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Application of photocured hydrogels in the treatment of bone defect diseases

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Abstract. Photocured hydrogels are materials with great potential, offering a novel approach in the treatment of bone defects. They exhibit excellent biocompatibility, tunable degradation characteristics, and the ability to incorporate cells and growth factors. This paper explores the mechanisms and advantages of photocured hydrogel applications in the treatment of bone defects, focusing on bone formation promotion, drug-loading and antimicrobial properties, and enhancement of vascularization in the surrounding tissues. Research indicates that photocured hydrogels can serve as scaffolds, drug delivery systems, and tissue engineering materials, promoting bone cell proliferation, osteogenic differentiation, inhibiting bone resorption and osteolysis, fostering vascularization, and providing drug-loading antimicrobial effects. Nevertheless, the application of photocured hydrogels in the treatment of bone defect diseases faces challenges, such as long-term stability and interface adaptability. Further research and development are required to overcome these challenges, facilitating the widespread clinical use of photocured hydrogels and improving the treatment outcomes and quality of life for patients with bone defects.

Keywords: Photocured Hydrogels, Bone Defect Diseases, Osteogenesis And Osteolysis, Vascularization, Drug-Loading Antimicrobial.

1. Introduction

Bone defects represent a severe condition in bone tissue, commonly arising from fractures, surgical resections of bone tumors, or age-related osteoporosis. These conditions significantly impact patients' quality of life and functional recovery. Traditional methods for bone defect repair, such as autogenous bone grafts, allogenic bone grafts, and artificial material implants, are associated with various limitations and complications. In recent years, the rapid development in the field of biomaterials has introduced innovative solutions for bone defect repair. Among these, hydrogels, characterized by their high biocompatibility, low immunogenicity, and tunable physicochemical properties, have gained unprecedented attention in the biomedical field [1]. Photocured hydrogels, in particular, have demonstrated exceptional performance in bone defect treatment.

Hydrogels are three-dimensional, polymer materials with hydrophilic groups that can absorb and swell in water without dissolution [2, 3]. Their high water content resembles that of human tissues, providing an ideal microenvironment for cell adhesion and growth. Furthermore, hydrogels exhibit favorable mechanical properties and biodegradability, gradually providing support for new bone

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formation and promoting bone regeneration. Photocured hydrogels are a subset of hydrogels cured through photochemical reactions initiated by photosensitizers. They offer controllable gelation rates, excellent biocompatibility, and biodegradability, making them widely applicable in the field of orthopedics [4].

This paper aims to comprehensively review the applications of photocured hydrogels in the treatment of bone defects, examining their characteristics, mechanisms, and advantages, while also providing insights into their future development. By delving into the use of photocured hydrogels in bone defect repair, it is hoped that this research will offer feasible solutions for clinical bone defect treatment and serve as a theoretical guide for materials scientists regarding hydrogel design and performance regulation.

2. Literature Review

Hydrogels, owing to their biocompatibility, biodegradability, and potential as scaffolds for tissue regeneration, have emerged as promising biomaterials for treating bone defects. Photocured hydrogels, in particular, have attracted considerable interest because they can be injected as liquid precursors and subsequently cured in situ under light exposure, allowing them to fill irregularly shaped defects [5]. Zhang et al. developed a novel photocured composite hydrogel consisting of hyaluronic acid, gelatin, and hydroxyapatite nanoparticles, which promoted osteogenesis of stem cells and enhanced bone regeneration in a rat calvaria defect model. Several studies support the potential of photocured hydrogels in bone defect treatment. Yoon [6] found that growth factor-1 (TGF-β1) and transforming growth factor-β1 (TGF-β1) containing bone morphogenetic protein-2 (BMP-2) loaded in photocured chitosan hydrogels enhanced bone formation in a rat tibial defect model. Abdul-Monem [7] developed photocured hyaluronic acid composite hydrogels with nano-hydroxyapatite and chitosan, demonstrating improved mechanical properties and osteogenic potential. Gong [8] discussed the advantages of hydrogels as fillers for bone defects and carriers for local therapy. Bae [9] showed that photocured hyaluronic acid hydrogels containing growth and differentiation factor-5 (GDF-5) sustained release, promoting cell proliferation, differentiation, in vivo bone regeneration. These findings collectively suggest the potential of photocured hydrogel treatments in enhancing bone regeneration. In summary, due to their ability to fill complex defects in situ, photocured hydrogels hold promise for bone defect treatment. Hyaluronic acid-based hydrogels and nano-composite hydrogels containing hydroxyapatite have been explored for bone regeneration. Further work is required to translate these promising hydrogels into clinical applications.

3. Application of Photocured Hydrogels in the Treatment of Bone Defects

Photocured hydrogels are a novel material widely used in clinical bone defect repair. This paper comprehensively discusses their advantages in bone defect treatment, including osteogenesis, drug loading for antimicrobial purposes, and the promotion of peripheral tissue vascularization.

3.1. Promoting Osteogenesis and Bone Resorption

Photocured hydrogels are an innovative material with significant potential in the treatment of bone defects, offering numerous advantages in osteogenesis and bone resorption.

In terms of osteogenesis, photocured hydrogels facilitate the bone-forming process at the site of bone defects. This is achieved through the following mechanisms:

Scaffold structure and cell infiltration: Photocured hydrogels possess a scaffold structure that provides appropriate support for the bone defect site and channels for cell infiltration. This scaffold structure offers the three-dimensional space necessary for cell infiltration, allowing bone cells and other cells to enter the defect area. Additionally, the scaffold structure of photocured hydrogels can mimic the natural bone tissue structure, aiding in directing cell migration and osteogenesis [10].

Release of growth factors: Photocured hydrogels can serve as carriers to immobilize and release growth factors such as bone morphogenetic protein (BMP) and platelet-derived growth factor (PDGF). These factors are crucial for the proliferation and differentiation of bone cells. By controlling the rate

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and timing of growth factor release, photocured hydrogels provide sustained stimulation, promoting the proliferation of bone cells and the deposition of bone matrix. These growth factors can activate bone cells and stem cells, facilitating their differentiation into osteoblasts and stimulating the deposition and mineralization of bone matrix.

Cell adhesion and proliferation: The surface of photocured hydrogels exhibits excellent biocompatibility and cell adhesiveness, promoting the attachment and proliferation of bone cells. When bone cells adhere to the surface of the hydrogel, adhesion proteins such as integrins on the cell surface interact with the structural components of the hydrogel, facilitating cell adhesion and spreading. This adhesion and proliferation process increases cell density at the site of the bone defect, providing a solid cellular foundation for osteogenesis.

Carrier degradation and replacement: Photocured hydrogels are typically biodegradable, gradually degrading and being replaced by newly formed tissue within an appropriate timeframe. This degradation and replacement process supports new bone tissue by providing the necessary support and space, enabling the filling of the bone defect and fusion with surrounding bone tissue [11].

Regarding bone resorption, photocured hydrogels have the potential to inhibit bone absorption and bone dissolution. By adjusting the composition and release mechanisms of the hydrogel, they can reduce the activity of osteoclasts, thereby inhibiting bone absorption and reducing bone loss [10]. A study has demonstrated the use of photosensitive hydrogels carrying low doses of cinnamic acid, which, when photo-stimulated, inhibits osteoclasts, thus suppressing the process of bone dissolution. This adjustable bone resorption inhibition strategy offers a new approach to treating bone-resorptive diseases [12].

In summary, the application of photocured hydrogels in the treatment of bone defects demonstrates their potential in osteogenesis and bone resorption. By regulating their degradation characteristics and release mechanisms, photocured hydrogels can promote the proliferation of bone cells and the deposition of bone matrix while inhibiting bone absorption and dissolution processes. Although there are still some challenges to overcome, the use of photocured hydrogels in the treatment of bone defects holds promise for providing more effective clinical treatment strategies.

3.2. Drug Delivery and Antibacterial Properties

The application of photocured hydrogels in bone defect treatment for drug delivery and antibacterial purposes demonstrates its potential in improving treatment outcomes and infection prevention. By embedding drugs and antibacterial agents within photocured hydrogels, it is possible to effectively extend drug release time, increase local drug concentrations, and inhibit bacterial growth and infection. In the treatment of bone defects, photocured hydrogels serve as drug carriers, incorporating antibiotics, growth factors, and other drugs. Through photopolymerization, the hydrogel is affixed to the bone defect site, facilitating sustained drug release. Research indicates that photocured hydrogels can modulate the rate of drug release, ensuring a sufficient drug concentration is maintained within the treatment area over a period of time. This sustained drug release helps in suppressing the growth and spread of pathogenic microorganisms, reducing the risk of infection. Additionally, the antibacterial properties of photocured hydrogels can be employed to prevent and treat infections in the bone defect area. Substances with antibacterial activity, such as antibiotics and silver ions, can be added to the photocured hydrogel. These substances can kill or inhibit bacterial growth, lowering the risk of infection. A study utilized photocured hydrogels to repair bone defects and successfully embedded silver nanoparticles with antibacterial activity within them [13]. The results demonstrated that silver nanoparticles effectively inhibited bacterial infections and biofilm formation, thereby enhancing the treatment of bone defects. Despite the broad potential of photocured hydrogels in drug delivery and antibacterial applications for bone defect treatment, several challenges exist. These challenges include drug stability, the interface adaptability of the hydrogel with bone defect tissue, and the persistence of antibacterial effects. Furthermore, the safety and biocompatibility of photocured hydrogels require further research and validation. Firstly, drug stability is a critical consideration in the use of photocured hydrogels for bone defect treatment. The photopolymerization process can be affected by light and heat, potentially leading to the degradation or loss of drug activity. Therefore, it is essential to ensure drug stability and activity

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are maintained when selecting drug carriers and adjusting photopolymerization conditions. This may require a series of experiments and optimization efforts to ensure the long-term stability of drugs within photocured hydrogels. Secondly, the interface adaptability of the hydrogel with bone defect tissue is also a crucial consideration. Good interface adaptability promotes the integration of the hydrogel with surrounding tissue, providing stable support and drug delivery platforms. However, achieving ideal interface adaptability remains challenging due to the morphological diversity and individual differences in defect areas [14]. Therefore, further research and improvement in hydrogel design and preparation techniques are needed to achieve better interface adaptability and compatibility. Moreover, the persistence of antibacterial effects is a challenge in the use of photocured hydrogels for bone defect treatment. Although adding antibacterial agents can suppress bacterial growth and infection to a certain extent, enhancing the long-term antibacterial effects requires further investigation. Using substances with persistent antibacterial functionality within photocured hydrogels, combined with appropriate release mechanisms, is a focal point for future research. Finally, the safety and biocompatibility of photocured hydrogels are crucial factors in bone defect treatment. While photocured hydrogels have shown good biocompatibility in experiments and initial studies, more in-depth safety assessments and clinical trials are necessary for their clinical application. This necessitates further in vitro and in vivo studies to evaluate the toxicity of photocured hydrogels and their impact on surrounding tissue, ensuring their safety and reliability.

In conclusion, the application of photocured hydrogels in bone defect treatment for drug delivery and antibacterial purposes shows significant potential. By adjusting drug release and incorporating antibacterial substances, photocured hydrogels can enhance the treatment of bone defects and prevent infections. Although challenges remain, photocured hydrogels offer new options and opportunities for clinical use in bone defect treatment.

3.3. Promoting Peripheral Tissue Vascularization

The application of photocured hydrogels in the treatment of bone defects for promoting peripheral tissue vascularization demonstrates its potential to enhance blood supply and facilitate bone tissue repair. By loading active substances such as growth factors and cytokines and regulating the biocompatibility and degradation rate of photocured hydrogels, it is possible to effectively stimulate angiogenesis and promote bone tissue regeneration. Angiogenesis plays a crucial role in bone tissue repair by providing oxygen and nutrients to the repair area and supporting newly formed cells and bone matrix [15]. Photocured hydrogels can carry growth factors such as vascular endothelial growth factor (VEGF) and cytokines like granulocyte colony-stimulating factor (G-CSF) to promote angiogenesis and enhance blood supply. Studies have shown that VEGF in photocured hydrogels can significantly increase vascular density and endothelial cell proliferation in the bone defect area, thereby promoting vascular formation. Furthermore, loading cells with angiogenic activity is a common strategy. Photocured hydrogels provide support for cell adhesion and proliferation, facilitating the survival and differentiation of implanted cells in the defect area. For example, by embedding endothelial cells or mesenchymal stem cells into photocured hydrogels, the formation of new blood vessels and improvements in blood supply can be achieved. This synergy between cells and the hydrogel better promotes vascularization and repair of bone tissue. When applied in bone defect treatment, photocured hydrogels can promote vascularization in peripheral tissues, thereby improving blood supply and accelerating bone tissue repair and regeneration. The following will provide a detailed explanation of the principles behind photocured hydrogels promoting angiogenesis:

Release of Growth Factors: Photocured hydrogels can serve as carriers to immobilize and release growth factors. Growth factors are a class of signaling molecules capable of stimulating cell proliferation and differentiation, including factors closely related to angiogenesis, such as vascular endothelial growth factor (VEGF). Growth factors fixed in photocured hydrogels gradually release after implantation into the treatment area, stimulating peripheral tissue angiogenesis. VEGF can bind to its receptor, activating a series of signaling pathways, including apoptosis inhibition, increased vascular permeability, endothelial cell migration, and differentiation, thus promoting the formation of new blood vessels [12].

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Photocured hydrogels, through controlling the rate and timing of growth factor release, can provide continuous stimulation, facilitating directed migration of endothelial cells and the formation of new blood vessels in the defect area.

Regulation of Cytokines: Cytokines within photocured hydrogels can also promote angiogenesis. For example, granulocyte colony-stimulating factor (G-CSF) can stimulate the proliferation and differentiation of bone marrow mesenchymal stem cells, thereby promoting angiogenesis. G-CSF, upon binding to its receptor, triggers downstream signaling pathways, such as STAT3, AKT, and more, activating endothelial cell proliferation, migration, and inducing branching of blood vessels [14]. Photocured hydrogels can provide an appropriate environment and time window for the release and regulation of cytokine expression to promote the process of angiogenesis.

Matrix Structure and Cell-Matrix Interaction: The scaffold structure of photocured hydrogels plays a significant role in providing an appropriate environment for vascular cells, promoting their directed migration and vascular construction. The pore structure and microenvironment parameters of the hydrogel (such as biomechanical properties, permeability, etc.) directly influence vascular cell activity. By adjusting the physical and chemical properties of the hydrogel, it is possible to affect cell morphology, migration direction, and signal transduction in cell-matrix interactions, thus promoting endothelial cell migration and vascular network formation. Photocured hydrogels can provide the structure and signals necessary to support and guide vascular generation, contributing to the formation of a well-developed vascular network [12].

In summary, photocured hydrogels can promote vascularization in peripheral tissues around bone defect areas by mechanisms such as the release of growth factors, regulation of cytokines, and interactions between the matrix structure and cells. This process helps improve blood supply, providing the necessary nutrients and oxygen for bone tissue repair and accelerating the healing of bone defects.

4. Conclusion

Photocured hydrogels have demonstrated vast prospects in the treatment of bone defects. Leveraging their tunable properties and biocompatibility, photocured hydrogels can serve as scaffold materials, drug delivery systems, and tissue engineering constructs, enabling the repair and regeneration of bone defects. Photocured hydrogels can promote bone cell proliferation, osteogenic differentiation, and bone matrix synthesis, thereby contributing to the repair and regeneration of bone defects [16]. They hold potential in the treatment of osteolytic diseases by controlling osteoclast activity and inhibiting bone resorption and dissolution processes. In drug-loaded antimicrobial applications, photocured hydrogels can prolong drug release, enhance local drug concentrations, and inhibit infection occurrence in bone defect treatment. Furthermore, in terms of vascularization, by loading active substances like growth factors and cytokines, photocured hydrogels can stimulate angiogenesis and improve blood supply, facilitating vascularization in the bone defect area and bone tissue regeneration. Although photocured hydrogels are considered a promising innovative material, their application in bone defect treatment still faces challenges such as long-term stability, interface adaptability, and safety. Further research and development are required to overcome these challenges and promote the widespread application of photocured hydrogels in clinical practice, ultimately providing better treatment outcomes and improved quality of life for patients with bone defects.

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