVA), Methacrylated chondroitin sulfate (MeCS) and polyacrylic acid (PAA).

#### **2.2.1. Polyethylene glycol (PEG)**

PEG- based hydrogels have been studied extensively for their potential in periodontal regeneration. PEG is a synthetic, water-soluble polymer that can form hydrogels through chemical crosslinking. These

hydrogels have several properties that make them attractive as scaffolds for periodontal tissue engineering.

Firstly, PEG hydrogels are highly biocompatible and non-immunogenic, which means they are unlikely to cause any adverse reactions in the body. They are also easily modifiable with different functional groups, allowing for customization of the hydrogel properties such as degradation rate and mechanical strength. Secondly, PEG hydrogels have high water content, which allows for efficient transport of nutrients and oxygen to support cell growth and proliferation. This property is particularly important for regenerating periodontal tissues, which require a constant supply of nutrients and oxygen from the blood vessels in the surrounding tissues (16).

Thirdly, PEG hydrogels have been shown to promote the attachment and proliferation of various cell types relevant to periodontal regeneration, including periodontal ligament cells and mesenchymal stem cells. This is likely due to the hydrophilic nature of PEG, which helps to mimic the extracellular matrix of natural tissues and facilitate cellular interactions. Finally, PEG hydrogels can be loaded with bioactive molecules such as growth factors or antibiotics to enhance their regenerative properties. These molecules can be released in a controlled manner over time, providing sustained delivery to the regenerated tissues (17).

### **2.2.2. Polyacrylic acid (PAA)**

(PAA) is a synthetic polymer that has been investigated for use in periodontal regeneration. The idea behind using PAA is that it can bind to the tooth surface and create a barrier against bacteria, while also promoting the growth of new tissue. Studies have shown that PAA can improve the attachment of cells to the tooth surface and enhance the proliferation of periodontal ligament cells. It has also been found to stimulate the production of extracellular matrix components, which are essential for the formation of new tissue. In addition, PAA has been used as a delivery system for growth factors such as platelet-derived growth factor (PDGF) and bone morphogenetic protein (BMP), which are known to promote periodontal regeneration. While the results of studies on PAA for periodontal regeneration are promising, more research is needed to determine its efficacy and safety in humans. Nonetheless, PAA is an interesting area of research for the treatment of periodontal disease and regeneration of periodontal tissues (17), (18).

### **2.2.3. Polyvinyl alcohol (PVA)**

PVA is a water-soluble, synthetic polymer that has been investigated for its potential use in periodontal regeneration. Periodontal regeneration refers to the regrowth of tissues such as bone, ligaments, and

connective tissue in the periodontium, which supports and anchors the teeth. In preclinical studies using animal models, PVA has shown promising results in promoting periodontal regeneration. PVA has been used as a scaffold material to support the growth of new tissue in the periodontium. The porous structure of PVA allows for the ingrowth of cells and the deposition of extracellular matrix components such as collagen. In addition to its scaffold properties, PVA has also been shown to have anti-inflammatory and antibacterial effects. This is important in the context of periodontal regeneration, as inflammation and bacterial infection can interfere with the healing process (19).

In conclusion, hydrogels show great promise as a scaffold for periodontal regeneration. They can provide a natural-like environment for tissue growth, promote cell adhesion, proliferation, and differentiation, and can be engineered to release growth factors. Chitosan-based hydrogels and hyaluronic acid-based hydrogels are two types of hydrogels that have shown particular promise in periodontal tissue regeneration. Also synthetic polymers can produce the same effect as natural polymers in addition they have high mechanical strength and long degradation rate than natural polymers. Further research is needed to determine the optimal conditions for their use in clinical settings.

## **3. REFERENCES**

1. **Batool F, Strub M, Petit C, Bugueno IM, Bornert F, Clauss F, et al.** Periodontal tissues, maxillary jaw bone, and tooth regeneration approaches: From animal models analyses to clinical applications. *Nanomaterials*. 2018;8(5).
2. **Aljateeli M, Koticha T, Bashutski J, Sugai J V., Braun TM, Giannobile W V., et al.** Surgical periodontal therapy with and without initial scaling and root planing in the management of chronic periodontitis: A randomized clinical trial. *Journal of Clinical Periodontology*. 2014;41(7):693–700.
3. **Jepsen S, Gennai S, Hirschfeld J, Kalemaj Z, Buti J, Graziani F.** Regenerative surgical treatment of furcation defects: A systematic review and Bayesian network meta-analysis of randomized clinical trials. *Journal of Clinical Periodontology*. 2020;47(S22):352–74.
4. **Liu J, Ruan J, Weir MD, Ren K, Schneider A, Wang P, et al.** Periodontal Bone-Ligament-Cementum Regeneration via Scaffolds and Stem Cells. *Cells*. 2019 Jun;8(6).
5. **Abboud AR, Ali AM, Youssef T.** Preparation and characterization of insulin-loaded injectable hydrogels as potential adjunctive periodontal treatment. *Dental and Medical Problems*. 2020;57(4):377–84.
6. **Yuan W, Wang H, Fang C, Yang Y, Xia X, Yang B, et al.** Microscopic local stiffening in a

- supramolecular hydrogel network expedites stem cell mechanosensing in 3D and bone regeneration. *Mater Horiz* [Internet]. 2021;8(6):1722–34. Available from: <http://dx.doi.org/10.1039/D1MH00244A>
7. **Pan J, Deng J, Yu L, Wang Y, Zhang W, Han X, et al.** Investigating the repair of alveolar bone defects by gelatin methacrylate hydrogels-encapsulated human periodontal ligament stem cells. *Journal of Materials Science: Materials in Medicine* [Internet]. 2020;31(1). Available from: <http://dx.doi.org/10.1007/s10856-019-6333-8>
  8. **Kreller T, Distler T, Heid S, Gerth S, Detsch R, Boccaccini AR.** Physico-chemical modification of gelatine for the improvement of 3D printability of oxidized alginate-gelatine hydrogels towards cartilage tissue engineering. *Materials & Design* [Internet]. 2021;208:109877. Available from: <https://www.sciencedirect.com/science/article/pii/S0264127521004305>
  9. **Guo S, He L, Yang R, Chen B, Xie X, Jiang B, et al.** Enhanced effects of electrospun collagen-chitosan nanofiber membranes on guided bone regeneration. *Journal of Biomaterials Science, Polymer Edition* [Internet]. 2020 Jan 22;31(2):155–68. Available from: <https://doi.org/10.1080/09205063.2019.1680927>
  10. **Janjić K, Agis H, Moritz A, Rausch-Fan X, Andrukhov O.** Effects of collagen membranes and bone substitute differ in periodontal ligament cell microtissues and monolayers. *Journal of Periodontology*. 2022;93(5):697–708.
  11. **Binlath T, Thammanichanon P, Rittipakorn P, Thinsathid N, Jitprasertwong P.** Collagen-Based Biomaterials in Periodontal Regeneration: Current Applications and Future Perspectives of Plant-Based Collagen. *Biomimetics*. 2022;7(2).
  12. **Yan XZ, Van Den Beucken JJJP, Cai X, Yu N, Jansen JA, Yang F.** Periodontal tissue regeneration using enzymatically solidified chitosan hydrogels with or without cell loading. *Tissue Engineering - Part A*. 2015;21(5–6):1066–76.
  13. **Bansal J, Kedige SD, Anand S.** Hyaluronic acid: a promising mediator for periodontal regeneration. *Indian journal of dental research : official publication of Indian Society for Dental Research*. 2010;21(4):575–8.
  14. **Bhati A, Fageeh H, Ibraheem W, Fageeh H, Chopra H, Panda S.** Role of hyaluronic acid in periodontal therapy (Review). *Biomedical reports*. 2022 Nov;17(5):91.
  15. **Rahimi M, Charmi G, Matyjaszewski K, Banquy X, Pietrasik J.** Recent developments in natural and synthetic polymeric drug delivery systems used for the treatment of osteoarthritis. *Acta Biomaterialia* [Internet]. 2021;123:31–50. Available from: <https://doi.org/10.1016/j.actbio.2021.01.003>
  16. **Sun S, Cui Y, Yuan B, Dou M, Wang G, Xu H, et al.** Drug delivery systems based on polyethylene glycol hydrogels for enhanced bone regeneration. *Frontiers in bioengineering and biotechnology*. 2023;11:1117647.
  17. **Li M, Lv J, Yang Y, Cheng G, Guo S, Liu C, et al.** Advances of Hydrogel Therapy in Periodontal Regeneration-A Materials Perspective Review. *Gels (Basel, Switzerland)*. 2022 Sep;8(10).
  18. **Jeong JO, Park JS, Kim EJ, Jeong SI, Lee JY, Lim YM.** Preparation of radiation cross-linked poly(Acrylic acid) hydrogel containing metronidazole with enhanced antibacterial activity. *International Journal of Molecular Sciences*. 2020;21(1).
  19. **Ayala-Ham A, López-Gutierrez J, Bermúdez M, Aguilar-Medina M, Sarmiento-Sánchez JI, López-Camarillo C, et al.** Hydrogel-Based Scaffolds in Oral Tissue Engineering. *Frontiers in Materials*. 2021;8(July):1–26.