Transactions on Environment, Energy and Earth Sciences
ISSN: 2960-1924, eISSN: 2960-2300 | Volume 5
EMCEME 2025

Application and Improvement of Shape Memory Polymer Stents in Bone Defect Repair

Pengyu Fu [1], Binqian Xu [2,*], and Ximing Zhang [3]

[1] School of Material Science and Engineering, Chang'an University, Xian, 710018, China

[2] Department of Chemistry, University of Manchester, Manchester, M13 9PL, United Kingdom

[3] Zhengzhou New Oriental School, Zhengzhou, 450046, China

* Corresponding Author Email: binqian.xu@student.manchester.ac.uk

Abstract. The PLLA-TMC-GA shape memory polymer scaffold effectively addresses critical limitations of traditional bone repair scaffolds, such as inadequate geometric adaptability and mismatched mechanical properties. However, it still suffers from insufficient performance in drug release behavior and distribution uniformity. Building on previous studies, this work proposes that incorporating intelligent hydrogel-mediated controlled release and nano/micro-scale drug loading strategies can significantly enhance the controllability, distribution homogeneity, and release intelligence of drug delivery in PLLA-TMC-GA shape memory scaffolds. These improvements are anticipated to promote osteogenic activity and reduce potential toxicity risks. This study offers a comprehensive strategy to address the critical drug delivery challenges associated with existing shape memory scaffolds, while simultaneously laying a foundational framework for the development of next-generation intelligent bone repair materials that exhibit superior therapeutic efficacy and broader clinical applicability. This research provides a crucial theoretical basis and technical path for the development of a new generation of intelligent bone repair materials that possess excellent mechanical adaptability, precise drug-controlled release capabilities, and good biological safety.

Keywords: Shape Memory Polymer; Bone Tissue Engineering; Geometric Compatibility; Controlled Drug Release; Ph-Responsive Hydrogel.

1. Introduction

Globally, bone tissue defects caused by disease, malnutrition, and aging have raised increasing public concern. Data shows that between 1990 and 2019, the global incidence of fractures increased by 33.4%. In 2019, the number of people affected reached 455 million, with the prevalence rate rising by 70.1% compared to 1990 [1], thereby imposing a heavy burden on healthcare systems worldwide. Recent research has increasingly focused on developing materials capable of enabling minimally invasive implantation, providing customized geometric adaptation for complex defect sites, and delivering integrated structural support through controlled bioactive release to promote bone regeneration while minimizing risks.

Traditional polymer bone scaffolds are widely used in bone repair. However, they suffer from several limitations, such as poor geometric adaptability to irregular defects, mismatched mechanical properties, and insufficient bioactivity, all of which restrict their clinical efficacy. In contrast, PLLA-TMC-GA shape memory polymers exhibit excellent mechanical strength, biocompatibility, and exceptional shape-matching capability. Hu et al. demonstrated that incorporating PHA significantly increased the compressive modulus of the scaffold from 21.8 MPa in the pure polymer group to 124 MPa [2], providing sufficient mechanical support for bone regeneration. Additionally, this composite scaffold effectively promoted new bone and collagen formation in a rat cranial defect model, demonstrating excellent biocompatibility and osseointegration capability. Moreover, its outstanding shape memory property directly addresses the critical limitation of geometric mismatch inherent in traditional scaffolds. The material rapidly recovers its preset shape under body temperature (37 °C) stimulation, achieving high-precision adaptation to complex defect margins. This capability significantly simplifies implant surgery while providing a stable mechanical environment conducive

to new bone growth. Nevertheless, scaffolds made from this material still exhibit deficiencies in drug delivery.

This study aims to systematically review recent advances and improvement strategies related to drug delivery in PLLA-TMC-GA shape memory polymer scaffolds. Based on recent literature, a feasible approach for enhancing drug delivery capacity has been summarized. By incorporating a multi-level structural design, the scaffold achieves both geometric adaptability and controlled drug release. Furthermore, two innovative modification methods are proposed to improve existing strategies, with the goal of achieving superior drug delivery performance.

2. Limitations of Conventional Bone Scaffolds in Geometric Compatibility and Bioactivity

Traditional bone scaffolds, such as porous structures fabricated from synthetic polymers like polylactic acid (PLLA) and polycaprolactone (PCL), are widely employed in bone defect repair. However, their inherent geometric and biofunctional shortcomings often limit clinical efficacy [3]. First of all, poor geometric compatibility is a major challenge. Irregular bone defects are commonly found in trauma or debridement surgery. However, conventional pre-formed scaffolds cannot dynamically adapt to complex and variable defect contours. This results in gaps between the implant and the bone, leading to poor integration, compromised mechanical load transfer, and creating the risk of infection [4]. Secondly, mechanical property mismatch represents another significant challenge. The elastic modulus of many polymer scaffolds differs considerably from that of human cancellous bone (approximately 0.1–2 GPa), predisposing to the "stress-shielding" effect. In this scenario, the scaffold bears excessive mechanical load, shielding the surrounding bone from essential physiological stress stimuli, which can lead to bone resorption and eventual implant failure [5]. Additionally, inadequate bioactivity also restricts the effect of repair. Traditional scaffolds often lack bioactive cues to actively promote osteogenic differentiation and vascularization, only providing passive support. This frequently results in slow bone integration and suboptimal repair quality [6]. As Wu et al. emphasized [7], ideal scaffolds should closely mimic the biochemical and structural characteristics of the native extracellular matrix; traditional manufacturing methods are difficult to achieve such mult-stage biomimetic structures.

3. Advantages of Shape Memory Polymer Scaffolds in Geometric Compatibility

To overcome the geometric constraints of traditional scaffolds, Shape Memory Polymer (SMP) scaffolds have been developed. Their biggest advantage lies in enabling precise morphological adaptation following minimally invasive implantation. These materials can be programmed into a temporary shape (e.g., compressed strip) ex vivo, implant the stent into the body through a small incision, and subsequently recover their original preset permanent shape upon exposure to biological environmental stimulation or at body temperature conditions（37℃）, thereby achieving intimate conformal contact with the complex interface of irregular bone defects [8]. A recent study by Hu et al. on a microsphere scaffold composed of a polylactic acid-trimethylene carbonate-glycolic acid (PLLA-TMC-GA) ternary copolymer perfectly demonstrates this characteristic [2]. The scaffold was temporarily shaped into a star configuration, requiring approximately 320 seconds to fully deploy at 25°C (simulating surgical conditions), but only about 100 seconds at 37°C (body temperature). It can return to its original shape, achieving high-fidelity conformal matching with the defect boundaries. This dynamic adaptation capability not only simplifies surgical procedures and minimizes tissue trauma but also provides a stable mechanical environment for the growth of new bone tissue and significantly improves the success rate of osseointegration by eliminating micromotion and bone gaps. In summary, this polymer scaffold demonstrates marked superiority over traditional scaffolds in terms of geometric compatibility, enabling perfect conformation to the bone defect site during repair. What's more, it can provide stable mechanical support throughout the process. Its dynamic adaptation capability substantially enhances the precision of morphological matching between the scaffold and bone during bone repair.

4. Limitations of Shape-memory Polymer Scaffolds in Drug Release Properties

Although the microsphere scaffold demonstrates great performance in geometric adaptability, limitations towards drug release exist. The experimental data indicate that approximately 45% of icariin was released within the first four days. This is primarily due to the rapid diffusion of the drug from the microsphere surface [2]. The initial burst release may promote early osteogenic differentiation, but the elevated local drug concentration may carry potential cytotoxic risks [9]. Subsequently, the release rate becomes remarkably slower, with cumulative release reaching 75% by day 25, indicating that the residual drug is difficult to release effectively within a short timeframe. Although sustained release may continuously stimulate the osteoblast proliferation and differentiation whilst inhibiting excessive osteoclast activity, this release pattern may lack uniformity. Fluctuations in local drug concentrations over time may compromise the maintenance of stable therapeutic levels. Besides, even though PHA demonstrates superior drug dispersion within microspheres compared to unmodified nHA, spatial variations in drug distribution may still occur [2]. There was research that indicates that drugs tend to aggregate on microsphere surfaces or within hydrophilic networks, while another study observed that structural heterogeneity leads to uneven drug distribution [10][11]. As icariin primarily permeates through hydrogels into the interstitial spaces between microspheres, local variations in PHA concentration may affect hydrogel cross-linking density, which may indirectly cause significant differences in release rate across distinct regions. Furthermore, the drug release mechanism is highly dependent on the degradation rate of the scaffold material. If material degradation is not synchronized with bone regeneration rates, it may result in a mismatch between drug supply and tissue regeneration demand, thereby compromising the overall therapeutic efficacy [12]. Overall, while the scaffold demonstrates strong geometric adaptability, problems such as limited drug release capacity, unstable release rates, and uneven distribution continue to constrain its potential for long-term bone regeneration applications.

5. Strategies for Improving Drug Transport in Existing Scaffolds

5.1. Intelligent Hydrogel Controlled Release Strategy: Evolution from Sustained Release to On-Demand Response

Addressing the insufficient bioactivity of traditional scaffolds, integrating hydrogels as drug carriers presents an effective solution. Hu et al. combined a sodium alginate hydrogel loaded with Icariin (Ica) with the shape memory microsphere scaffold [2], successfully constructing a PTG/PHA/Ica composite scaffold. However, there is a problem with this system. It exhibited a significant burst release with 45.2% of the drug released within the initial 4 days, potentially inducing local cytotoxicity and hindering the maintenance of long-term osteogenic effects. To address this challenge, pH-responsive intelligent hydrogels offer a more advanced controlled release strategy. The core is to use the difference of the pH between the acidic microenvironment typical of bone infection sites (pH < 6.0) and normal physiological conditions (pH ~7.4) to achieve precise, on-demand drug release. For instance, inspired by the approach of Lu et al. [13], Ica could be co-loaded with $CaCO_3$ nanoparticles. Under normal neutral pH, the hydrogel network remains stable, facilitating slow drug diffusion and effectively suppressing the initial burst release. Upon infection-induced acidification, $CaCO_3$ rapidly decomposes, neutralizing the acidity while concurrently inducing structural changes in the hydrogel network, thereby triggering targeted and accelerated drug release precisely at the infection site. This precise mode, which can be released slowly in normal environments and automatically accelerates release in acidic environments, not only solves the safety concerns associated with conventional drug carriers but also endows the scaffold with the capability to actively respond to pathological changes and enable spatially targeted therapy [14]. Consequently, incorporating a pH-responsive mechanism represents a critical advancement over traditional sodium alginate hydrogel systems. It shifts the drug release paradigm from passive sustained release to an intelligent, on-demand modality, greatly enhancing the targeting efficacy and therapeutic effectiveness for treating infected bone defects.

5.2. Improvement of Drug Delivery via Nano/Micro-scale Drug Loading in Shape-Memory Polymer Scaffolds

For the deficiencies in drug release from shape-memory polymer (SMP) scaffolds, nano/micro-scale drug loading has been proposed as an effective strategy to enhance the drug delivery performance of SMP scaffolds. Embedding drugs into nanostructures or fibre networks improves uniform distribution within the scaffold, thereby enhancing the controllability of the release. The research conducted by Zare et al. employed electrospinning to fabricate nanofibrillated SMP scaffolds with uniformly embedded drugs within the fibre network. The results showed uniform drug distribution while maintaining shape-memory effects. This also provides excellent biomechanical support for cells [15]. Meanwhile, PCL nanofibre composite membranes were constructed by Le et al. Incorporating functional nanoparticles loaded with bioactive molecules enabled on-demand release and optimised drug distribution while preserving shape-memory properties. This also demonstrates favorable antimicrobial performance [16]. These studies provide valuable references for optimising the drug delivery of SMP scaffolds by dealing with nanoscale or microscale drug loading. This offers a more stable, reliable, and controllable therapeutic pathway for bone defect repair.

6. Conclusion

This paper systematically analyzed the application potential of PLLA-TMC-GA shape memory polymer scaffolds for bone defect repair, mainly focusing on their advantages in geometric compatibility and the limitations in drug release. By proposing a Three-level structure design, further introducing an intelligent response mechanism, it leads to two innovative controlled drug release strategies. The first involves a pH-responsive intelligent hydrogel system for on-demand drug release within the infected microenvironment. The second utilizes nano/micro-scale drug loading technologies to enhance drug distribution uniformity and release controllability within the scaffold. These strategies significantly improve the scaffold's bioactivity and targeted treatment.

To further advance the clinical translation of this scaffold system, subsequent research should focus on a systematic evaluation of the match between the scaffold’s long-term degradation behavior and the natural bone regeneration process, with particular emphasis on clarifying the biological impact of its degradation products on local tissue repair. Concurrently, large-animal studies are essential to comprehensively assess the scaffold’s biocompatibility, retention of mechanical properties, and osteogenic efficacy within a complex physiological environment. Building on these foundations, future efforts may integrate clinical imaging data with advanced 3D printing technologies to develop personalized scaffold designs that achieve high fidelity to patient-specific morphology. Such an approach would significantly improve anatomical adaptation, repair accuracy, and ultimately, clinical applicability.

Authors Contribution

All the authors contributed equally, and their names were listed in alphabetical order.

References

[1] GBD 2019 Fracture Collaborators. Global, regional, and national burden of bone fractures in 204 countries and territories, 1990–2019: a systematic analysis from the Global Burden of Disease Study 2019. The Lancet Healthy Longevity, 2021, 2(9): 580-592.

[2] Hu X, Yang S, Zhao W, et al. Novel multi-functional microsphere scaffold with shape memory function for bone regeneration. Biomaterials Advances, 2024, 163: 213958.

[3] Wang, W. and Yeung, K.W.K. Bone grafts and biomaterials substitute for bone defect repair: A review[J]. Bioactive Materials, 2017, 2(4): 224-247.

[4] Yang, S., Leong, K.F., Du, Z., et al. The design of scaffolds for use in tissue engineering. Part I. Traditional factors. Tissue Engineering, 2001, 7(6): 679-689.

[5] Chaudhary, M., Payghan, S.A., Bhamare, N., et al. Advanced manufacturing techniques and advancements in biodegradable biomaterials[J]. Materials Today: Proceedings, 2021, 47: 6686-6692.

[6] Haidar, Z.S., Hamdy, R.C., and Tabrizian, M. Delivery of recombinant bone morphogenetic proteins for bone regeneration and repair. Part A: Current challenges in BMP delivery. Biotechnology Letters, 2009, 31(12): 1817-1824.

[7] Wu, S., Liu, X., Yeung, K.W.K., et al. Biomimetic porous scaffolds for bone tissue engineering[J]. Materials Science and Engineering: R: Reports, 2014, 80: 1-36.

[8] Wan, Z., Zhang, P., Liu, Y., et al. Four-dimensional bioprinting: current developments and applications in bone tissue engineering. Acta Biomaterialia, 2020, 101: 26-42.

[9] Smagina V, Yudaev P, Kuskov A, et al. Polymeric gel systems cytotoxicity and drug release as key features for their effective application in various fields of addressed pharmaceuticals delivery. Pharmaceutics, 2023, 15(3): 830.

[10] Chabane A, Bouchal F, Hentabli M, et al. Investigation of the candesartan cilexetil antihypertensive drug microencapsulation by PLA-PVP K30 biodegradablepolymers: Experimental optimization and release kinetics modelling. Canadian Journal of Chemical Engineering, 2023, 101(8): 4446-4459.

[11] Uboldi M, Pasini C, Pandini S, et al. Expandable drug delivery systems based on shape memory polymers: impact of film coating on mechanical properties and release and recovery performance. Pharmaceutics, 2022, 14(12): 2814.

[12] Tajvar S, Hadjizadeh A, Samandari S S. Scaffold degradation in bone tissue engineering: an overview. International Biodeterioration & Biodegradation, 2023, 180: 105599.

[13] Lu, J., Li, M., Guo, R., et al. CaCO3-assistant synthesis of pH/near-infrared light-responsive and injectable sodium alginate hydrogels for melanoma synergistic treatment. Journal of Colloid and Interface Science, 2023, 633: 657-667.

[14] Berberich, C., Schelling, A., Feuerstein, A., et al. [Bone cement as a local antibiotic carrier][J]. Orthopadie (Heidelb), 2023, 52(12): 981-991.

[15] Zare M, Davoodi P, Ramakrishna S. Electrospun shape memory polymer micro-/nanofibers and tailoring their roles for biomedical applications. Nanomaterials, 2021, 11(4): 933.

[16] Le L T, Nguyen H T, Bui H T T, et al. Drug release system based on a composite polycaprolactone nanofiber membrane with dual functionality of shape memory effect and antibacterial ability. RSC Advances, 2024, 14(37): 26884-26895.