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REVIEW

Derleme

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Smart and Bioactive Hydrogels in Dentistry: Emerging Regenerative Applications

Diş Hekimliğinde Akıllı ve Biyoaktif Hidrojeller: Yeni Rejeneratif Uygulamalar

ABSTRACT

Smart and bioactive hydrogels offer significant potential for regenerative applications in dentistry. Their biocompatibility, capacity to carry bioactive agents, and function as tissue engineering scaffolds are opening new horizons in oral tissue regeneration. They provide advanced solutions for a variety of dental problems such as periodontal disease, endodontic lesions, and bone defects. With ongoing research and technological advancements, smart and bioactive hydrogels represent future options for improving dental practice and providing better treatment outcomes at affordable prices. This review examines the re-creation and stored records of smart and bioactive hydrogels in dentistry. It highlights the transformative potential of hydrogels in oral tissue engineering in the face of the limitations of traditional treatment methods. In particular, recent research and advancements discuss how these advanced biomaterials are shaping, or will shape, dental practice.

Key Words

Hydrogels, Regenerative, Biomedicine

ÖZ

Akıllı ve biyoaktif hidrojeller, diş hekimliğinde rejeneratif uygulamalar için büyük bir potansiyel sunmaktadır. Biyouyumlulukları, biyoaktif ajanları taşıma yetenekleri ve doku mühendisliği iskeleleri olarak işlev görmeleri, oral doku rejenerasyonunda yeni ufuklar açmaktadır. Periodontal hastalıklar, endodontik lezyonlar ve kemik defektleri gibi çeşitli diş hekimliği sorunlarına yönelik yenilikçi çözümler sunmaktadırlar. Devam eden araştırmalar ve teknolojik gelişmelerle birlikte, akıllı ve biyoaktif hidrojellerin gelecekte diş hekimliği pratiğini dönüştürmesi ve hastalar için daha iyi tedavi sonuçları sağlaması beklenmektedir. Bu derlemede, diş hekimliğinde akıllı ve biyoaktif hidrojellerin rejeneratif uygulamalarını derinlemesine incelemektedir. Geleneksel tedavi yöntemlerinin sınırlılıkları karşısında, hidrojellerin oral doku mühendisliğindeki dönüştürücü potansiyeli vurgulanmaktadır. Özellikle son yıllardaki güncel araştırmalar ve ilerlemeler, bu yenilikçi biyomateryallerin diş hekimliği pratiğini nasıl şekillendirdiği veya şekillendireceğinden bahsedilmektedir.

Anahtar Sözcükler

Hidrojeller, Rejeneratif, Biyotıp

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INTRODUCTION

Hydrogels are three-dimensional polymer networks capable of absorbing vast quantities of biological fluids or water. In the field of biomedicine, they have evolved into materials that are versatile, especially in dentistry (1). Their unique properties, such as biocompatibility, adjustable mechanical properties, and the ability to respond to different stimuli, make them indispensable for a wide range of dental applications, from targeted drug delivery and tissue regeneration to faster wound healing. Hydrogels are suitable for regenerative endodontics and periodontics because they can replicate the natural extracellular matrix (ECM). They provide crucial requirements for tissue development, including regulated biodegradability and viscoelasticity (2,3). Long-term stability in the aqueous oral environment is further guaranteed by their exceptional hydrophilicity, which is crucial for sustained performance (2).

The oral cavity environment hinders drug delivery because of the way chemicals and physical interactions operate. By acting as supporting carriers for various bioactive substances and cells, hydrogels effectively overcome these challenges (4,5). The porous structure of hydrogels facilitates metabolic waste removal disposal and nutrient delivery, both of which are essential for cellular viability and proliferation in tissue engineering applications (3,6). Innovative antibacterial hydrogels provide a promising approach for addressing dental tissue infections, which often result in significant discomfort and tooth loss, by mimicking the original extracellular matrix of soft tissues (7). The creation of multifunctional hydrogels is essential for addressing infections, reducing inflammation, and alleviating oxidative stress, therefore enhancing dental regeneration methods (3).

This paper seeks to underscore the expanding potential of smart hydrogels (SHs) in the treatment of diverse oral pathologies. This review aims to highlight their developing functionalities as responsive, bioactive platforms in endodontics, periodontal regeneration, and oral and maxillofacial tissue reconstruction, emphasizing their translational significance in modern dental medicine.

SHs in Periodontology

Periodontal disease is a highly prevalent chronic inflammatory condition affecting a significant proportion of the global population and remains one of the leading causes of tooth loss in adults. Its treatment primarily consists of professional supragingival debridement to remove calculus and plaque deposits during the first treatment visit, along with behavioral changes related to the patient, especially the improvement of oral hygiene habits. The second therapeutic step consists of scaling and root planning, especially in the presence of subgingival calculus and periodontal pockets exceeding 4 mm in probing depth. Despite adequate plaque control and the removal of local contributing factors, certain sites may continue to exhibit residual periodontal pockets greater than 4 mm, associated with bleeding on probing. These pockets can also be associated with vertical intrabony defects characterized by 1-, 2-, or 3-wall bony configurations. In such situations, regenerative surgical therapy may be considered. As a result of their hydrophilic nature and ability to act as carriers for a variety of bioactive agents, hydrogels offer a promising adjunctive option in the regenerative management of these defects. Additionally, their injectability makes them easy to apply. In order to improve their stability and extended therapeutic action within the defect site, advanced formulations can be designed to undergo polymerization in response to thermal stimuli or ultraviolet light.

A thermo-reversible polyisocyanopeptide-based hydrogel, augmented with doxycycline and lipoxin A4, exhibited considerable therapeutic efficacy in an experimental periodontitis model including 41 Beagle dogs. The local application of this injectable hydrogel significantly reduced subgingival bacterial load, accompanied by a significant decrease in pro-inflammatory interleukin-8 levels. These findings highlight the dual antimicrobial and immunomodulatory effects of this material, supporting its potential role as an adjunctive therapeutic strategy in periodontal regenerative approaches (8).

In a murine model, PiezoGEL, another novel formulation based on gelatin methacryloyl (GelMA) combined with biocompatible piezoelectric barium titanate fillers, has shown encouraging outcomes both *in vitro* and *in vivo.* With the addition of piezoelectric fillers, hydrogels can produce localized electrical charges in response to biomechanical forces like mastication. By upregulating important osteogenic markers like RUNX2, COL1A1, and ALP, this property enhances bone marrow stem cell viability and promotes osteogenic differentiation while also significantly reducing pathogenic biofilm biomass. *In vivo* data demonstrated that PiezoGEL considerably enhanced bone tissue regeneration and decreased periodontal inflammation as compared to control groups, underscoring its promise as a versatile electroactive platform for periodontal regenerative therapy (9).

SHs in Endodontics

A naturally occurring cationic polysaccharide, chitosan is well-known for its cost-effectiveness, biocompatibility, and biodegradability. It can be mixed with the non-toxic anionic substance β-glycerophosphate (β-GP) to form an injectable thermosensitive hydrogel via electrostatic interactions at physiological temperature. In order to assist conventional periodontal therapies and encourage tissue repair, Ma *et al.* (10) created a delivery system that regulates the release of antioxidants and antimicrobial peptides. *In vitro* tests demonstrated the hydrogel's ease of production, biocompatibility, and potent antibacterial, anti-inflammatory, and antioxidant qualities. The hydrogel demonstrated the potential of thermosensitive chitosan hydrogels as flexible platforms for combined antimicrobial and host-modulatory approaches in periodontal regeneration by successfully reducing alveolar bone loss and significantly reducing local inflammation in a rat periodontitis model.

As previously mentioned, hydrogels show great potential in the management of periodontal, however, their clinical applicability extends far beyond periodontal therapy. They are increasingly being explored as potential alternatives to conventional root canal treatment, as hydrogels are considered promising scaffolds capable of triggering dental pulp regeneration in devitalized human teeth. *In vitro* cellular studies have shown that the incorporation and controlled delivery of exosomes significantly enhance the regenerative capacity of hydrogels, promoting both odontogenesis and angiogenesis. In a study that examined a thermosensitive hydrogel based on hydroxypropyl chitin and chitin whisker, it was demonstrated that *in vivo* animal trials had already produced newly created pulp-like tissues within implanted tooth root models. These results support the importance of hydrogel-based platforms as multifunctional biomaterials that can orchestrate complicated tissue regeneration processes, suggesting their translational potential in regenerative endodontics (11).

These findings have led to additional advancements in hydrogel-based endodontic treatments, which reinforce their capacity for regeneration. Using a Schiff base reaction between carboxymethyl chitosan and polyethylene glycol aldehyde (OHC-PEG-CHO) to create a complex system, an injectable hydrogel containing modified triple antibiotic drugs (mTAD) has demonstrated encouraging outcomes. In addition to enabling localized and sustained antimicrobial release, this system created an environment that was conducive to tissue regeneration. The outcome of the experiment demonstrated that mTCP hydrogel significantly promoted the ongoing growth of roots and aided in the healing of periapical tissue. All these findings suggest that these innovative, medication-loaded injectable hydrogels could be used as a minimally invasive method of regenerative endodontic therapy and root canal disinfection (12).

Enterococcus faecalis is a well-recognized pathogen frequently associated with persistent root canal infections and endodontic treatment failure (13). These are due to their remarkable resistance to conventional irrigants and intracanal medicaments (14). The inhibitory effect of calcium hydroxide is often limited because of the complex root canal anatomy, where complete penetration is difficult to achieve. Its use has been associated with undesirable side effects, including postoperative discomfort and potential weakening of the dentinal structure over time. The development of novel intracanal therapeutic strategies capable of effectively suppressing bacterial growth and improving the clinical success rate of pulpitis treatment remains of paramount importance. To reduce these pathogens' activity, antimicrobial agents should be taken into consideration. While chlorhexidine works against bacteria by changing the permeability of the bacterial cytoplasmic membrane, which causes cell lysis and intracellular component leakage, metronidazole has shown antimicrobial activity against anaerobic pathogens, such as *Enterococcus faecalis*. In one study, an *in vitro* evaluation of a UV-responsive hydrogel loaded with either metronidazole or chlorhexidine shown significant inhibitory effects against recognized endodontic pathogens. These results highlight the promise of intelligent, photoresponsive hydrogels as innovative intracanal drug delivery devices in endodontic therapy (15).

SHs in Oral and Maxillofacial Surgery

In modern dentistry, alveolar bone regeneration and prevention of subsequent ridge resorption continue to be major obstacles, especially in aesthetically demanding areas. Biocompatible and biodegradable biomaterials with osteoconductive and osteoinductive qualities are necessary for effective bone regenerating techniques. Crucially, these materials should mimic important structural and functional characteristics of the extracellular matrix of natural bone, promoting the recruitment, adhesion, proliferation, and differentiation of stem cells to facilitate the new bone formation. The good cytocompatibility, large loading capacity for bioactive chemicals, and versatile mechanical properties of injectable hydrogels have made them appealing platforms in bone tissue engineering. These systems can further improve their regenerative performance when paired with nano-hydroxyapatite, a bioceramic that closely resembles the mineral phase of human bone. Nano-hydroxyapatite is the main inorganic component of bone extracellular matrix and reflects the crystalline structure and chemical makeup of skeletal tissue. To help preserve the alveolar ridge after tooth extraction, composite scaffolds that combine inorganic hydroxyapatite particles with organic hydrogel matrices like hyaluronan and chitosan-known as hydrogel-hydroxyapatite systems- have been proposed. Hydrogels' inherent porous structure makes it easier for endogenous stem cells to migrate into the defect site and adapt to irregular post-extraction bone cavities. Additionally, the mineral phase and the hydrogel network work in concert to produce a favorable microenvironment that encourages osteoconduction and osteoinduction, which improves *in vivo* bone regeneration (16).

High-performance polymer polyetheretherketone (PEEK) has drawn more interest as a metal-free titanium substitute in implant dentistry. It is biocompatible and has good mechanical qualities. Researchers have added PEEK to injectable hydrogel systems made of silk fibroin (SF) and aldehyde-modified cellulose nanocrystals (ADCNCs) to increase its regeneration capacity. These composite hydrogels combine the structural stability of PEEK with the bioactive and adaptable characteristics of the polymeric matrix. PEEK-integrated ADCNCs/SF hydrogels may promote bone regeneration in craniofacial defects, especially in peri-implant areas where implant stability is jeopardized by bone loss, according to preclinical research.

Such injectable systems offer a promising approach to boosting peri-implant bone regeneration and enhancing long-term implant success by offering a supportive scaffold and a favorable microenvironment for cellular infiltration and osteogenic activity (17).

Despite the encouraging outcomes that have been reported so far, it is important to point out several significant limitations. Most of the existing evidence related to hydrogel-based therapies in dentistry has been obtained using *in vitro* studies and *in vivo* animal models. While these studies are certainly useful for gaining a deeper understanding of the mechanisms and proof-of-concept, they cannot fully reflect the biological complexity, microbiological diversity, and mechanical forces that are present in the human oral environment. Future studies should aim to provide a more detailed examination of individual hydrogel systems rather than attempting to broadly assess a variety of heterogeneous formulations. Standardized experimental protocols, the utilization of well-established and pathology-specific animal models, and multicenter preclinical validation studies are all critical steps that must be taken before attempting to enter human clinical trials. In addition, it will be necessary to utilize high-quality methodological approaches and long-term outcome measures in order to accurately assess safety, efficacy, and true regenerative potential.

CONCLUTION

Within the context of the existing level of evidence, hydrogels are a relatively modern and highly promising alternative to existing therapeutic approaches in dentistry. The multifunctional nature of these systems makes them innovative platforms that have the potential to alter future regenerative and minimally invasive dental therapies.

Abbreviations

ECM: Extracellular Matrix, GelMA: Gelatin Methacryloyl, β-GP: β-glycerophosphate, mTAD: Modified Triple Antibiotic Drug, PEEK: Polyetheretherketone, SF: Silk Fibroin, ADCNCs: Aldehyde-Modified Cellulose Nanocrystals

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Authors' Contributions

Concept: A-M.B-Ş., Z.B-V., E.S.B.; Supervision: A-M.B-Ş., Z.B-V., E.S.B.; Resources: A-M.B-Ş., Z.B-V., E.S.B.; Materials: A-M.B-Ş., Z.B-V., E.S.B.; Data Collection and/or Processing: A-M.B-Ş., Z.B-V., E.S.B.; Analysis and/ or Interpretation: A-M.B-Ş., Z.B-V., E.S.B.; Literature Search: A-M.B-Ş., Z.B-V.; Writing Manuscript: A-M.B-Ş., Z.B-V., E.S.B.; Critical Review: E.S.B.

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Data Availability

Data is available from the corresponding author upon request.

Ethics Approval

Not required.

Conflicts of Interest

The authors declare no conflicts of interest.

AI Declaration

No AI tools were used.

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REFERENCES

1. Huang M, Huang Y, Liu H, *et al.* Hydrogels for the treatment of Oral and Maxillofacial diseases: current research, challenges, and future directions. Biomater. Sci. 2022; 10: 6413-46. doi: 10.1039/D2BM01036D

2. Fratila DN, Virvescu DI, Luchian I, *et al.* Advances and functional integration of hydrogel composites as drug delivery systems in contemporary dentistry. Gels. 2024; 10: 661. doi: 10.3390/gels10100661

3. Atila D, Kumaravel V. Advances in antimicrobial hydrogels for dental tissue engineering: regenerative strategies for Endodontics and Periodontics. Biomater Sci. 2023; 11: 6711-47. doi: 10.1039/D3BM00719G

4. Wang X, Zheng Z, Zhang Y, *et al.* Application of hydrogel-loaded dental stem cells in the field of tissue regeneration. Human Cell. 2024; 38: 2.doi: 10.1007/s13577-024-01134-2.

5. Hoveizi E, Naddaf H, Ahmadianfar S, *et al.* Encapsulation of human endometrial stem cells in chitosan hydrogel containing titanium oxide nanoparticles for dental pulp repair and tissue regeneration in male wistar rats. J Biosci Bioeng. 2023; 135: 331-40. doi: 10.1016/j.jbiosc.2022.12.009.

6. Ma Y, Wang X, Su T, *et al.* Recent advances in macroporous hydrogels for cell behavior and tissue engineering. Gels. 2022; 8: 606. doi: 10.3390/gels8100606

7. Flores-Espinoza AI, Garcia-Contreras R, Guzman-Rocha DA, *et al.* Gelatin–chitosan hydrogel biological, antimicrobial and mechanical properties for dental applications. Biomimetics (Basel). 2023; 8: 575. doi: 10.3390/biomimetics8080575

8. Wang B, Booij-Vrieling HE, Bronkhorst EM, *et al.* Antimicrobial and anti-inflammatory thermo-reversible hydrogel for periodontal delivery. Acta Biomater. 2020; 116: 259-67. doi: 10.1016/j.actbio.2020.09.018

9. Roldan L, Montoya C, Solanki V, *et al.* A novel injectable piezoelectric hydrogel for periodontal disease treatment. ACS Appl Mater Interfaces. 2023; 15: 43441-54. doi: 10.1021/acsami.3c08336

10. Ma S, Lu X, Yu X, *et al.* An injectable multifunctional thermo-sensitive chitosan-based hydrogel for periodontitis therapy. Biomater Adv. 2022; 142: 213158. doi: 10.1016/j.bioadv.2022.213158

11. Wang S, Xing X, Peng W, *et al.* Fabrication of an exosome-loaded thermosensitive chitin-based hydrogel for dental pulp regeneration. J Mater Chem B. 2023; 11: 1580-90. doi: 10.1039/D2TB02073D

12. Cao M, Wu D, Tu H, *et al.* Injectable hydrogel as intracanal medication for root canal disinfection. J Dent Res. 2025; 104: 503-12. doi: 10.1177/00220345241309865

13. Parga A, Mattu J, Belibasakis GN, *et al.* A polymicrobial perspective into the ecological role of Enterococcus faecalis in dental root canal infections. NPJ Biofilms Microbiomes. 2025; 11: 83. doi: 10.1038/s41522-025-00722-w

14. Sharma J, Jhamb S, Mehta M, *et al.* Characterization of Enterococcus faecalis associated with root canal failures: virulence and resistance profile. J Conserv Dent Endod. 2025; 28: 602. doi: 10.4103/JCDE.JCDE_190_25

15. Yan Y, Zhou P, Lu H, *et al.* Potential apply of hydrogel-carried chlorhexidine and metronidazole in root canal disinfection. Dent Mater J. 2021; 40: 986-93. doi: 10.4012/dmj.2020-299

16. Pan Y, Zhao Y, Kuang R, *et al.* Injectable hydrogel-loaded nano-hydroxyapatite improves bone regeneration and alveolar ridge promotion. Mater Sci Eng C Mater Biol Appl. 2020; 116: 111158. doi: 10.1016/j.msec.2020.111158

17. Alipour M, Ghorbani M, Johari Khatoonabad M, *et al.* A Novel injectable hydrogel containing polyetheretherketone for bone regeneration in the craniofacial region. Sci Rep. 2023; 13: 864. doi: 10.1038/s41598-022-23708-6