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Research Progress of Hydrogels in the Treatment of Periodontitis

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Abstract. Periodontitis is a chronic infectious disease driven by dental plaque biofilms. Its core pathological features are local microbiome dysbiosis, immune homeostasis disruption, and progressive destruction of periodontal support tissue. Traditional mechanical debridement combined with conventional medications struggles to overcome key clinical limitations, such as poor drug retention in deep periodontal pockets, ineffective eradication of refractory biofilms, and insufficient alveolar bone regeneration. In recent years, hydrogels have become an ideal platform for periodontal local minimally invasive drug delivery and tissue engineering due to their highly hydrated three-dimensional networks, excellent biocompatibility, and adjustable physical and chemical properties. This review systematically presents the latest research progress of functionalized hydrogels in the treatment of periodontitis. Firstly, the material basis underlying their adaptation to the complex periodontal pocket microenvironment is discussed from three aspects: wet adhesion, in-situ injectability, and controlled degradability. Secondly, the smart response drug release mechanism based on pathological microenvironment markers such as local acidity (pH), high levels of reactive oxygen species (ROS), specific enzymes, and glucose is elaborated. On this basis, the review deeply analyzes the multi-dimensional mechanism by which hydrogels promote the remodeling of the periodontal immune-inflammatory microenvironment and alveolar bone regeneration through the delivery of various bioactive agents such as antibiotics, antioxidants, osteogenic inducers, etc. Finally, the key challenges faced by hydrogels in clinical transformation are discussed, including mechanical adaptability, predictability of in vivo degradation timing, and coordinated multi-tissue regeneration, and future research directions are proposed to support precision-targeted, functional regenerative therapies for periodontitis.

Keywords: Periodontitis, Hydrogels, Localized drug delivery, Microenvironmental regulation, Periodontal tissue regeneration

1. Introduction

Periodontitis is a chronic inflammatory disease characterized by progressive destruction of periodontal supporting tissues. Owing to its high prevalence and serious impact on both oral and systemic health, it has caused a significant global public health burden. Epidemiological evidence has shown that approximately 1.1 billion individuals worldwide were affected by severe

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periodontitis in 2021, and the number is projected to increase further by 2040 [1]. The pathogenesis of periodontitis is initiated by dysbiosis within the dental plaque biofilm. The continuous stimulation of pathogenic microorganisms can induce the imbalance of host immune-inflammatory response, which in turn triggers the release of inflammatory factors, the abnormal accumulation of reactive oxygen species (ROS), and activation of matrix metalloproteinases (MMPs), ultimately leading to irreversible damage to periodontal supporting tissues. The main clinical manifestations are attachment loss, periodontal pocket deepening, and bleeding on probing. In severe cases, it can develop into tooth loosening or even falling off.

At present, the clinical treatment of periodontitis remains based on mechanical debridement, including supragingival scaling, subgingival scaling, and root planning, supplemented by local or systemic antimicrobial therapy. However, traditional treatment strategies still have several drawbacks, such as limited drug retention time of drugs within periodontal pockets, incomplete biofilm removal, systemic drug-related adverse reactions, and the risk of antimicrobial resistance. Furthermore, they often fail to simultaneously achieve treatment of infection control, inflammation regulation, and tissue regeneration [2]. Therefore, the construction of a novel therapeutic system that integrates long-term local retention, controlled drug release, and multifunctional synergistic therapy has become a crucial development direction in the field of periodontitis treatment.

As a three-dimensional network structure material formed by cross-linking of hydrophilic polymers, hydrogels possess excellent biocompatibility and adjustable physical and chemical properties. They can adapt to the complex anatomical structure of periodontal pockets, enabling efficient local delivery and sustained release of drugs. In recent years, functionalized hydrogels with antibacterial, anti-inflammatory, and tissue-regenerative capabilities have shown considerable potential, offering a new strategy for integrated therapy based on the concept of "infection control—inflammation regulation—tissue repair."

2. Performance design of hydrogels applied to periodontal microenvironment

The periodontal pocket is a dynamic, humid, and microbial-intensive pathological microenvironment. Its irregular shape, persistent exposure to gingival crevicular fluid, and chewing mechanical load put forward strict requirements for hydrogel design.

2.1. Wet adhesion

Hydrogels must be stably retained on the surface of wet tooth roots and soft tissues, taking into account low mucosal stimulation and strong wet adhesion. Although polymers such as polyacrylic acid and chitosan are commonly used to construct adhesive hydrogels, the hydration of polymer chains in the oral environment often weakens their interactions with tissues. At the same time, the interfacial water layer blocks direct contact, resulting in a significant reduction in adhesion. In order to overcome the interference of the water layer, Dong et al. introduced hydrophobic drug-loaded microcapsules into chitosan hydrogels. The microcapsules distributed on the surface of the gel dispersed the interfacial water molecules, promoted direct contact between the gel and the substrate, thereby significantly improving the wet adhesion performance [3].

2.2. In-situ injectability

The injectability enables hydrogels to be delivered to the periodontal pocket in a minimally invasive manner. An ideal system should exhibit appropriate rheological behavior: keep flowing during the

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injection process, and rapidly form a stable three-dimensional network structure after entering the periodontal pocket to resist saliva erosion and chewing force. The shear-thinning hydrogel designed by Hu et al. showed decreased viscosity under shear stress, which was convenient for injection; once the shear stress was eliminated, the viscosity recovered, and a gel state was formed. The characteristics of this non-Newtonian fluid made it suitable for minimally invasive treatment of periodontal pockets [4]. Furthermore, thermosensitive hydrogel carriers prepared with agarose, chitosan, poloxamer, or poly N-isopropylacrylamide maintain a fluid state under ambient conditions but undergo gelation upon contacting with body temperature, thereby adapting seamlessly to the complex morphology of periodontal pockets [5].

2.3. Controlled degradability

Hydrogel degradation generally occurs through hydrolysis of covalent bonds, enzymatic cleavage, or weakening of non-covalent interactions. The degradation rate needs to match the tissue regeneration cycle. Crosslinking density is a key regulatory factor; that is, networks with high crosslinking density degrade more slowly, and the degradation behavior can be adjusted by changing the type and concentration of crosslinking agent. Specific chemical modifications can also directly affect the degradation rate. For instance, the incorporation of caprolactone moieties has been reported to delay hydrolysis, while lactide moieties accelerate this process [6]; Cai et al. further demonstrated that the hydrogel prepared by carboxymethyl chitosan and oxidized dextran at a volume ratio of 10:1 showed the best degradation performance [7], underscoring the importance of the chemical ratio between the matrix and the crosslinking agent.

3. Drug release behavior of smart responsive hydrogels

Smart responsive hydrogels can detect pathological microenvironment signals, realize microenvironment-triggered controlled drug release, thus avoiding the burst release issues commonly observed with traditional drug delivery systems, and improving the targeting and timeliness of treatment. Pathological cues associated with periodontitis, including acidic pH, ROS overload, elevated levels of specific enzymes, and, in diabetic patients, abnormal glucose concentration, provide a biological foundation for designing multi-signal-triggered delivery systems.

3.1. pH-responsive hydrogels

Periodontal lesions exhibit slightly acidic conditions (pH＜6.0) owing to bacterial metabolism, enhanced inflammatory responses, and local hypoxia, which is significantly different from physiological pH 7.4. Chitosan dissolves under acidic conditions due to protonation of its amino groups, forming a positively charged polyelectrolyte capable of gel formation in inflammation sites. By contrast, it remains stable under slightly alkaline conditions, making it a viable pH-responsive carrier [7].In addition, both metal ions and H^+ can act as Lewis acids to compete for ligand binding, thereby conferring pH responsiveness to metal-ligand bonds. For example, Mou et al. developed a pH-sensitive delivery system based on the interaction of zinc-albumin ligand. The cumulative drug release rate was 80 % at pH 6.5 for 24 hours, and less than 50 % at pH 7.4 [8].

3.2. ROS-responsive hydrogels

The host immune response triggered by pathogens colonizing in the subgingival plaque of periodontitis patients may lead to excessive production of ROS, which causes oxidative stress-

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mediated injury to periodontal tissues. ROS-responsive hydrogels often introduce sensitive groups such as phenylboronic acid, thioketones, or selenium/sulfide bonds. Zhao et al. used the high sensitivity of phenylboronic acid to hydrogen peroxide to construct a ROS-responsive hydrogel formed by the cross-linking of oxidized dextran and phenylboronic acid-functionalized poly(ethyleneimine). The nitrogen atom in the drug molecule formed a B-N coordination bond with the boron atom, which was cleaved under a high ROS environment, thereby triggering drug release [9].

3.3. Enzyme-responsive hydrogels

During the progression of periodontitis, MMPs are abnormally upregulated and participate in extracellular matrix degradation and periodontal tissue destruction. Among them, the level of MMP-8 in gingival crevicular fluid correlates closely with disease severity. Based on this, Guo et al. utilized the cleavage characteristics of MMP-8 toward the CGPQG↓IWGQC peptide crosslinker to construct a polyethylene glycol-based enzyme-responsive hydrogel loaded with minocycline hydrochloride. This hydrogel demonstrated significantly accelerated drug release in a 20 nM MMP-8 solution for about 48 hours [10].

3.4. Glucose-responsive hydrogels

For diabetic periodontitis, where hyperglycemia contributes to disease progression, glucose-responsive hydrogels are expected to achieve more precise therapeutic intervention. Typically, glucose oxidase (GOx) is immobilized in pH-sensitive materials. GOx catalyzes the oxidation of glucose into gluconic acid, thereby decreasing the local pH and inducing drug release through hydrogel swelling or contraction. To mitigate the cytotoxicity of traditional chemical crosslinking agents such as glutaraldehyde, recent research tends to favor natural crosslinkers like genipin and citric acid, or alternative methods such as photocrosslinking approaches [11].

3.5. Light-responsive hydrogels

Light-responsive hydrogels have attracted increasing interest in drug delivery because of their low cost, non-invasive operation, and precise control over release behavior. According to the principle of controlled release, they can be divided into photocrosslinked type, photoisomerization-based type, and photothermal-triggered system. Photocrosslinked hydrogels achieve in-situ gelation by photo-initiated free radical polymerization to form a dense three-dimensional network to limit drug diffusion. For example, UV-crosslinked GelMA/ZIF-8 hydrogels exhibited sustained Zn^{2+} release following Fickian diffusion [12]. The photoisomerization type incorporates photosensitive groups such as azobenzene and spiropyran, whose reversible cis-trans isomerization modulates network porosity and enables pulsatile drug release. The photothermal-triggered release type uses photothermal agents such as gold nanocages to induce the phase transition of thermosensitive polymers under near-infrared light to achieve on-demand drug release [13].

4. Functional strategies of hydrogel-based drug delivery system

As functional drug delivery carriers, hydrogels have multiple advantages, such as in-situ forming, controllable release, and lesion targeting. Through in-situ gelation, they enable minimally invasive administration and adapt well to the irregular morphology of periodontal defects. Moreover, their three-dimensional network structure delays drug diffusion rate, thereby achieving sustained release

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and extending the local treatment window. In addition, ligand modifications or incorporation of pathological microenvironment-responsive mechanisms can further enhance lesion-specific delivery. Consequently, hydrogels can serve as multifunctional platforms to load active molecules with antibacterial, anti-inflammatory, and osteogenic properties. By synergistically regulating the inflammatory microenvironment and promoting bone regeneration, these systems ultimately facilitate the structural and functional restoration of periodontal tissues (Figure 1).

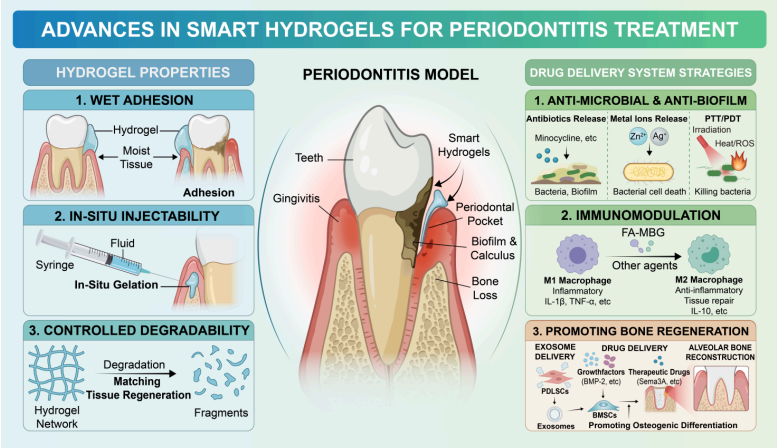


Figure 1. Schematic overview of smart hydrogel-based therapeutic strategies for periodontitis

4.1. Role and mechanisms of hydrogels in regulating the periodontal inflammatory microenvironment

4.1.1. Targeting periodontal pathogens and biofilms

Bacterial infection and plaque biofilm imbalance are the initiating factors of periodontitis. Mature dental plaque biofilm is composed of a variety of microorganisms embedded within an extracellular polymeric matrix, which provides a mechanical barrier and metabolic protection for pathogens, helping limit the penetration of antimicrobial agents and evade host immune clearance. Porphyromonas gingivalis (P. gingivalis) is widely recognized as a key bacterium that drives disease progression. It adheres to periodontal tissues through fimbriae, colonizes plaque biofilms, and releases virulence factors such as lipopolysaccharides and proteases, thus driving chronic inflammation and tissue destruction.

Currently, hydrogel-based systems exert antibacterial and anti-biofilm effects through the following ways. Firstly, antibiotic loading enables hydrogels to maintain effective concentrations locally through sustained release, thereby overcoming the biofilm penetration barrier. Commonly incorporated antibiotics include penicillins, cephalosporins, tetracyclines, macrolides, etc. The minocycline in-situ hydrogel developed by Wang et al. sustained drug release for approximately 48 hours after a single injection, with in vitro antibacterial activity comparable to that of commercially available minocycline ointment [14]. However, it may still be limited by antimicrobial resistance risk and insufficient eradication of mature biofilms. Secondly, metal ion loading provides broad-spectrum antibacterial activity. Metal ions such as Zn^{2+}, Cu^{2+}, and Ag^{+} play antibacterial roles by disrupting bacterial membrane integrity, enzyme activity, and metabolic pathways. Popescu et al. developed a silver nanoparticles/polyvinyl alcohol/chitosan composite hydrogel that enabled controlled Ag^{+} release and exhibited enhanced antibacterial activity with increasing silver loading [15]. Nevertheless, the potential cytotoxicity of metal ions toward host tissues at high concentrations

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remains a major concern. Thirdly, photothermal and photodynamic therapies offer non-antibiotic strategies for biofilm eradication. Upon near-infrared irradiation, photothermal agents generate heat, whereas photosensitizers produce ROS. The T8IC nanoparticle-loaded hydrogel reported by Wang et al. achieved a mild photothermal effect of about 45°C under 808 nm laser irradiation while simultaneously generating ROS, significantly enhancing bacterial inactivation within biofilms [16]. This strategy is less likely to induce drug resistance, but the danger of thermal injury to surrounding tissues must be carefully monitored. Finally, intrinsically antimicrobial materials provide a drug-free strategy. Through electrostatic attraction to the anionic surface of bacterial membranes, cationic agents—including chitosan and quaternary ammonium compounds—compromise membrane integrity, eventually leading to bacterial demise [17].

4.1.2. Regulation of inflammatory cell polarization and immune microenvironment remodeling

Periodontitis is not only an infectious disease but also a chronic inflammatory disease dominated by host immunity imbalance. Compared with free drugs or nanoparticles, hydrogels can be used as immunomodulatory delivery platforms to interfere with the function of inflammatory cells and reconstruct local immune homeostasis of periodontal tissues by virtue of their local retention, sustained release performance, and multi-factor co-loading ability, laying a foundation for subsequent bone regeneration.

Macrophages have a core regulatory role in periodontitis-related immune cells. According to different functional statuses, they are broadly classified into pro-inflammatory M1 phenotype and anti-inflammatory/pro-reparative M2 phenotype. In periodontitis lesions, persistent pathogen stimulation and excessive accumulation of ROS can activate inflammatory signaling pathways such as NF-κB, inhibit Nrf2-mediated antioxidant defense, thus disrupting macrophage polarization balance, which not only hinders inflammation regression but also adversely affects the recruitment and differentiation of osteoblasts. Yu et al. developed a Pluronic F127 (PF127) thermosensitive injectable hydrogel loaded with folic acid-modified mesoporous bioactive glass nanoparticles (FA-MBG) and doxycycline, which could be gelled in situ and target macrophages to scavenge ROS, thereby promoting polarization toward the M2 phenotype in animal models.

In addition, the homeostasis of the periodontal immune system relies critically on the Th17/Treg cell axis. In the inflammatory microenvironment, pro-inflammatory signals derived from M1 macrophages drive Th17 differentiation and aggravate bone resorption, whereas M2-associated anti-inflammatory factors support Treg function and tissue repair. Li et al. developed a thermosensitive hydrogel containing quercetin-loaded microemulsions that targeted macrophages through folate receptors, released quercetin and peppermint oil to synergistically remove excessive ROS in cells, promote the transformation of M1 to M2, and ultimately reconstruct Th17/Treg immune homeostasis [18].

4.1.3. Regulating periodontal inflammation-related cytokine network

The continuous progress of periodontitis is closely related to dysregulation of the local cytokine network. Increased levels of pro-inflammatory cytokines, such as IL-6, IL-1β, and TNF-α, have been identified in the gingival crevicular fluid and periodontal tissues of individuals suffering from chronic periodontitis, and their levels are positively correlated with periodontal pocket depth and the extent of alveolar bone resorption. In contrast, anti-inflammatory cytokines, including IL-10 and TGF-β, help suppress excessive inflammation and promote tissue repair. Therefore, targeted

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regulation of the cytokine network is another important strategy through which hydrogel-based systems may ameliorate the pathological microenvironment in periodontitis.

Previous studies have shown that periodontal pathogens such as P. gingivalis can activate the NOD-like receptor family pyrin domain-containing 3 (NLRP3) inflammasome in macrophages and induce excessive release of pro-inflammatory cytokines. Liu et al. developed a dual-crosslinked hydrogel that achieved rapid in-situ gelation and dual pH/ROS responsiveness through dynamic boronate ester bond and photocrosslinking. This hydrogel was loaded with the NLRP3 inflammasome inhibitor MCC950 to block the downstream inflammatory cascade mediated by IL-1β and IL-18 [19]. Besides small-molecule inhibitors, Hygor et al. used carbomer-based gel as a delivery system, loaded with the natural heteropolysaccharide cashew gum, leveraging the adhesive properties of the matrix to achieve local retention and sustained release. In a rat model of experimental periodontitis, 15% cashew gum gel significantly reduced the overexpression of pro-inflammatory related genes such as COX-2 in the gingival tissue, and its effect is equivalent to 2% chlorhexidine gel [20].

4.1.4. Scavenging excessive reactive oxygen species

Eliminating excessive ROS is a key strategy for intervening in the progression of periodontitis. Oxidative stress is a central driver of the initiation and development of this disease. Studies have shown that patients with periodontitis exhibit significantly increased ROS and their metabolite levels in saliva, gingival crevicular fluid, and serum, while the total antioxidant capacity is relatively reduced. Excessive ROS not only directly induces protein oxidation, lipid peroxidation, and DNA damage, resulting in apoptosis of gingival fibroblasts and injury to periodontal ligament cells, thereby aggravating gingival recession and alveolar bone resorption, but also amplifies the inflammatory responses by activating the NLRP3 inflammasome and signaling pathways such as NF-κB and JNK. In addition, ROS promotes osteoclast differentiation and activation by regulating the RANKL/OPG axis. Therefore, eliminating excessive ROS and restoring local redox homeostasis are important therapeutic directions for periodontitis. Hydrogels can function as localized delivery platforms for antioxidant agents, including curcumin [17], epigallocatechin gallate (EGCG) [4], and polydopamine [21], or be designed as ROS-responsive structures to enable local free radical scavenging. For example, the injectable Laponite/gelatin hydrogel developed by Hu et al. encapsulated EGCG-Cu complexes to achieve multi-pathway ROS scavenging through the synergistic effect of polyphenols and Cu^{2+}, while up-regulating the glutathione metabolic pathway of macrophages to enhance endogenous antioxidant capacity [4].

4.2. Hydrogel-mediated periodontal bone regeneration strategies and mechanisms

Alveolar bone resorption is the main pathological basis leading to tooth loosening and shedding; therefore, promoting alveolar bone regeneration is essential for the functional repair of periodontal tissue. Bone marrow mesenchymal stem cells (BMSCs), as adult stem cells derived from mesoderm, possess self-renewal capacity and multilineage differentiation potential. Under the stimulation of an appropriate microenvironment, BMSCs can differentiate into osteoblasts, thus facilitating new bone formation, repairing osseous defects, and finally realizing the reconstruction of alveolar bone structure and the recovery of tooth stability. Owing to their excellent tissue-bionic characteristics and controllable delivery capability, hydrogels are considered ideal bone regeneration carriers. By forming stable three-dimensional scaffolds in the lesion area, the local retention and continuous

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release of re-living factors can be realized, so as to foster a conducive milieu for BMSC retention, multiplication, and subsequent osteogenic transformation.

Growth factors such as bone morphogenetic protein-2 (BMP-2), vascular endothelial growth factor (VEGF), and stromal cell-derived factor-1α (SDF-1α) can inhibit inflammation, promote angiogenesis and bone formation by regulating cell proliferation, migration, and differentiation. Among them, BMP-2 is a classical osteogenic inducing factor that markedly enhances alkaline phosphatase activity and promotes bone matrix mineralization. SDF-1α recruits BMSCs to the bone defect sites mainly through chemotaxis, providing a cell source for local bone repair. The SDF-1α-loaded thermosensitive hydrogel constructed by Liu et al. can continuously release bioactive factors after in-situ gelation, promote BMSC recruitment, and activate the Wnt/β-catenin pathway, thereby significantly improving osteogenesis in rat models of bone defects [22].

Bioactive metal ions such as Ca^{2+}, Zn^{2+}, Mg^{2+}, and Cu^{2+} [4] also participate in bone repair by promoting osteogenic differentiation, enhancing angiogenesis, and regulating the expression of osteogenesis-related genes. Among them, Ca^{2+}, as an important component of bone minerals, can not only inhibit inflammatory responses through calcium receptor activation, but also promote BMP-2 secretion, which plays a central role in bone remodeling. Since the obvious concentration dependence of the biological effects of metal ions, hydrogels can maintain the local effective therapeutic concentration while minimizing cumulative toxicity by virtue of their controllable release characteristics, and have become an ideal carrier for ion delivery. The polydopamine-modified graphene oxide / nano-hydroxyapatite composite conductive scaffold constructed by Li et al. can promote Ca^{2+} influx under electrical stimulation, up-regulate the expression of osteogenesis-related genes such as COL1A1, Osterix, and ALP, and significantly enhance the osteogenic differentiation ability of BMSCs [23].

In recent years, the cell-free therapy strategy based on the paracrine mechanism of stem cells has gradually become a research hotspot in periodontal tissue engineering. Compared with direct stem cell transplantation, exosomes (Exos), as important paracrine products of mesenchymal stem cells, are nanosized extracellular vesicles that carry bioactive components of source cells. They are involved in intercellular information transmission and tissue repair regulation with low immunogenicity and favorable biosafety. In this context, hydrogels have been widely explored as platforms for the localized retention and sustained release of exosomes, thereby improving their bioavailability. For example, the composite hydrogels loaded with periodontal ligament stem cell-derived exosomes (PDLSCs-Exos) formed a porous three-dimensional network structure through Ca^{2+}-mediated crosslinking, which can enhance exosome retention in local defect areas. Studies have shown that the uptake of PDLSC-Exos by BMSCs can significantly promote their proliferation and osteogenic differentiation, and induce greater new bone formation in rat alveolar bone defect models [24]. In addition, the PF127 thermosensitive hydrogel constructed by He et al. was capable of sustained release of BMSC-derived exosomes overexpressing CTNNB1 and effectively increased the new bone formation by regulating the CTNNB1/miR-146a-5p/IRAK1/TRAF6 signaling axis [25].

Moreover, the incorporation of osteoregenerative drugs into hydrogels represents a direct strategy to promote periodontal bone regeneration. Through controlled-release systems, agents such as melatonin [26], metformin [9], and Semaphorin3A [27] can be stably delivered locally, thereby preserving their bioactivity while avoiding burst release, and enhancing their efficacy in the defect area.

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5. Conclusion and outlook

Hydrogels provide a promising strategy for local periodontal therapy due to their advantages of injectability, wet adhesion, and intelligent responsiveness. By integrating antibacterial, anti-inflammatory, immunomodulatory, and osteogenic functions, hydrogel-based systems are expected to overcome the shortcomings of traditional treatments, especially in local retention, targeted drug release, and tissue repair.

However, several challenges still hinder its clinical transformation. First, there is an inherent contradiction between the mechanical strength and injectability of hydrogels, because the improvement of mechanical properties is often accompanied by a decrease in injectability and plasticity. Secondly, the degradation of hydrogels in vivo is affected by various factors such as local inflammatory state, enzyme activity, and fluid dynamics, and it is difficult to accurately match with the tissue regeneration process. Thirdly, periodontal regeneration requires the coordinated repair of multiple tissues such as alveolar bone, periodontal ligament, and cementum; however, the existing research mainly focuses on bone regeneration, while the bionic reconstruction of functional soft tissues, especially the highly ordered periodontal ligament, is relatively less studied. Finally, precise time control over the transition from early anti-inflammation to subsequent promotion of regeneration is still insufficient, both due to the incomplete understanding of the dynamic healing process of periodontitis and the limited durability and efficacy of current biosurfactants in complex lesion microenvironments.

Future research should focus on overcoming these challenges. With the continuous development of material engineering and the in-depth understanding of the potential biological mechanisms of periodontal regeneration, the hydrogel system is anticipated to achieve optimized mechanical adaptability, controllable degradation characteristics, enhanced multi-tissue synergistic regeneration ability, and more accurate space-time regulation. In general, these advances will promote the development of periodontal therapy in the direction of functional effectiveness, personalization, and regenerative therapy.

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