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Biopolymer-Based 3D Composite Scaffolds for Bone Tissue Engineering: Photothermal-Responsive Systems with Controlled Pt (IV) Prodrug Release

Pasunuti Durga[1*], C. Hazarathaiah Yadav[2], Darwin R.S.[3], Mahesh Kumar Thota[4]

Abstract

Biopolymer-based composite scaffolds have attracted significant attention as multifunctional platforms at the intersection of polymer science, regenerative medicine, and cancer nanotherapy. In this study, a dual-functional scaffold was developed for simultaneous osteosarcoma treatment and bone regeneration using poly (L-lactic acid) (PLLA) reinforced with bioactive glass (BG) and integrated with a glutathione-responsive platinum (IV) prodrug system (PDA@Pt). To improve interfacial adhesion, photothermal conversion efficiency, and tumor-specific activation, the Pt (IV) prodrug was conjugated onto polydopamine (PDA) nanoparticles. These nanofillers were uniformly embedded within the PLLA/BG matrix via selective laser sintering (SLS), enabling precise architectural control, optimized porosity, and enhanced mechanical stability suitable for load-bearing bone applications.

The engineered scaffold exhibited a highly interconnected porous structure that supported nutrient transport, vascularization, and cell infiltration, while maintaining improved compressive strength due to synergistic reinforcement from bioactive glass and polymer crystallinity. Under near-infrared (NIR) irradiation, the scaffold generated localized hyperthermia, enabling efficient tumor ablation and simultaneously triggering the reduction of Pt (IV) to cytotoxic Pt (II) species in the glutathione-rich tumor microenvironment. The drug release profile showed sustained and stimuli-responsive kinetics governed by matrix degradation and redox-sensitive cleavage mechanisms, ensuring controlled therapeutic delivery.

In vitro studies demonstrated strong cytotoxicity against osteosarcoma cells, along with induction of immunogenic cell death and activation of the cGAS–STING signaling pathway, highlighting its promise for polymer-mediated cancer immunotherapy. Concurrently, the scaffold promoted osteogenic differentiation of bone marrow mesenchymal stem cells, as evidenced by increased alkaline phosphatase activity and osteocalcin expression.

In vivo results further confirmed effective tumor suppression under NIR exposure and accelerated bone regeneration in critical-sized defects with improved tissue integration. Overall, this work highlights the potential of integrating polymer matrices, bioactive inorganic phases, and multifunctional nanocarriers to develop advanced scaffolds with synchronized therapeutic and regenerative functions for regenerative oncology and personalized biomedical applications.

Keywords: Biopolymeric composites, 3D polymer scaffolds, Photothermal-responsive materials, Polymer-based drug delivery systems, Platinum-based prodrugs, Controlled release kinetics, Tissue engineering matrices

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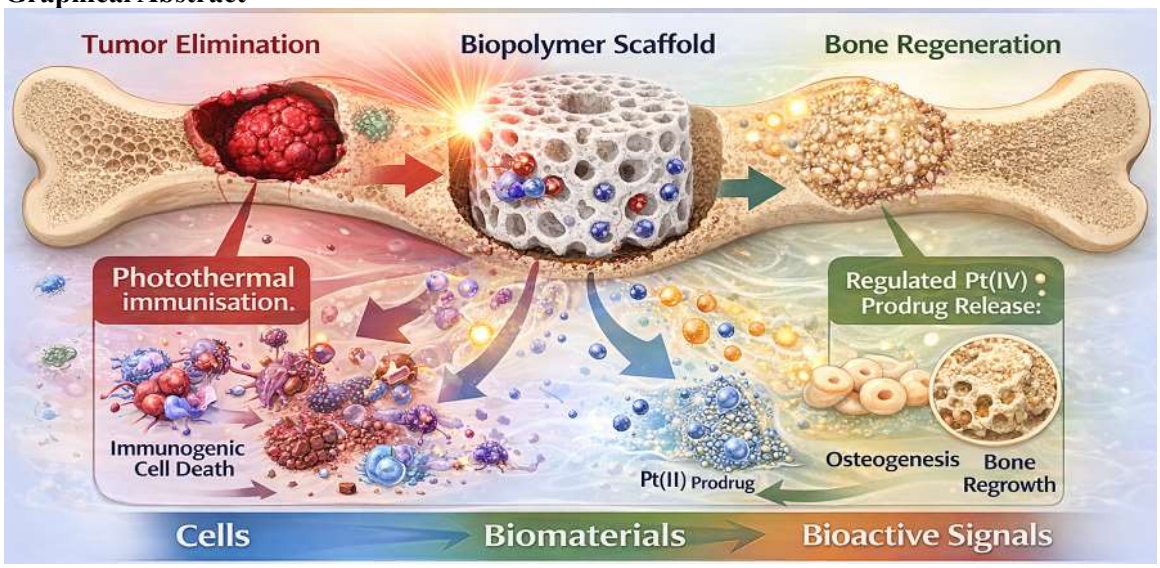
Graphical Abstract



Research Highlights

- For targeted therapy, a glutathione-responsive Pt (IV) prodrug (PDA@Pt) was developed.
- Using selective laser sintering, a prodrug is integrated into a PLLA/BG biopolymer scaffold, allowing controlled release of Pt (II) in microenvironments that resemble tumors.
- Robust photothermal conversion for synergistic treatment under NIR.
- Significant in vitro cytotoxicity against osteosarcoma cells.
- Activation of antitumor immune pathways (cGAS-STING).
- Support for osteogenic differentiation of stem cells in vitro. ∗Enhanced bone repair and local tumor inhibition in vivo.

SCOPE

This study focuses on the design, fabrication, and evaluation of a multifunctional biopolymer-based composite scaffold for applications in post-tumor bone reconstruction. The work addresses limitations associated with conventional systemic chemotherapy and bone grafting, including poor localized drug delivery and insufficient mechanical support for effective tissue regeneration. To overcome these challenges, a composite scaffold system was engineered by integrating a biodegradable polymer matrix with a glutathione-responsive platinum (Pt(IV)) prodrug and photothermal agents, enabling simultaneous structural reinforcement, localized therapeutic delivery, and stimuli-responsive functionality. The research encompasses: (1) synthesis and physicochemical characterization of the polymer–drug composite, including analysis of polymer morphology, interfacial interactions, and thermal stability; (2) evaluation of scaffold properties such as porosity, mechanical strength, degradation behavior, and controlled drug release kinetics; and (3) biological investigations, including in vitro cytocompatibility, photothermal efficiency, and osteogenic differentiation potential. Furthermore, in vivo studies were conducted to assess the composite scaffold's performance in tumor suppression and bone tissue regeneration using established animal models. Special emphasis was placed on structure–property–function relationships within the polymer composite system to ensure optimal performance. Quantitative analyses of drug release behavior, mechanical integrity, and host response were carried out to demonstrate the scaffold's potential as an advanced polymeric composite for biomedical applications. [Figure 1] [1,2].

The use of biopolymers such as collagen, chitosan, and bioactive glass in scaffold construction to promote cellular development and deliver therapeutic chemicals is in line with this integrative approach. For scaffold functioning in tissue engineering, biopolymers are chosen for their intrinsic

biocompatibility, biodegradability, and adjustable qualities. Such scaffolds have been demonstrated to boost tissue regeneration results, reduce systemic toxicity, and improve localised medication delivery.Prior research has mostly concentrated on discrete elements, such as tissue regeneration or anticancer delivery, but this study connects these fields to provide a multipurpose platform that can be employed in clinical settings. The findings have implications for the study communities of biomaterials, oncology, and regenerative medicine, and they present a possible novel therapeutic approach for combined anticancer and repair treatment [3-15].

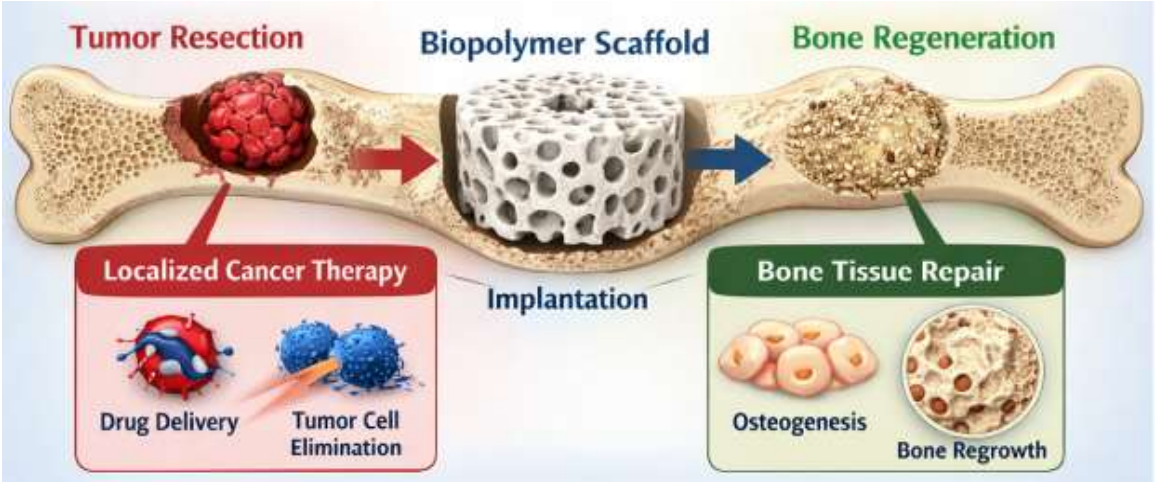


Figure 1. Development of multifunctional bio-polymer scaffold for post-tumor resection reconstructive surgery

INTRODUCTION

Tissue engineering has rapidly evolved within the domain of polymer and composite science, offering innovative strategies for the repair and regeneration of damaged tissues through the integration of cells, polymeric biomaterials, and bioactive cues. In this context, biopolymers such as collagen, chitosan, and their composite derivatives play a pivotal role in scaffold fabrication owing to their excellent biocompatibility, controlled biodegradability, and close resemblance to the native extracellular matrix (ECM). Recent advances emphasize the development of polymer-based composite scaffolds with enhanced mechanical strength, tunable physicochemical properties, and functional versatility. Despite these advancements, tissue defects associated with malignant tumors pose a significant challenge, as they require not only effective structural reconstruction but also the incorporation of therapeutic functionalities to inhibit tumor recurrence. Consequently, the design of multifunctional polymeric and composite scaffolds capable of simultaneous tissue regeneration and localized anticancer activity has become a critical focus in the Journal of Polymer and Composites research landscape. [Figure:2] [16].

Tissue engineering has emerged as an advanced interdisciplinary field that integrates polymer science, biomaterials engineering, and biological systems to restore or replace damaged tissues. In this context, biopolymers such as collagen and chitosan have gained significant attention due to their intrinsic biocompatibility, biodegradability, and structural resemblance to the natural extracellular matrix (ECM). These characteristics make them highly suitable candidates for the fabrication of polymeric scaffolds with tailored physicochemical and biological properties [17]. From a polymer and composites perspective, the development of multifunctional scaffold systems requires precise control over composition, architecture, and functional responsiveness. Tissue abnormalities associated with malignant tumours present dual challenges: structural degradation and the risk of local cancer recurrence. Recent advances in polymer-based composite systems have enabled the design of stimuli-responsive drug delivery platforms, where biochemical triggers such as elevated glutathione (GSH) concentrations in tumour microenvironments can initiate controlled drug release. Incorporation of redox-responsive Pt (IV) prodrugs within polymer matrices facilitates site-specific activation, thereby

enhancing therapeutic efficiency while minimizing systemic toxicity [18]. Furthermore, functional modification of polymer composites using polydopamine (PDA) introduces photothermal properties, enabling near-infrared (NIR)-induced localized hyperthermia. This synergistic approach combines polymer-mediated drug delivery with thermal therapy, highlighting the versatility of engineered composite scaffolds [19]. In addition, polymer composites incorporating bioactive glass (BG) and poly (L-lactic acid) (PLLA) demonstrate enhanced mechanical strength, osteoconductivity, and structural stability, making them suitable for load-bearing bone tissue applications. The dispersion of inorganic phases such as BG within polymer matrices promotes mineralization and facilitates new tissue formation, illustrating the critical role of composite design in achieving desirable biological and mechanical performance. By integrating biodegradable polymers, inorganic bioactive fillers, and functional nanocoatings, multifunctional composite scaffolds can be engineered to support cell adhesion, proliferation, and differentiation, while simultaneously enabling anticancer activity and immunomodulation. Despite substantial progress, most systems remain at a preliminary stage, with limited studies demonstrating simultaneous tissue regeneration and anticancer efficacy in clinically relevant models [20]. To address these challenges, the present work focuses on the development of a glutathione-responsive Pt(IV) prodrug-functionalized polymer composite scaffold (PDA@Pt) fabricated via selective laser sintering. This advanced processing technique allows precise control over scaffold porosity and architecture. The designed composite system exhibits NIR-triggered photothermal behavior, redox-responsive drug release, and enhanced osteogenic differentiation of mesenchymal stem cells. Such a multifunctional polymer composite platform offers significant potential as a theranostic system for simultaneous bone regeneration and suppression of tumour recurrence [21-50].

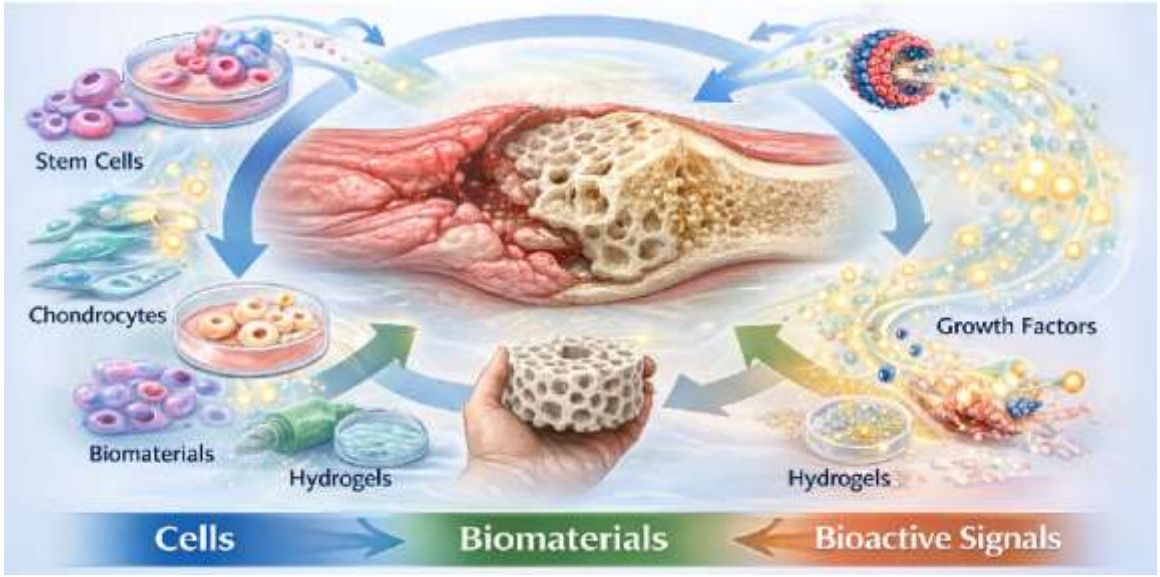


Figure 2. Using a combination of cells, biomaterials, and bioactive signals, tissue engineering has become a revolutionary science focused on replacing or mending damaged biological tissues.

RESEARCH AND METHODOLOGIES

Supplies and the Fabrication of Scaffolds

Synthesis of the Prodrug: Pt (IV) prodrug was created by amidation grafting onto polydopamine (PDA), which produced PDA@Pt nanoparticles.

Scaffold Matrix: A biocompatible matrix was produced by combining bioactive glass (BG) particles with poly(L-lactic acid) (PLLA).

Fabrication Method: PDA@Pt was encapsulated in porous 3D scaffolds made via selective laser sintering (SLS) [51-60].

Techniques for Characterisation

Morphology: Pore architecture can be examined using scanning electron microscopy (SEM).

Compression Tests are used in Mechanical Testing to Determine Modulus

Drug Release: Pt (II) release at different GSH levels is measured using high performance liquid chromatography (HPLC).

Infrared thermal imaging under NIR irradiation (808 nm) demonstrated photothermal efficiency [Table 1] [61-70].

Table 1. Data: Scaffold Characterization

Parameter	Value / Range	Method
Porosity	68–74%	SEM Image Analysis
Mean Pore Size	200–350 μm	SEM
Compressive Modulus	50–120 MPa	Mechanical Test
Pt Loading Efficiency	15.3 ± 1.2%	HPLC
Cumulative Pt(II) Release (10 mM GSH, 72 h)	78 ± 4%	HPLC
Photothermal Temp Increase (NIR, 5 min)	+22 ± 2 °C	IR Imaging

RESULTS AND DISCUSSION

In Vitro Anticancer Efficacy

The composite scaffold exhibited GSH-triggered rapid Pt (II) release, mimicking tumor intracellular environments. Under NIR irradiation, significant temperature elevations were recorded, confirming strong photothermal capability, which enhances cytotoxic effects via hyperthermia [Table 2] [71].

Table 2. Cell Viability (MG-63 Osteosarcoma Cells):

Treatment Group	Viability (%) at 72 h
Control	100 ± 3
Scaffold (no drug)	92 ± 5
Scaffold + Pt	42 ± 4
Scaffold + Pt + NIR	18 ± 3

The synergistic effect of chemotherapy and PTT significantly reduced cell viability, demonstrating enhanced therapeutic efficacy [72].

Immunogenic Response

Upregulation of cGAS-STING pathway markers confirmed immunogenic cell death, suggesting not only direct tumor cell killing but also potential immune activation [73,74].

Osteogenic Differentiation

BMSCs cultured on scaffolds showed increased osteogenic markers over 21 days [Table 3].

Table 3. Marker and Fold Change

Marker	Fold Change vs Control
ALP activity	2.8 ± 0.4
OCN expression	3.2 ± 0.5
Mineralization (alizarin red)	1.9 ± 0.3

This indicates that the scaffold supports bone regeneration, likely linked to BG's bioactivity [75].

In Vivo Findings

Scaffolds containing PDA@Pt under NIR demonstrated improved bone growth in the critical cranial defect model without appreciable inflammation, as demonstrated by histology and μCT imaging. Recent developments in multifunctional scaffold design that combine immunotherapy, controlled drug delivery, and structural support are consistent with these findings [76]. The functionality of natural polymers in biomedical scaffolds has been strengthened by the usage of biopolymers such as collagen and chitosan in comparable settings for tissue restoration and medication delivery [77].

FUTURE PERSPECTIVES

Multifunctional biopolymer scaffolds must overcome a number of obstacles before they may be used in therapeutic settings. First and foremost, it is crucial to optimise degradation profiles to correspond with healing timescales. In order to preserve mechanical stability, scaffold materials must be adjusted to degrade in tandem with tissue regeneration. For more accurate therapeutic release, future materials might incorporate smart polymers that react to several stimuli (temperature, pH, and enzymes).

Second, patient-specific treatments may be transformed by the expansion of fabrication methods such as selective laser sintering for customised implants. Coupling with imaging data (e.g., CT scans) may enable patient-tailored scaffold designs.

Further research is necessary to fully understand the integration of immunotherapy techniques. The cGAS-STING pathway's reported activation raises the possibility that systemic immune responses could be primed by local scaffold-mediated treatment. Investigating combination tactics with adjuvants or checkpoint inhibitors may increase the effectiveness of anticancer treatments.

Diversification of biopolymers is another area. Additional biological cues are provided by natural polymers like collagen and chitosan, even though this study used a synthetic polymer blend (PLLA/BG). While chitosan's antibacterial and mucoadhesive qualities can lower the risk of infection, collagen's resemblance to the native extracellular matrix may improve cell adherence and differentiation. Promising are hybrid scaffolds that combine natural biological signals with synthetic strength.

Scaffold performance could be further customised by using nanotechnology components like growth factors or nanoparticles. One known limiting factor in the repair of big defects is vascularization, which may be accelerated by embedding angiogenic agents.

It is still crucial to conduct thorough clinical research on long-term safety, immunocompatibility, and functional results. To speed up translation, regulatory procedures for combination products—those that serve as both drug carriers and devices—need more precise frameworks.

In conclusion, by combining structural and therapeutic properties, the multifunctional scaffold created here represents a step toward next-generation regenerative oncology therapeutics. In order to fully realise the potential of biopolymer-based therapeutic scaffolds, future research should concentrate on improving immune involvement, smart response, and personalised scaffold construction.

CONCLUSIONS

This study demonstrates the development of a multifunctional biopolymer-based composite scaffold designed for simultaneous bone regeneration and localized anticancer therapy. A three-dimensional porous polymeric matrix was engineered to incorporate a glutathione-responsive Pt(IV) prodrug, enabling controlled and stimuli-responsive drug release under tumor-specific biochemical conditions. Additionally, near-infrared (NIR)-responsive components were integrated into the composite system to facilitate photothermal therapy, thereby enhancing therapeutic efficiency. The physicochemical and mechanical characterization of the scaffold revealed an interconnected porous architecture, suitable compressive strength, and structural stability, all of which are critical for bone tissue engineering

applications. The polymer composite exhibited favorable degradation behavior and sustained drug release profiles, highlighting its potential as an advanced functional biomaterial. Biological evaluations indicated that the composite scaffold possesses significant cytotoxic effects against osteosarcoma cells, along with the ability to stimulate immune responses. Furthermore, the scaffold promoted osteogenic differentiation in vitro and supported new bone formation in vivo, confirming its dual functionality as both a regenerative and therapeutic platform. The synergistic integration of polymer-based structural support with controlled drug delivery and photothermal functionality represents an innovative approach in composite biomaterials. This work underscores the importance of tailoring polymer composition, microstructure, and functional additives to achieve enhanced performance in biomedical applications, particularly for conditions requiring concurrent tissue regeneration and cancer treatment. Overall, the findings highlight the potential of advanced polymer–composite scaffolds as next-generation multifunctional systems, combining mechanical integrity, bioactivity, and therapeutic responsiveness for improved clinical outcomes. [Table 4]:

Table 4. Key Data Summary

Parameter	**Outcome**
Pt (II) Release Efficiency	High in tumor-like conditions
Photothermal Response	> +20°C under NIR
Tumor Cell Viability	Significantly reduced
Osteogenic Differentiation	Markedly enhanced
Bone Regeneration	Demonstrable in vivo

Larger animal models, immunomodulatory adjuncts, and clinical translation pathways should all be explored in future research, with an emphasis on manufacturing and regulatory issues. Precision medicine and cutting-edge biomaterials can be combined to improve patient outcomes with multifunctional biopolymer scaffolds like the one created here, providing a viable foundation for integrated regenerative cancer.

REFERENCES

1. Sindhi, K., Pingili, R. B., Beldar, V., Bhattacharya, S., Rahaman, J., & Mukherjee, D. (2025). The role of biomaterials-based scaffolds in advancing skin tissue construct. Journal of Tissue Viability, 34(2), 100858. https://doi.org/10.1016/j.jtv.2025.100858
2. Yan, Z., Deng, Y., Huang, L., Zeng, J., Wang, D., Tong, Z., Fan, Q., Tan, W., Yan, J., Zang, X., & Chen, S. (2025). Biopolymer-based bone scaffold for controlled Pt (IV) prodrug release and synergistic photothermal-chemotherapy and immunotherapy in osteosarcoma. Journal of Nanobiotechnology, 23(1), 286. https://doi.org/10.1186/s12951-025-03253-w
3. Sultana, N., Cole, A., & Strachan, F. (2024). Biocomposite scaffolds for tissue Engineering: materials, fabrication techniques and future directions. Materials, 17(22), 5577. https://doi.org/10.3390/ma17225577
4. Garot, C.; Bettega, G.; Picart, C. Additive Manufacturing of Material Scaffolds for Bone Regeneration: Toward Application in the Clinics. Adv. Funct. Mater. 2020, 31, 2006967.
5. Aldana, A.A.; Abraham, G.A. Current advances in electrospun gelatin-based scaffolds for tissue engineering applications. Int. J. Pharm. 2017, 523, 441–453.
6. Gregor, A.; Filová, E.; Novák, M.; Kronek, J.; Chlup, H.; Buzgo, M.; Blahnová, V.; Lukášová, V.; Bartoš, M.; Nečas, A.; et al. Designing of PLA scaffolds for bone tissue replacement fabricated by ordinary commercial 3D printer. J. Biol. Eng. 2017, 11, 31.
7. Mao, A.S.; Mooney, D.J. Regenerative medicine: Current therapies and future directions. Proc. Natl. Acad. Sci. USA 2015, 112, 14452–14459.
8. Dzobo, K.; Thomford, N.E.; Senthebane, D.A.; Shipanga, H.; Rowe, A.; Dandara, C.; Pillay, M.; Motaung, K.S.C.M. Advances in Regenerative Medicine and Tissue Engineering: Innovation and Transformation of Medicine. Stem Cells Int. 2018, 2018, 2495848.

9. Kaul, H.; Ventikos, Y. On the genealogy of tissue engineering and regenerative medicine. Tissue Eng. Part B Rev. 2015, 21, 203–217.
10. Krishani, M.; Shin, W.Y.; Suhaimi, H.; Sambudi, N.S. Development of Scaffolds from Bio-Based Natural Materials for Tissue Regeneration Applications: A Review. Gels 2023, 9, 100.
11. Marques, C.F.; Diogo, G.S.; Pina, S.; Oliveira, J.M.; Silva, T.H.; Reis, R.L. Collagen-based bioinks for complex tissue engineering applications: A comprehensive review. J. Mater. Sci. Mater. Med. 2019, 30, 32.
12. Silver, F.H.; Jaffe, M.; Shah, R.G. Structure and behavior of collagen fibers. In Handbook of Properties of Textile and Technical Fibers; Woodhead Publishing: Sawston, UK, 2018; pp. 345–365.
13. Fan, J.; Abedi-Dorcheh, K.; Sadat Vaziri, A.; Kazemi-Aghdam, F.; Rafieyan, S.; Sohrabinejad, M.; Ghorbani, M.; Rastegar Adib, F.; Ghasemi, Z.; Klavins, K.; et al. A Review of Recent Advances in Natural Polymer-Based Scaffolds for Musculoskeletal Tissue Engineering. Polymers 2022, 14, 2097.
14. Afewerki, S.; Sheikhi, A.; Kannan, S.; Ahadian, S.; Khademhosseini, A. Gelatin-polysaccharide composite scaffolds for 3D cell culture and tissue engineering: Towards natural therapeutics. Bioeng. Transl. Med. 2018, 4, 96–115.
15. Kuttappan, S.; Mathew, D.; Nair, M.B. Biomimetic composite scaffolds containing bioceramics and collagen/gelatin for bone tissue engineering—A mini-review. Int. J. Biol. Macromol. 2016, 93 Pt B, 1390–1401.
16. Norouzi, S., Shemshaki, N. S., Norouzi, E., Latifi, M., Azimi, B., Danti, S., Qiao, X., Miao, Y., Yang, S., Gorji, M., Petrovic, V., Aboudzadeh, M. A., & Bagherzadeh, R. (2024). Recent advances in biomaterials for tissue-engineered constructs: Essential factors and engineering techniques. Materials Today Chemistry, 37, 102016. https://doi.org/10.1016/j.mtchem.2024.102016
17. Hatem, S., Abdel-Gawad, R., Hussein, D.K. et al. Biological modulation and repair using plant-derived bioactives: advancements in tissue engineering and regenerative medicine. Futur J Pharm Sci 12, 14 (2026). https://doi.org/10.1186/s43094-026-00933-8
18. Norouzi, S., Shemshaki, N. S., Norouzi, E., Latifi, M., Azimi, B., Danti, S., Qiao, X., Miao, Y., Yang, S., Gorji, M., Petrovic, V., Aboudzadeh, M. A., & Bagherzadeh, R. (2024). Recent advances in biomaterials for tissue-engineered constructs: Essential factors and engineering techniques. Materials Today Chemistry, 37, 102016. https://doi.org/10.1016/j.mtchem.2024.102016
19. Huang, R., Yang, W., Wang, T., Cao, X., Sun, S., Jiang, J., Liu, H., & Peng, J. (2025). Photothermally-activated nano-delivery system for on-demand treatment of diabetic wound infections. International Journal of Pharmaceutics X, 11, 100464. https://doi.org/10.1016/j.ijpx.2025.100464
20. Ellakwa, D.ES., Abu-Khadra, A.S. & Ellakwa, T.E. Insight into bioactive glass and bio-ceramics uses: unveiling recent advances for biomedical application. Discov Mater 5, 78 (2025). https://doi.org/10.1007/s43939-025-00254-2
21. Nshimiyimana, P., Major, I., Colbert, D. M., & Buckley, C. (2025). Progress in the Biomedical application of Biopolymers: An Overview of the status quo and outlook in managing intrauterine adhesions. Macromol—A Journal of Macromolecular Research, 5(2), 25. https://doi.org/10.3390/macromol5020025
22. Savioli Lopes, M.; Jardini, A.L.; Maciel Filho, R. Poly (lactic acid) production for tissue engineering applications. Procedia Eng. 2012, 42, 1402–1413.
23. Wang, J.; Yang, C.; Xie, Y.; Chen, X.; Jiang, T.; Tian, J.; Hu, S.; Lu, Y. Application of Bioactive Hydrogels for Functional Treatment of Intrauterine Adhesion. Front. Bioeng. Biotechnol. 2021, 9, 1–16.
24. Buckley, C.; Murphy, E.J.; Montgomery, T.R.; Major, I. Hyaluronic Acid: A Review of the Drug Delivery Capabilities of This Naturally Occurring Polysaccharide. Polymers 2022, 14, 3442.
25. Murphy, E.J.; Fehrenbach, G.W.; Abidin, I.Z.; Buckley, C.; Montgomery, T.; Pogue, R.; Murray, P.; Major, I.; Rezoagli, E. Polysaccharides—Naturally Occurring Immune Modulators. Polymers 2023, 15, 2373.

26. Lee, S.S.; Kim, H.D.; Kim, S.H.L.; Kim, I.; Kim, I.G.; Choi, J.S.; Jeong, J.; Kim, J.H.; Kwon, S.K.; Hwang, N.S. Self-healing and adhesive artificial tissue implant for voice recovery. ACS Appl. Bio Mater. 2018, 1, 1134–1146.
27. Pina, S.; Oliveira, J.M.; Reis, R.L. Natural-based nanocomposites for bone tissue engineering and regenerative medicine: A review. Adv. Mater. 2015, 27, 1143–1169.
28. Gwak, S.J.; Lee, Y.B.; Lee, E.J.; Park, K.H.; Kang, S.W.; Huh, K.M. The use of acetylation to improve the performance of hyaluronic acid-based dermal filler. Korean J. Chem. Eng. 2023, 40, 1963–1969.
29. Lee, S.S.; Du, X.; Kim, I.; Ferguson, S.J. Scaffolds for bone-tissue engineering. Matter 2022, 5, 2722–2759.
30. Roupa, Z.; Polikandrioti, M.; Sotiropoulou, P.; Faros, E.; Koulouri, A.; Wozniak, G.; Gourni, M. Causes of Infertility in Women at Reproductive Age. Heal. Sci. J. 2009, 3, 80–87.
31. Han, Q.; Du, Y. Advances in the Application of Biomimetic Endometrium Interfaces for Uterine Bioengineering in Female Infertility. Front. Bioeng. Biotechnol. 2020, 8, 1–9.
32. Feng, L.; Wang, L.; Ma, Y.; Duan, W.; Martin-Saldaña, S.; Zhu, Y.; Zhang, X.; Zhu, B.; Li, C.; Hu, S.; et al. Engineering self-healing adhesive hydrogels with antioxidant properties for intrauterine adhesion prevention. Bioact. Mater. 2023, 27, 82–97.
33. Schmerold, L.; Martin, C.; Mehta, A.; Sobti, D.; Jaiswal, A.K.; Kumar, J.; Feldberg, I.; Munro, M.G.; Lee, W.C. A cost-effectiveness analysis of intrauterine spacers used to prevent the formation of intrauterine adhesions following endometrial cavity surgery. J. Med. Econ. 2024, 27, 170–183.
34. Huang, C.Y.; Chang, W.H.; Cheng, M.; Huang, H.Y.; Horng, H.C.; Chen, Y.J.; Lee, W.L.; Wang, P.H. Crosslinked hyaluronic acid gels for the prevention of intrauterine adhesions after a hysteroscopic myomectomy in women with submucosal myomas: A prospective, randomized, controlled trial. Life 2020, 10, 67.
35. Wang, P.H.; Yang, S.T.; Chang, W.H.; Liu, C.H.; Liu, H.H.; Lee, W.L. Intrauterine adhesion. Taiwan. J. Obstet. Gynecol. 2024, 63, 312–319.
36. Kou, L.; Jiang, X.; Xiao, S.; Zhao, Y.Z.; Yao, Q.; Chen, R. Therapeutic options and drug delivery strategies for the prevention of intrauterine adhesions. J. Control. Release 2020, 318, 25–37.
37. Nie, N.; Gong, L.; Jiang, D.; Liu, Y.; Zhang, J.; Xu, J.; Yao, X.; Wu, B.; Li, Y.; Zou, X. 3D bio-printed endometrial construct restores the full-thickness morphology and fertility of injured uterine endometrium. Acta Biomater. 2023, 157, 187–199.
38. Huang, X.W.; Lin, M.M.; Zhao, H.Q.; Powell, M.; Wang, Y.Q.; Zheng, R.R.; Ellis, L.B.; Xia, W.T.; Lin, F. A prospective randomized controlled trial comparing two different treatments of intrauterine adhesions. Reprod. Biomed. Online 2020, 40, 835–841.
39. Cen, J.; Zhang, Y.; Bai, Y.; Ma, S.; Zhang, C.; Jin, L.; Duan, S.; Du, Y.; Guo, Y. Research progress of stem cell therapy for endometrial injury. Mater. Today Bio 2022, 16, 100389.
40. De Wilde, R.L.; Devassy, R.; Ten Broek, R.P.G.; Miller, C.E.; Adlan, A.; Aquino, P.; Becker, S.; Darmawan, F.; Gergolet, M.; Habana, M.A.E.; et al. The Future of Adhesion Prophylaxis Trials in Abdominal Surgery: An Expert Global Consensus†. J. Clin. Med. 2022, 11, 1476.
41. Deans, R.; Abbott, J. Review of Intrauterine Adhesions. J. Minim. Invasive Gynecol. 2010, 17, 555–569.
42. Tabeeva, G.; Silachev, D.; Vishnyakova, P.; Asaturova, A.; Fatkhudinov, T.; Smetnik, A.; Dumanovskaya, M. The Therapeutic Potential of Multipotent Mesenchymal Stromal Cell—Derived Extracellular Vesicles in Endometrial Regeneration. Int. J. Mol. Sci. 2023, 24, 9431.
43. Zhu, Q.; Yao, S.; Ye, Z.; Jiang, P.; Wang, H.; Zhang, X.; Liu, D.; Lv, H.; Cao, C.; Zhou, Z.; et al. Ferroptosis contributes to endometrial fibrosis in intrauterine adhesions. Free Radic. Biol. Med. 2023, 205, 151–162.
44. Santamaria, X.; Roson, B.; Perez-Moraga, R.; Venkatesan, N.; Pardo-Figuerez, M.; Gonzalez-Fernandez, J.; Llera-Oyola, J.; Fernández, E.; Moreno, I.; Salumets, A.; et al. Decoding the endometrial niche of Asherman's Syndrome at single-cell resolution. Nat. Commun. 2023, 14, 5890.

45. Hooker, A.B.; de Leeuw, R.A.; Emanuel, M.H.; Mijatovic, V.; Brolmann, H.A.M.; Huirne, J.A.F. The link between intrauterine adhesions and impaired reproductive performance: A systematic review of the literature. BMC Pregnancy Childbirth 2022, 22, 837.
46. Hanstede, M.M.F.; Van Der Meij, E.; Goedemans, L.; Emanuel, M.H. Results of centralized Asherman surgery, 2003–2013. Fertil. Steril. 2015, 104, 1561–1568.e1.
47. Ang, C.J.; Skokan, T.D.; Mckinley, K.L. Mechanisms of Regeneration and Fibrosis in the Endometrium. Annu. Rev. Cell Dev. Biol. 2023, 39, 197–221.
48. Wang, J.; Zhan, H.; Wang, Y.; Zhao, L.; Huang, Y.; Wu, R. Current advances in understanding endometrial epithelial cell biology and therapeutic applications for intrauterine adhesion. Stem Cell Res. Ther. 2024, 15, 379.
49. Lee, W.L.; Liu, C.H.; Cheng, M.; Chang, W.H.; Liu, W.M.; Wang, P.H. Focus on the primary prevention of intrauterine adhesions: Current concept and vision. Int. J. Mol. Sci. 2021, 22, 5175.
50. Hooker, A.B.; Lemmers, M.; Thurkow, A.L.; Heymans, M.W.; Opmeer, B.C.; Brölmann, H.A.M.; Mol, B.W.; Huirne, J.A.F. Systematic review and meta-analysis of intrauterine adhesions after miscarriage: Prevalence, risk factors and long-term reproductive outcome. Hum. Reprod. Update 2014, 20, 262–278.
51. Wang, Y., Duan, H., Zhang, Z., Chen, L., & Li, J. (2024). Research progress on the application of natural medicines in biomaterial coatings. Materials, 17(22), 5607. https://doi.org/10.3390/ma17225607
52. Fu, Y.; Liu, T.; Wang, H.; Wang, Z.; Hou, L.; Jiang, J.; Xu, T. Applications of nanomaterial technology in biosensing. J. Sci. Adv. Mater. Devices 2024, 9, 100694.
53. Vigneshvar, S.; Sudhakumari, C.C.; Senthilkumaran, B.; Prakash, H. Recent Advances in Biosensor Technology for Potential Applications—An Overview. Front. Bioeng. Biotechnol. 2016, 4, 11.
54. Ertas, Y.N.; Mahmoodi, M.; Shahabipour, F.; Jahed, V.; Diltemiz, S.E.; Tutar, R.; Ashammakhi, N. Role of biomaterials in the diagnosis, prevention, treatment, and study of corona virus disease 2019 (COVID-19). Emergent Mater. 2021, 4, 35–55.
55. Cai, L.; Xu, J.; Yang, Z.; Tong, R.; Dong, Z.; Wang, C.; Leong, K.W. Engineered biomaterials for cancer immunotherapy. MedComm 2020, 1, 35–46.
56. Xiao, M.; Tang, Q.; Zeng, S.; Yang, Q.; Yang, X.; Tong, X.; Zhu, G.; Lei, L.; Li, S. Emerging biomaterials for tumor immunotherapy. Biomater. Res. 2023, 27, 47.
57. Niziołek, K.; Słota, D.; Sobczak-Kupiec, A. Polysaccharide-Based Composite Systems in Bone Tissue Engineering: A Review. Materials 2024, 17, 4220.
58. Gao, C.; Peng, S.; Feng, P.; Shuai, C. Bone biomaterials and interactions with stem cells. Bone Res. 2017, 5, 253–285.
59. Sun, W.; Ye, B.; Chen, S.; Zeng, L.; Lu, H.; Wan, Y.; Gao, Q.; Chen, K.; Qu, Y.; Wu, B. Neuro–bone tissue engineering: Emerging mechanisms, potential strategies, and current challenges. Bone Res. 2023, 11, 65.
60. Ansari, M. Bone tissue regeneration: Biology, strategies and interface studies. Prog. Biomater. 2019, 8, 223–237.
61. Li, Y., & Li, R. (2025). Preparation and characterization of a GSH-responsive drug-loaded polymer nanoparticle/silk fibroin composite hydrogel. Frontiers in Bioengineering and Biotechnology, 13, 1643800. https://doi.org/10.3389/fbioe.2025.1643800
62. BryantS. J. (2016). SP0088 hydrogels for osteoarthritis treatment. Ann. Rheum. Dis.75, 22. 10.1136/annrheumdis-2016-eular.6408
63. ChelikeD. K.AlagumalaiA.AcharyaJ.KumarP.SarkarK.ThangaveluS. A. G.et al (2020). Functionalized iron oxide nanoparticles conjugate of multi-anchored schiff's base inorganic heterocyclic pendant groups: cytotoxicity studies. Appl. Surf. Sci.501, 143963. 10.1016/j.apsusc.2019.143963
64. ChenH.ZhuangQ.WangH.ZhaiX.ZhangK.DengH.et al (2022). Ultrafine gold nanoparticles dispersed in conjugated microporous polymers with sulfhydryl functional groups to improve the reducing activity of 4-nitrophenol. Colloids Surf. Physicochem. Eng. Asp.649, 129459. 10.1016/j.colsurfa.2022.129459

65. ChenQ.YanM.HuA.LiangB.LuH.ZhouL.et al (2024). Injectable nanorobot-hydrogel superstructure for hemostasis and anticancer therapy of spinal metastasis. Nano-Micro Lett.16, 259. 10.1007/s40820-024-01469-3
66. FengJ.LiZ.TianL.MuP.HuY.XiongF.et al (2022). Efficacy and safety of curcuminoids alone in alleviating pain and dysfunction for knee osteoarthritis: a systematic review and meta-analysis of randomized controlled trials. BMC Complement. Med. Ther.22, 276. 10.1186/s12906-022-03740-9
67. FuS.RempsonC. M.PucheV.ZhaoB.ZhangF. (2022). Construction of disulfide containing redox-responsive polymeric nanomedicine. Methods199, 67–79. 10.1016/j.ymeth.2021.12.011
68. HoelderS.ClarkeP. A.WorkmanP. (2012). Discovery of small molecule cancer drugs: successes, challenges and opportunities. Mol. Oncol.6, 155–176. 10.1016/j.molonc.2012.02.004
69. KimS. H.YeonY. K.LeeJ. M.ChaoJ. R.LeeY. J.SeoY. B.et al (2018). Precisely printable and biocompatible silk fibroin bioink for digital light processing 3D printing. Nat. Commun.9, 1620. 10.1038/s41467-018-03759-y
70. KovrlijaI.MenshikhK.AbreuH.CochisA.RimondiniL.MarsanO.et al (2024). Challenging applicability of ISO 10993-5 for calcium phosphate biomaterials evaluation: towards more accurate in vitro cytotoxicity assessment. Biomater. Adv.160, 213866. 10.1016/j.bioadv.2024.213866
71. Jiao, Y., Zhang, Y., Dong, C., Zhu, J., Chen, W., Xu, T., Ye, S., & Du, Y. (2025). Recent advances in inorganic nanocomposites for the photothermal therapy of bone tumors. Nanoscale Horizons. https://doi.org/10.1039/d5nh00692a
72. Naik, G. a. R. R., Gupta, A., Datta, D., More, M., Roy, A. A., Kudarha, R., Hedayat, P., Moorkoth, S., Mutalik, S., & Dhas, N. (2025). Synergistic combinational photothermal therapy-based approaches for cancer treatment. FlatChem, 50, 100834. https://doi.org/10.1016/j.flatc.2025.100834
73. Xu, H., Jiang, Y., Zhang, R., Wang, D., Feng, J., & Zhang, H. (2026). Multiple-pathway cGAS-STING activation with enhanced mild photothermal therapy through glycolysis regulation for boosting gastric cancer immunotherapy. Materials Today Bio, 37, 102790. https://doi.org/10.1016/j.mtbio.2026.102790
74. Yan, Y., Tan, X., Song, B., Yi, M., Chu, Q., & Wu, K. (2025). Breaking barriers: The cGAS-STING pathway as a novel frontier in cancer immunotherapy. Cancer Communications, 45(11), 1513–1546. https://doi.org/10.1002/cac2.70067
75. Afsharian, Y. P., Rahimnejad, M., Rabiee, S. M., Feizi, F., & Seitz, H. (2025). Recent advances in promoting bone regeneration in Type 2 diabetes using drug delivery vehicles and Vehicle-Free therapeutics. Advanced Therapeutics, 8(2). https://doi.org/10.1002/adtp.202400400
76. Yang Q, Lou S, Zhang Y, Fang Z, Xing C, Wang W, Han M, Wang Z, Tang BZ, Zhang M. NIR-II Responsive Multifunctional Scaffold Enabling "Kill-Modulation-Build" Synergistic Therapy for Infectious Bone Defects. Adv Sci (Weinh). 2025 Dec;12(47):e08948. doi: 10.1002/advs.202508948.
77. Jabeen, N., & Atif, M. (2023). Polysaccharides based biopolymers for biomedical applications: A review. Polymers for Advanced Technologies, 35(1). https://doi.org/10.1002/pat.6203

