International Journal of Research and Review
[Indexed, Peer-Reviewed Journal]
Volume 12; Issue: 5; May 2025
Website: www.ijrrjournal.com
Review Paper
E-ISSN: 2349-9788; P-ISSN: 2454-2237

Hydrogels in Dentistry: A Step Forward in Dental Innovation

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DOI: https://doi.org/10.52403/ijrr.20250558

ABSTRACT

Oral diseases are a widespread global health concern, primarily involving microbial infections, inflammation and the degradation of oral tissues. While maintaining oral health is critical to overall well-being, effective treatment and regeneration of damaged dental structures remain significant challenges. Despite advances in dental medicine, current therapies are often limited by the performance of the materials used. This has driven growing interest in the development of advanced biomaterials to meet the complex demands of oral and craniofacial therapies. Biomaterials are engineered to interact with biological systems for diagnosis, treatment or tissue replacement. Hydrogels have garnered significant attention due to their capacity to replicate the natural tissue environment and facilitate cellular functions.
Hydrogels are three-dimensional structures with an insoluble crosslinked network of hydrophilic co-polymers, which endows them with the ability to adsorb and retain large amount of water in their swollen states, closely mimicking the natural extracellular matrix (ECM). Their highwater content, biocompatibility, porosity and viscoelastic properties support cell attachment, proliferation and differentiation. Though hydrogels do not directly heal tissues, they serve as effective carriers for drugs, cells or minerals creating a favourable microenvironment that enhances therapeutic outcomes in oral tissue repair and regeneration.
This article is the concise overview of hydrogel and their multifaceted application for treating various oral and maxillofacial conditions, including infection management and defect repair.

Keywords: Biomaterials, Extracellular matrix, Hydrogel, Polymeric network.

INTRODUCTION

Hydrogels are three-dimensional networks composed of insoluble, crosslinked hydrophilic copolymers, enabling them to absorb and retain large amounts of water in their swollen state, resembling the extracellular matrix.[1] Conventional materials often fail to satisfy the full spectrum of biological and functional criteria necessary for biomedical applications. As a result, research has increasingly turned toward developing advanced biomaterials, leading to the emergence of hydrogels as highly adaptable systems with improved biocompatibility, functionality and interaction with living tissues. Due to these advantages, hydrogels have attracted considerable interest in the biomedical field. They play a vital role in various therapeutic and clinical applications, such as tissue repair, drug delivery, and cell transplantation.[2]

Structurally, hydrogels consist of crosslinked polymer chains, with key characteristics such as mesh size and the molecular weight between crosslinks influencing their mechanical strength and ability to allow substances to diffuse through them. Hydrogels can be classified in various ways: by their origin (natural, synthetic and hybrid), by their composition (homopolymeric, copolymeric or interpenetrating polymer networks), by the type of crosslinking (chemical or physical), by their charge properties (neutral, ionic or ampholytic), by their degradability (biodegradable or non-biodegradable), by their structural arrangement ranging from amorphous to crystalline and by their ability to respond to environmental stimuli.[3-4] Of particular interest are stimuli-responsive or "smart" hydrogels, which undergo physical or chemical changes in response to environmental cues such as pH, temperature or specific biomolecules. These intelligent systems offer significant promise for next-generation biomedical applications, enabling precise control and adaptability in therapeutic and regenerative contexts.[2]

APPLICATIONS OF HYDROGEL:

1) Dental Caries

Dental caries is one of the most prevalent diseases that destroys tooth enamel and dentin, and its progression is closely related to the imbalance between demineralization and remineralization of the tooth.

Currently, materials like resin composites, cements and amalgam are used to treat dental caries, but they lack the structural and chemical characteristics of natural enamel, such as crystal alignment and graded anisotropy. This leads to weak bonding at the tooth interface, often causing marginal leakage, secondary caries and restoration failure. To overcome these limitations, bioinspired strategies are being explored. For instance, Mukherjee *et al* [5] developed a chitosan hydrogel containing leucine-rich amelogenin peptide, which formed a dense, mineralized layer of enamel-like apatite crystals and restored over 87% of natural enamel hardness. Similarly, Ruan *et al* [6] tested an amelogenin-chitosan hydrogel under pH-cycling conditions and found that it promoted crystal regrowth and reduced lesion depth by up to 70%, showing promise for enamel regeneration.

For dentin regeneration, Campodoni *et al* [7] fabricated a gelatin chitosan hydrogel biomimetic mineralization system loaded with magnesium-doped-hydroxyapatite nanocrystals that resembled the characteristics of natural mineralized tissue. Han *et al* [8] reported an agarose hydrogel loaded with calcium and phosphate that induced the growth of an oriented and densely packed hydroxyapatite layer on the damaged dentin surface.

2) Dentin- Pulp Regeneration

Regenerating damaged tissues, including the dentin-pulp complex, is a major clinical challenge. Hydrogels have emerged as promising materials for dental pulp regeneration due to their ability to support cell growth and mimic the extracellular matrix. Injectable hydrogels are ideal for minimally invasive applications, adapting easily to the root canal. Hydrogel microspheres further enhance this by encapsulating stem cells or bioactive agents for targeted delivery.

Atila *et al* [9] used hyaluronic acid hydrogel with RG1-loaded chitosan microspheres to promote odontogenic and angiogenic differentiation of dental pulp stem cells. Similarly, Zhang *et al* [10] developed Gelatin Methacrylate (GelMA) microspheres with platelet lysate and Laponite, which enhanced stem cell proliferation, differentiation and vascularized tissue regeneration, highlighting the potential of hydrogel systems in pulp therapy.

3) Pulp Revascularization

Pulp revascularization is commonly used to treat immature teeth by encouraging stem cell migration and apical healing through induced bleeding. While it can promote root development, it has limitations such as pulp calcification and insufficient dentin-pulp regeneration.

Injectable hydrogels offer a more advanced approach by mimicking the extracellular matrix and delivering stem cells and growth factors for effective pulp regeneration. Studies have shown that hydrogel scaffolds like GelMA with human dental pulp stem cells (hDPSCs) and Human Umbilical Vein Endothelial Cells (HUVECs), or peptide-based and thermo-responsive hydrogels enhance cell differentiation, tissue growth and vascularization.[11] Additionally, 3D bioprinted hydrogels loaded with stem cells have shown great potential for regenerating the dentin–pulp complex by accurately replicating tissue structure and function.[12]

4) Pulp Canal Space Disinfection

Traditional root canal treatments rely on disinfectants to remove infected pulp, but the complex structure of dentinal tubules can hinder complete pathogen elimination. Higher antimicrobial doses may harm healthy tissues. To overcome this, new biomaterials with sustained antimicrobial properties have been developed for improved pulp space disinfection.

Afami *et al* [13] demonstrated that ultrashort peptides (fewer than 8 amino acids) can self-assemble into hydrogels and be tailored with antimicrobial features, such as lysine residues, to enhance their activity. In solution, these peptides effectively targeted S. aureus and E. faecalis biofilms, while their hydrogel form inhibited *E. faecalis* and *F. nucleatum*. Similarly, Aggarwala found that Bacitracin-derived Molecule 2, a D-decameric cationic peptide in gel form, exhibited strong antimicrobial effects against planktonic and biofilm cultures of *C. albicans, S. gordonii, S. mutans* and *E. faecalis*, even at concentrations eight times higher than in solution.[14]

Linares *et al* [15] incorporated diclofenac hydrogels for disinfection in regenerative endodontics and concluded that sodium diclofenac hydrogels demonstrate antimicrobial efficacy against endodontic biofilms.

5) Vital Pulp Therapy

Vital pulp therapy is a minimally invasive method aimed at preserving pulp vitality, dental structure, and tooth function. After pulp exposure, healing and tissue regeneration are promoted using biomaterials like hydrogels. These hydrogels reduce inflammation, support pulp healing, stimulate odontoblasts, and aid dentin bridge formation. Their tissue-like, hydrophilic structure makes them ideal for local drug delivery, enabling controlled agent release via micro-/nanosized systems placed near connective tissue to maintain pulp vitality.

In a study by Qiu *et al* [16] on Strontium Copper Tetrasilicate / Gelatin Methacryloyl (SrCuSi4O10 /GelMA) Composite Hydrogel-Mediated Vital Pulp Therapy, it was concluded that the prepared SrCuSi4O10 /GelMA hydrogel exhibited ion-release capability and NIR-induced photothermal properties. The study demonstrated that the SrCuSi4O10 /GelMA hydrogel, when combined with Near-Infrared irradiation, effectively reduced *S. mutans* and *L. casei*, inhibited biofilm formation *in vitro* and promoted dentin-pulp complex repair in a rat dental pulp infection model.

6) Treatment of Periodontal Diseases

Periodontal disease is a serious inflammatory condition caused by harmful microbes, leading to the destruction of tooth-supporting structures and eventual tooth loss. Traditional treatments like scaling and root planning remove plaque but often result in weak tissue regeneration. Effective therapy should control infection and restore damaged tissues. Hydrogels show promise as drug delivery systems to reduce inflammation and as scaffolds to support periodontal tissue regeneration.

Wong *et al* [17] reported that polymeric hydrogels loaded with chlorhexidine and silver nanoparticles had a significant antimicrobial effect against *P. gingivalis.* Vanitha *et al* [18] evaluated gelatin hydrogels for socket preservation and suggested their potential as a bone substitute due to their cost-effectiveness, low risk of rejection, and elimination of the need for a secondary surgical site.

7) Wound Healing

Hydrogels are effective wound dressings as they maintain moisture, absorb exudates, allow gas exchange, and support tissue regeneration. They can be applied as sprays or injectables, adapting to irregular wounds.

Examples include Gelatin Methacryloyl 3,4-Dihydroxyphenylalanine (GelMA-DOPA) hydrogel with antibacterial and antioxidant properties, silver nanoparticle-loaded hydrogels targeting drug-resistant bacteria, and antioxidant hydrogels with lignin that aid burn healing by promoting cell growth. Haidari *et al* [19] reported that the silver-nanoparticle-loaded pH hydrogel also showed the effective elimination of P. aeruginosa and S. epidermidis in in vitro antibacterial biofilm studies. This hydrogel provides a promising strategy to enhance the healing of drug-resistant-bacteria-infected wounds. Xu *et al* [20] prepared a thermo-responsive hydrogel using a combination of Polyethylene Glycol (PEG), polypropylene glycol (PPG), and polydimethylsiloxane (PDMS), which then incorporates the lignin (an antioxidant material). This hydrogel increases cell proliferation to promote the healing of burn wounds.

8) Treatment of Head and Neck Squamous Cell Carcinoma

Oral cancers, particularly oral squamous cell carcinoma, account for 90% of cases and are typically treated with chemotherapy and immunotherapy. However, these treatments often face challenges like poor drug solubility, low bioavailability, and systemic side effects. To address this, hydrogel-based drug delivery systems have been developed for targeted, localized therapy.

These hydrogels offer sustained or stimulus-triggered drug release, high drug-loading capacity, and reduced side effects. Adhesive hydrogels can be applied directly to oral tumours, and smart hydrogels can respond to pH, temperature, or light for controlled delivery. For example, hydrogels loaded with doxorubicin, or dual-drug systems using metal-organic frameworks, improve treatment precision.[21] Some hydrogels also enable combined therapies like chemotherapy and photothermal therapy for enhanced antitumor effects.

9) Orthodontic Tooth Movement

Orthodontic tooth movement (OTM) involves alveolar bone remodelling—bone resorption on the pressure side and formation on the tension side. Accelerating OTM is of growing interest to reduce treatment-related issues like caries, root resorption, and relapse. Hydrogel-based drug delivery systems have been explored to enhance OTM by promoting bone remodelling.

For example, Lu *et al* [22] used thermosensitive hydrogels loaded with sclerostin to accelerate OTM in rats by boosting osteoclast activity. Similarly, Xing *et al* [23] developed a peptide hydrogel for sustained release of Receptor Activator of Nuclear Factor Kappa-B Ligand (RANKL), a key regulator in bone remodelling, to enhance local osteoclastogenesis and speed up tooth movement.

10) Peri-Implantitis

Dental implants are a widely accepted modality for the replacement of missing teeth; however, peri-implantitis affecting up to 20% of patients remains a significant clinical complication.[24] Conventional therapeutic approaches often demonstrate limited efficacy due to the persistent risk of bacterial recolonization.

Hydrogels have emerged as promising solutions for peri-implantitis. They can coat implant surfaces to prevent bacterial growth and support healing without triggering inflammation. Boot *et al* [25] created antibiotic-loaded hydrogel coatings for titanium implants, showing they don't hinder bone integration. Layer-by-layer (LbL) techniques further enhance hydrogel functionality, enabling controlled, pH-responsive drug release. Hydrogels like chitosan/hydroxyapatite bilayers also boost antibacterial effects and biomineralization.

Beyond coatings, hydrogels serve as bioadhesives and scaffolds. For instance, Gelatin Methacryloyl–Antimicrobial Peptide (GelAMP) hydrogel controls inflammation and promotes bone regeneration, while silver lactate-alginate hydrogels with stem cells enhance both antimicrobial activity and bone healing.[26]

11) Oral Topical Anaesthesia

A major advancement in dentistry is the development of effective topical anaesthetics, addressing patients' fear of needles and improving treatment adherence. Current topical options, like the lidocaine-prilocaine eutectic cream (EMLA), are made for skin use and can cause oral ulcers, ineffective palatal numbness, and even systemic side effects when used in the mouth.

Nanostructured drug delivery systems such as nanostructured lipid carriers, offer improved stability, biocompatibility, and drug protection. Hydrogels are also promising for topical anaesthesia due to their strong adhesion and compatibility with oral tissues. Muniz *et al* [27] developed a CARBOPOL hydrogel with lidocaine and prilocaine nanocapsules, which outperformed commercial anaesthetics. Cubayachi *et al* [28] enhanced anaesthetic absorption using iontophoresis with hydrogel carriers. Combining microneedles with adhesive hydrogels, especially with stimuli like near-infrared light, further improves drug penetration and controlled release for pain-free anaesthesia.

12) Facial Aesthetics

Dermal fillers have become a popular, minimally invasive method to restore this lost volume and reduce visible signs of aging.

Hydrogels, particularly hyaluronic acid (HA) hydrogels, are widely used in dermal fillers for their water-retaining, tissue-like properties, high biocompatibility, and low risk of immune reactions. HA fillers last 6–9 months, require no allergy testing and can be reversed with hyaluronidase. They also promote collagen production by stimulating fibroblasts in the dermis.

Leading HA-based fillers like Juvéderm, Restylane and Revanesse Versa+ are commonly used for facial volume restoration, wrinkle correction, and lip augmentation, with many including lidocaine to reduce injection discomfort. Artefill, a permanent filler made from polymethylmethacrylate beads, is FDA-approved for deeper folds. A recent case study also showed that a PEG-crosslinked HA hydrogel (PEGDE-HA) was effective and well-tolerated for lip enhancement.[29]

13) Salivary Gland Regeneration

Replicating the complex structure of salivary glands (SGs) outside the body is difficult, but significant progress has been made over the past two decades using various in vitro and ex vivo models. To better mimic SG architecture, research shifted to 3D culture systems using both natural and synthetic hydrogels. These hydrogels support cell growth, gland development, and potential transplantation.

Matrigel, for example, enables acinar-like structure formation and the expression of key SG proteins like amylase. Low concentrations (2 mg/mL) promote cell differentiation. Collagen and fibrin gels also support acinar and ductal cell morphologies.[30]

Synthetic hydrogels like Polylactic-co-glycolic acid (PLGA) and PEG have been shown to promote branching in embryonic tissue and enhance the expression of acinar markers such as aquaporin 5, essential for creating functional artificial SGs.[31]

14) Bone and Cartilage Tissue Engineering

Cartilage has limited regenerative capacity, especially in older adults, due to its dense, avascular, aneural structure, which restricts blood supply and progenitor cell access. In contrast, bone can typically heal itself thanks to its vascularization, but severe injuries like non-union fractures or tumour removals often exceed its repair ability.

Current treatments for bone and cartilage repair are often complex, lengthy, and may not fully restore native tissue function. Hydrogels made from natural and synthetic biopolymers such as chitosan, collagen, gelatin, alginate, HA and PEG have shown promise in regenerative medicine due to their biocompatibility and viscoelastic properties.

For cartilage repair, Jeong *et al* [32] enhanced HA-based hydrogels with β-cyclodextrin, improving their mechanical strength, cell viability, and shear-thinning behaviour. Asadi *et al* [33] developed nanocomposite hydrogels using gelatin and Polycaprolactone–Polyethylene glycol–Polycaprolactone (PCL–PEG–PCL) nanoparticles loaded with Transforming Growth Factor Beta 1 (TGFβ1), significantly increasing the scaffold's stiffness and supporting cartilage regeneration.

In bone repair, hydrogels support integration with native tissue, reducing immune responses and eliminating the need for surgical removal. Lindsey *et al* [34] demonstrated that collagen-filled bone defects in rats showed improved healing compared to controls. Wang *et al* [35] created chitosan-collagen hydrogel microbeads loaded with bone marrow stem cells, which enhanced osteogenic marker expression and mineral deposition.

15) Treatment Of Oral Mucosal Diseases

Oral inflammatory diseases like xerostomia, stomatitis, and mucositis often lack effective local treatments. Oral drugs degrade in the GI tract while topical forms (e.g., lozenges, sprays) struggle with poor adhesion.

Hydrogels offer a promising alternative due to their strong mucosal adhesion, moisture retention, and ability to carry drugs like antibiotics, corticosteroids, and peptides. They mimic saliva's viscosity, reduce infection risk, and enhance drug stability and delivery especially when combined with iontophoresis.

Examples include poloxamer-based hydrogels with dexamethasone for lichen planus, fluconazole-loaded hyaluronic acid gels for candidiasis and Trimethyl Chitosan / Glycerophosphate hydrogels for mucositis. Selenium hydrogels have also shown success in treating erosive lichen planus, with results comparable to corticosteroids. [36-39]

CONCLUSION

In a nutshell, hydrogels have emerged as a transformative material in dentistry, combining biocompatibility, adaptability, and therapeutic potential. Their ability to mimic natural tissue environments, deliver drugs in a controlled manner, and conform to complex dental structures makes them ideal for a wide range of clinical applications—from tissue regeneration to targeted treatments. The development of smart, stimuli-responsive hydrogels further enhances their relevance, offering dynamic and responsive solutions to oral health challenges. As research continues to advance, hydrogels are set to become an integral part of next-generation dental care, significantly improving treatment outcomes and patient well-being.

Declaration by Authors

Ethical Approval: Not required
Acknowledgement: None
Source of Funding: None
Conflict of Interest: No conflicts of interest declared.

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How to cite this article: Ridhiman Raman, Shravan Rathi, Vineeta Nikhil. Hydrogels in dentistry: a step forward in dental innovation. *International Journal of Research and Review*. 2025; 12(5): 568-575.
DOI: *https://doi.org/10.52403/ijrr.20250558*

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