Open Journal of Nano
ISSN: 2147-0081
(2025) 10–1
Review Article

The use of poly(lactic acid) (PLA) in bone tissue engineering

[1] Rumeysa İNCESU, *[2] **Tarkan AKDERYA**, [2] Cem GÖK, [3] Cemal BİLİR,
[1] Gülbahar TABAKOĞLU, [1] Ataberk KAPLAN,

[1] Biyomedikal Mühendisliği, Lisansüstü Eğitim Enstitüsü, İzmir Bakırçay Üniversitesi, Menemen, İzmir 35660, Türkiye
[2] Biyomedikal Mühendisliği A.B.D., Mühendislik ve Mimarlık Fakültesi, İzmir Bakırçay Üniversitesi, Menemen, İzmir 35660, Türkiye
[3] Çocuk Cerrahisi A.B.D., Tıp Fakültesi, İzmir Bakırçay Üniversitesi, Menemen, İzmir 35660, Türkiye
*Corresponding author, e-mail: tarkan.akderya@bakircay.edu.tr

Submission Date: 09.01.2025 Acceptation Date: 27.03.2025

Abstract - Bone is a tissue that can regenerate and repair itself when minor damage occurs; however, it is insufficient to repair large defects. Today, various treatments to repair bone defects are limited due to risks such as lack of donors, genetic differences, infection, and tissue rejection. Although traditional metals are used extensively in bone treatments, these materials have many disadvantages. In recent years, biodegradable biopolymers such as poly(lactic) acid (PLA), polyetheretherketone (PEEK), polycaprolactone (PCL), and poly (glycolic acid) PGA have attracted growing interest due to their properties such as lightweight, high mechanical strength, biocompatibility, and high processability. In recent years, these polymer materials have been extensively used in the medical field. PLA is known to be preferred in bone tissue engineering applications as it is a biomaterial that supports cell processes, including migration, proliferation, distribution, and differentiation. In recent years, alongside traditional methods for producing bone scaffolds, innovative technological approaches have emerged. Traditional manufacturing methods, however, often lack precise control over scaffold porosity, prompting a shift towards advanced designs and rapid prototyping techniques. In bone scaffolds produced with additive manufacturing, it is possible to create 3D porous bone scaffolds with internal connections. In addition, PLA-based composite scaffolds have been studied to improve the mechanical and biological properties of pure PLA bone scaffolds, such as osteogenicity, porosity, and mechanical strength. This study presents a review of the PLA-based composite bone scaffolds in bone tissue engineering applications.

Keywords: Bone Tissue Engineering; Biopolymers; Polylactic Acid; Composite Bone Scaffolds; Additive Manufacturing Technologies

1. Introduction

Bone is a natural, complex, and living connective tissue that provides structural support to the body, protects internal organs, produces red and white blood cells, stores minerals, and enables movement [1], [2]. The bone cells, known as osteoblasts, are primarily surrounded by an extracellular matrix (ECM) composed of an inorganic phase containing hydroxyapatite (HA) and an organic phase containing typeI collagen. The primary role of the ECM is to provide mechanical support, mineralization, bone formation, bone repair, and homeostasis [1].

While bone tissue is able to regenerate and repair itself when experiencing minor damage, it is not sufficient in repairing large defects caused by trauma, osteoporosis, cancer, and congenital disorders, all of which significantly impact the quality of life and often require clinical intervention [1], [3]. Although autograft, allograft, and xenograft procedures are currently used to repair such large-scale bone defects, there are limitations due to risks such as donor shortage, genetic differences, infection, and tissue rejection [4].

At this point, regenerative medicine and its subfield, bone tissue engineering, have emerged to overcome these limitations. Bone tissue engineering, which uses cells and biomaterials to restore the lost functions of tissues, is based on osteoblasts and structural scaffolds. The use of biopolymer materials for scaffolds has attracted attention due to their biodegradable nature within the body.

DOI: 10.56171/ojn.1611817

Ideally, scaffolds produced with natural or synthetic biomaterials that are biocompatible and biodegradable, and that have appropriate structural and morphological characteristics, become structures that facilitate cell adhesion, proliferation, and growth [1], [4], [5].

Interest in bone tissue engineering, which aims for new bone formation through the combined use of biomaterials, cells, and growth factors, has increased over the years, and the development of this field has required the collaborative efforts of scientists, engineers, and physicians [5], [6].

Considering all these factors, polylactic acid (PLA), a synthetic biopolymer that is biocompatible, biodegradable, low-cost, and environmentally friendly has attracted the interest of researchers focusing on producing bone scaffolds. Its easy processability, low cost, and high mechanical strength make PLA a popular choice in bone tissue engineering applications [7]. This review article discusses the applications of PLA in bone tissue engineering and studies on composite bone scaffolds in which PLA is reinforced with other polymers to enhance the properties of bone scaffolds.

2. Biopolymers

In recent years, due to the environmental and ecological harm caused by petroleum-based materials, there has been a growing interest in the production of natural-based materials. As a result, attention has shifted towards polymer materials that could replace petroleum-based ones while also being environmentally friendly, biodegradable, lightweight, and having high specific strength. Known as "green polymers," biopolymers derive the prefix "bio" from their renewable or biological origins, which also confer biodegradable properties [8], [9].

Polymers are formed by the repetition of covalently bonded identical or different types of monomers and can exhibit both amorphous and crystalline structures. Additionally, monomer chains may be linearly, branched, or cross-linked. For in vivo applications in bone tissue scaffolds, it is vital to synthesize temperature-responsive polymers with a glass transition temperature (Tg) that does not exceed body temperature, as they become fluid above Tg [2].

Materials used in bone treatments are classified into two groups based on their degradation performance: bioinert and biodegradable. Although bioinert materials are successfully used in orthopedic implant applications, their persistence in the human body without degradation can lead to additional surgery in cases of replacement or functional disorder, thus increasing the patient's burden of pain and discomfort [10]. For this reason, researchers have focused on the use of biodegradable materials in bone tissue engineering, which possess properties that meet both the biochemical and biomechanical needs of bone tissue. Biodegradable bone scaffolds, placed in the damaged bone area, serve as a support for the attachment and growth of surrounding tissues and cells and biologically degrade in vivo without requiring surgical intervention once bone repair has occurred. The biologically degradable scaffold need to help the bone repair and healing process, provide mechanical support, and break down into non-toxic products that can be absorbed by the body [2].

Biopolymers, which are among biodegradable materials, are used as primary materials in bone tissue engineering studies and based on their origin are classified into two groups of natural and synthetic. The use of natural polymers is limited due to their rapid degradation rate, low mechanical properties, and high physiological activity. However, synthetic polymers possess superior properties compared to natural polymers, as they offer ease of design and display an appropriate degradation rate. These superior properties may result from the polymer chains being linked with other chains in either a linear or cross-linked manner, meaning the material can exhibit an amorphous or crystalline structure [10].

DOI: 10.56171/ojn.1611817

Open Journal of Nano
ISSN: 2147-0081
(2025) 10–1
Review Article

2.1 Polylactic Acid (PLA)

PLA, the most widely used biodegradable biopolymer in bone tissue scaffold applications, is an aliphatic polymer from the saturated Poly-α-hydroxy ester family (Figures 1 and 2). It exists in three stereoisomer forms: Poly (D-lactic acid) (PDLA), Poly (L-lactic acid) (PLLA), and D, L-PLA (PDLLA). Derived from renewable sources like corn and sugar, PLA is a polymer that offers ease of processing, high mechanical strength, biocompatibility, and biodegradability, making it suitable for 3D printing. Table 1 presents the physical and mechanical properties of PLA [6], [10], [11].

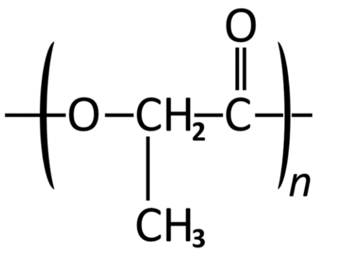

Figure 1. Structural formula of polylactic acid [2].

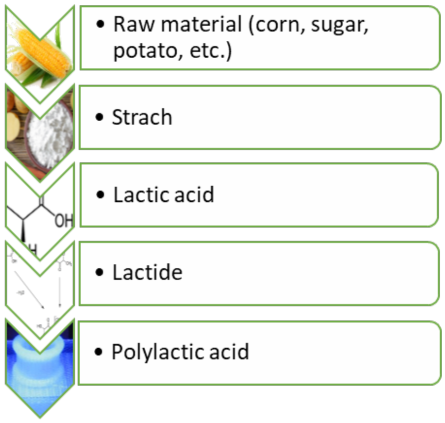

Figure 2. Production scheme of Polylactic Acid [6].

First identified in 1780 by Swedish chemist Scheele, PLA was first used in medical applications in the 1960s to treat fractured jawbones in dogs. In scaffolds produced for bone tissue engineering applications intended for clinical cases, L-PLA is preferred because it meets most requirements, including porous architecture, mechanical durability, biodegradability, and resistance to hydrolysis [2], [10].

Table 1. Physical and mechanical properties of PLA [12].

Özellikler	Birimler	PLA
ρ	g / cm^3	1.21 – 1.25
σ	MPa	21.0 – 60.0
E	GPa	0,35 – 3,50
ε	%	2,50 – 6,00
Tg	°C	45 – 60
Tm	°C	150 – 162

(ρ - polymer density, σ - tensile strength, E - tensile modulus, ε - ultimate strain, Tg - glass transition temperature, and Tm - melting temperature.)

DOI: 10.56171/ojn.1611817

Open Journal of Nano
ISSN: 2147-0081
(2025) 10–1
Review Article

For biodegradable polymer materials used in bone regeneration applications that are mechanically comparable to natural bone tissue, controlled and gradual degradation is expected, thereby eliminating the stress shielding effect and enabling the transfer of load to the bone tissue and soft tissue [13], [14]. Table2 compares the mechanical properties of PLA used in bone scaffold applications with those of natural bone tissue and discusses its areas of application.

Table 2. Comparison of the mechanical properties of natural bone tissue with PLA and clinical applications of PLA [15], [16], [17], [18], [19], [20], [21], [22], [23], [24].

Type of Material	Compressive Strength *(MPa)*	Tensile Strength *(MPa)*	Young's Modulus *(GPa)*	Elongation *(%)*	Degradation Time *(month)*	Tot 'ower *th)*	Application Areas
				Bone			
Human Cortical	131–224	35–283	17–20	1.07–2.10	Natural Bone Regeneration	-	Autograft and allograft utilized in defect filling, alveolar ridge augmentation, and sinus procedures
Human Cancellous Tissue	5–10	1.5–38	0,05–0,1	0,5–3	Natural Bone Regeneration	0,5–1	Augmentation, maintenance of dental ridge [25], [26], [27], [28], [29], [30], [31], [32], [33], [34]
				Biodegradable PLA			
PLLA	80–500	45–70	2.7	5–10	>24	3	BMP carrier, scaffolds, HA composite [35], [36], [37], [38], [39], [40]
D,L(PLA)	15–25	90–103	1.9	3–10	12–16	4	fracture stabilization, and interference screws [41], [42], [43]
L(PLA)	20–30	100–150	2.7	5–10	>24	3	Fracture stabilization, interference screws, scaffolds, bone graft material [36], [44], [45], [46], [47], [48]

(PLLA: Poly L-lactic acid; PLA: Polylactic acid; BMP: bone morphogenetic proteins; HA: hydroxyapatite.)

3. Bone Scaffold Design and Production Methods

The production technique and design of scaffolds designed for applications in bone tissue engineering must be developed in accordance with the structure and function of the target tissue. The scaffold's manufacturing technique, porosity, pore size, shape, osteoinductivity, biodegradability, and mechanical properties are all factors that affect the cells' growth and, consequently, tissues [3], [49].

In scaffold production, pore count and pore size are among the most critical considerations. As porosity increases, cell adhesion, proliferation, and the release of growth agents in scaffolds equipped with growth factors also increase. However, high porosity might decrease the mechanical strength of the scaffold, so producing a scaffold with ideal pore size is crucial for effective for bone tissue engineering applications. Although there are discrepancies in the literature on this topic, it is generally emphasized that the ideal pore size should be between 100 and 500 µm [3].

Bone tissue engineering applications are a multidisciplinary field with three main components: scaffold, cells, and growth factors, and this process is schematized in Figure 3.

DOI: 10.56171/ojn.1611817

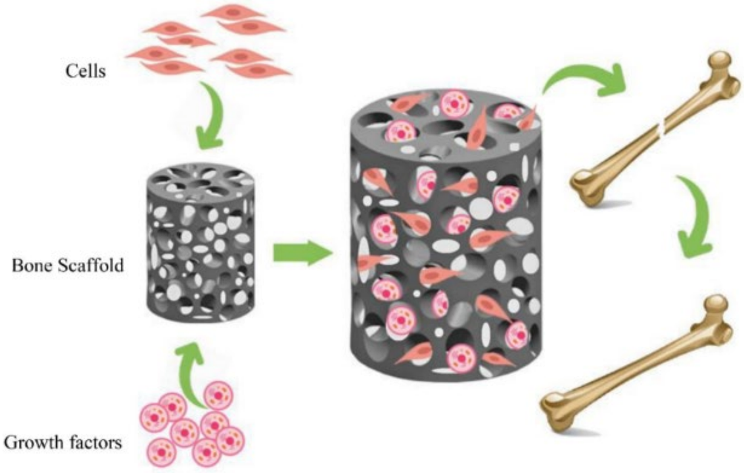

Figure 3. Bone tissue engineering process [54].

PLA has attracted interest in bone tissue applications as a biopolymer due to its biodegradability in implanted areas over time and its biocompatibility, both of which are essential for natural tissue regeneration. PLA's mechanical strength, comparable to human bone, making it an optimal matrix for bone tissue scaffolds. However, its low osteoconductivity, poor cellular adhesion on its surface, and brittleness limit its use. Reinforcing PLA with other polymer materials to create composite scaffolds and employing different production techniques have provided solutions to these disadvantages. The benefits of using PLA in bone tissue engineering scaffolds are listed below [1], [50].

- Although the hydrophobic surface of PLA reduces cell adhesion to some extent, surface modification can be achieved to make it hydrophilic by adjusting the production technique and incorporating other biomaterials.
- Enables the production of scaffolds in an interconnected porous form.
- The lactic acid byproduct resulting from PLA degradation is metabolized in vivo without cytotoxic effects on living tissue.
- PLA-based scaffolds were reported by Zhang et al. [51] in recent years to prevent insufficient nutrition and promote vascularization in the ossifying region.
- Despite occasional inadequacies in PLA's mechanical strength, it can be reinforced or coated with other biomaterials, enhancing its durability.

Today, both traditional and innovative technological approaches are accessible for scaffold fabrication in bone tissue engineering applications. Traditional methods include phase separation, solvent casting with particle leaching, gas foaming, solid freeform techniques, freeze-drying, melt molding, and electrospinning [1], [52]. However, as these traditional production techniques lack precise control over scaffold porosity, the focus has shifted to new design and rapid prototyping methods with advancing technology [49].

Open Journal of Nano
ISSN: 2147-0081
(2025) 10–1
Review Article

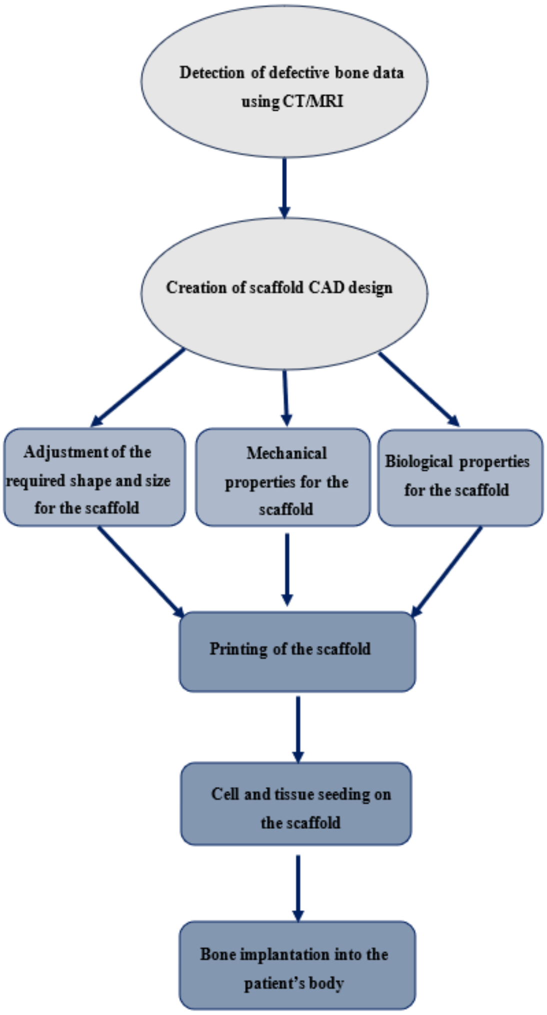

Figure 4. Steps used in additive manufacturing for bone tissue engineering [5].

3D printing technologies, commonly referred to as additive manufacturing technologies, enable the layer-by-layer construction of materials, offering high efficiency and the capability to fabricate intricate 3D scaffold structures that are challenging to create utilizing traditional techniques [53]. Additive manufacturing technologies comprise photopolymerization, material extrusion, material jetting, sheet lamination, binder jetting, powder bed fusion, and directed energy deposition [6]. One of the significant advantages provided by additive manufacturing since its inception in the 1980s is the ability to print patient-specific bone scaffolds using a 3D image of the impaired bone area gathered from computed tomography (CT) or magnetic resonance imaging (MRI) [5], [53]. The necessary process steps for scaffold production via additive manufacturing technologies are illustrated in Figure 4.

4. Bone Tissue Engineering with PLA and Other Biomaterials

Bone tissue engineering has emerged as a pivotal field aimed at addressing the limitations of conventional bone repair techniques, leveraging biocompatible and biodegradable materials to support cellular proliferation and tissue regeneration. Poly (lactic acid) (PLA), a widely studied aliphatic polyester, stands out for its high biodegradability, favorable mechanical properties, and ease of fabrication into various scaffold geometries. However, PLA's inherent hydrophobicity, low cell adhesion, and limited bioactivity present challenges for its standalone application in bone tissue engineering. To overcome these limitations, researchers have focused on combining PLA with bioactive materials such as hydroxyapatite (HA), Ti6Al4V (Ti64), pearl powder, collagen, and polycaprolactone (PCL), creating composite systems tailored for bone regeneration applications.

DOI: 10.56171/ojn.1611817

The integration of PLA with hydroxyapatite (HA) is particularly promising, as HA is a naturally occurring mineral found in bone that promotes osteoinduction and enhances biocompatibility. In PLA/HA composites, PLA provides a mechanically robust scaffold, while HA introduces a bone-mimicking mineral phase, facilitating the adhesion, proliferation, and differentiation of osteoblasts. This synergy enhances the overall osteogenic scaffold's potential and accelerates bone tissue formation. Moreover, by optimizing the distribution and concentration of HA particles, the mechanical properties of the composites can be fine-tuned to match those of native bone, making them suitable for load-bearing applications. Studies have demonstrated the ability of PLA/HA composites to support rapid bone cell adhesion and mineralization both in vitro and in vivo, reinforcing their clinical relevance [55]

The study by Zarei et al. (2023) was conducted to assess the potential of Ti64 as an alternative PLA metallic reinforcement. Using FDM-based 3D printing, 3D scaffolds of PLA-Ti64 with various Ti64 contents (0, 3, 6 and 9 wt%) were created and investigated from mechanical, physical, thermal, biological aspects [17]. 3D PLA-Ti6Al4V (Ti64) scaffolds with open pores and interconnected channels were successfully produced using the material extrusion technique. The study found that incorporating 3-6 wt% Ti64 into PLA significantly enhanced its mechanical properties. Specifically, the ultimate compressive strength and compressive modulus of PLA-3Ti64 were increased to 49.9 MPa and 1.9 GPa, respectively. This improvement demonstrates the potential of Ti64 as an effective reinforcement material for PLA, offering a promising approach for developing mechanically robust scaffolds in applications such as bone tissue engineering. [56].

In a study conducted by Dai et al. (2016), polylactic (PLA) nanofibrous scaffolds produced through the electrospinning process to enhance the biocompatibility and mineralization potential of PLA and supplemented with (0, 1, 2, 3 wt%) pearl powder were produced and marked as EP0, EP1, EP2 and EP3, respectively. Pearl powder was used to promote hydroxyapatite (HA) deposition and cell culture [18]. According to the result of the study; while the surface of pure PLA was very smooth, it became rough on PLA/pearl nano. In this case, it was understood that the rough surface was due to the addition of pearl powder. A small increase in hydrophilicity was obtained in PLA/pearl scaffolds. The mineralization process caused the deposition of HA particles on the sample surfaces and the PLA/pearl scaffold was completely covered with HA, while only partially covering the pure PLA scaffold. In vitro evaluations, including MTT assay and SEM analysis, demonstrated enhanced cell proliferation and improved adhesion morphology in the PLA/pearl scaffold, indicating that pearl can improve the poor biocompatibility of PLA. Therefore, a PLA/pearl composite nanostructure would be superior to a pure PLA scaffold, implying great potential applications in bone tissue engineering [57].

Similarly, PLA-collagen composites represent another innovative approach to mimic the extracellular matrix (ECM) of bone tissue. Collagen, a primary structural protein in the ECM, is well-known for its exceptional biocompatibility, biodegradability, and ability to support cellular integration and proliferation. The combination of PLA and collagen offers a scaffold that balances structural integrity with biological functionality. PLA ensures the mechanical stability and controlled degradation of the scaffold, while collagen promotes cell adhesion and proliferation by providing bioactive cues. This combination has been successfully employed to fabricate 3D porous scaffolds that enable cell infiltration and nutrient exchange, making them ideal for bone regeneration. Furthermore, crosslinking techniques can enhance the stability and durability of PLA-collagen scaffolds, ensuring their long-term performance in tissue engineering applications [58].

In a study conducted by Nadi et. al. [59], the combination of PLA with polycaprolactone (PCL), a biodegradable polymer with superior flexibility and elongation properties, has shown significant potential. PCL complements PLA by reducing its brittleness and enhancing the elasticity of the

DOI: 10.56171/ojn.1611817

resulting composite, making it particularly suitable for dynamic mechanical environments such as bone repair sites. PLA/PCL blends exhibit balanced mechanical properties and extended degradation times, allowing the scaffold to provide long-term support as new bone tissue forms. To further improve bioactivity, these composites can be functionalized with osteoactive coatings, growth factors, or nanoparticles to enhance cellular responses and promote bone regeneration. Recent advancements in 3D printing technologies have enabled the precise fabrication of PLA/PCL scaffolds with complex architectures, opening new avenues for personalized and patient-specific bone grafts [59].

In conclusion, the combination of PLA with bioactive materials such as HA, collagen, and PCL represents a transformative strategy in bone tissue engineering. These composites not only address the limitations of individual materials but also create multifunctional scaffolds that meet the mechanical, biological, and degradative requirements for successful bone regeneration. By tailoring the composition and architecture of these materials, researchers can develop innovative solutions that align with the complex demands of personalized medicine, ultimately advancing the field of regenerative medicine and improving patient outcomes.

5. Conclusions And Future Perspective

PLA is a widely used biopolymer in the biomedical field due to its processability, biocompatibility, and high mechanical properties. However, the characteristics of PLA-based bone scaffolds need enhancement to address limitations such as PLA's slow degradation rate, low cell adhesion, and potential for in vivo inflammation. For this reason, PLA is often reinforced and coated with bioceramics, metals, and other polymers. Studies have reported the advantages of pure PLA bone scaffolds, yet further research is necessary to move closer to clinical applications in this field.

Scaffolds with complex properties must be tailored to the mechanical properties of the defective cancellous or cortical bone section where they will be applied. Therefore, as the mechanical properties and internal structure of bone scaffolds will be highly diverse and complex, 3D printing technology is required. Topics and suggestions for material selection and additive manufacturing technology are listed below:

- By establishing an AI-based material selection system, intelligent choices can be made to select the appropriate material and design for the target bone region.
- The bone scaffold material used for bone revision should possess antibacterial and anticancer properties. Otherwise, pathological factors could compromise the effectiveness of the bone scaffolds.
- The degradation rate of bone scaffolds produced with biodegradable materials must be adjustable. While biodegradable biopolymers are preferred to avoid long-term adverse effects from implant materials on the human body, the micro-material behaviors due to early or late degradation of biodegradable materials should be analyzed and evaluated.
- Composite bone scaffolds combining PLA with other biopolymers should be expanded and their performance enhanced. The prepared composite bone scaffolds should be evaluated in terms of biocompatibility, morphological structure, biodegradability, and growth factors that support osteogenesis.
- Real-time control of bone scaffold production with additive manufacturing technology and maintain standardization for each production in 3D manufacturing are problems that need to be addressed.

DOI: 10.56171/ojn.1611817

Peer-review: Externally peer - reviewed.

Author contributions: Concept – R.İ., T.A., C.G., C.B.; Literature Search – R.İ., G.T., A.K.; Writing – T.A., C.G, R. İ., G. T.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

References

[1] M. S. Alavi *et al.* (2023) Applications of poly (lactic acid) in bone tissue engineering: A review article," *Artificial Organs*, vol. 47, no. 9. doi: 10.1111/aor.14612.

[2] Z. Sheikh, S. Najeeb, Z. Khurshid, V. Verma, H. Rashid, and M. Glogauer (*2015*) Biodegradable Materials for Bone Repair and Tissue Engineering Applications," *Materials 2015, Vol. 8, Pages 5744-5794*, vol. 8, no. 9*, pp. 5744–5794, Aug. doi: 10.3390/MA8095273.*

[3] N. İ. Büyük et al. (2023) Effect of different pore sizes of 3D printed PLA-based scaffold in bone tissue engineering *International Journal of* Polymeric Materials and Polymeric Biomaterials, vol. 72, no. 13, pp.1021–1031.doi: 10.1080/00914037.2022.2075869.

[4] S. Salehi, H. Ghomi, S. A. Hassanzadeh-Tabrizi, N. Koupaei, and M. Khodaei, "The effect of polyethylene glycol on printability, physical and mechanical properties and osteogenic potential of 3D-printed poly (l-lactic acid)/polyethylene glycol scaffold for bone tissue engineering," *Int J Biol Macromol*, vol. 221, pp. 1325–1334, Nov. 2022, doi: 10.1016/J.IJBIOMAC.2022.09.027.

[5] A. Haleem, M. Javaid, R. H. Khan, and R. Suman, "3D printing applications in bone tissue engineering," J Clin Orthop Trauma, vol. 11, pp. S118–S124, Feb. 2020, doi: 10.1016/J.JCOT.2019.12.002.

[6] P. K. A. Terzioğlu, "(PDF) Kemik Doku Mühendisliği Uygulamaları için Polilaktik Asit-Hidroksiapatit Kompozitler." Accessed: Jan. 01, 2024.

[7] M. Jouyandeh, H. Vahabi, N. Rabiee, M. Rabiee, M. Bagherzadeh, and M. R. Saeb, "Green composites in bone tissue engineering," *Emergent Materials 2021 5:3*, vol. 5, no. 3, pp. 603–620, Aug. 2021, doi: 10.1007/S42247-021-00276-5.

[8] L. Ravikumar and D. Chandramohan, "Bending Test on Hybrid Bio Composite Materials," Indian Journal of Science and Technology, vol. 10, no. 7, 2017, doi: 10.17485/ijst/2017/v10i7/108478.

[9] B. Çetin, B. Mühendisliği, and A. Dalı, "Doğal lif ile güçlendirilmiş polilaktik asit/polipropilen kompozitlerin mekanik ve termal özellikleri," 2019, Accessed: Jan. 24, 2024.

[10] F. G. H. K. İ. U. O. Mert, "(PDF) Kemik Tedavilerinde Kullanılan Biyobozunur İmplant Malzemeler," 1. Uluslararası Plastik ve Kauçuk Teknolojileri Sempozyumu ve Sergisi, Ankara. Accessed: Jan. 01, 2024.

[11] V. DeStefano, S. Khan, and A. Tabada, "Applications of PLA in modern medicine," Engineered Regeneration, vol. 1, pp. 76–87, Jan. 2020, doi: 10.1016/J.ENGREG.2020.08.002.

[12] S. Farah, D. Anderson, and R. Langer, "Physical and mechanical properties of PLA, and their functions in widespread applications—A comprehensive review," *Advanced Drug Delivery Reviews*, vol. 107, pp. 367–392, 2016.

[13] Hutmacher, D., Hürzeler, M. B., & Schliephake, H. (1996). A review of material properties of biodegradable and bioresorbable polymers and devices for GTR and GBR applications. *The International Journal of Oral & Maxillofacial Implants*, 11(5), 667–678.

[14] C. Chanlalit, J. Fitzsimmons, K.-N. An, and M. E. Morrey, "Stress shielding around radial head prostheses," *The Journal of Hand Surgery*, vol. 37, no. 10, pp. 2118–2125, Oct. 2012, doi: 10.1016/j.jhsa.2012.06.020.

[15] K. A. Athanasiou, C. F. Zhu, D. R. Lanctot, C. M. Agrawal, and X. Wang, "Fundamentals of biomechanics in tissue engineering of bone," *Tissue Eng, vol. 6, no. 4, pp. 361–381, 2000, doi: 10.1089/107632700418083.*

[16] M. J. Yaszemski, R. G. Payne, W. C. Hayes, R. Langer, and A. G. Mikos, "Evolution of bone transplantation: Molecular, cellular and tissue strategies to engineer human bone," *Biomaterials*, vol. 17, no. 2, pp. 175–185, 1996, doi: 10.1016/0142-9612(96)85762-0.

[17] D. Eglin and M. Alini, "Degradable polymeric materials for osteosynthesis: Tutorial," European Cells and Materials, vol. 16, pp. 80–91, 2008, doi: 10.22203/eCM.v016a09.

[18] F. Tamimi, Z. Sheikh, and J. Barralet, "Dicalcium phosphate cements: Brushite and monetite," *Acta Biomater*, vol. 8, no. 2, pp. 474–487, 2012, doi: 10.1016/J.ACTBIO.2011.08.005.

[19] L. E. Claes, "Mechanical characterization of biodegradable implants," *Clin Mater*, vol. 10, no. 1–2, pp. 41–46, 1992, doi: 10.1016/0267-6605(92)90083-6.

[20] J. Blackburn, R. Hodgskinson, J. D. Currey, and J. E. Mason, "Mechanical properties of microcallus in human cancellous bone," *Journal of Orthopaedic Research*, vol. 10, no. 2, pp. 237–246, 1992, doi: 10.1002/JOR.1100100211.

[21] L. Tan, X. Yu, P. Wan, and K. Yang, "Biodegradable Materials for Bone Repairs: A Review," *J Mater Sci Technol*, vol. 29, no. 6, pp. 503–513, Jun. 2013, doi: 10.1016/J.JMST.2013.03.002.

[22] I. Armentano, M. Dottori, E. Fortunati, S. Mattioli, and J. M. Kenny, "Biodegradable polymer matrix nanocomposites for tissue engineering: A review," *Polym Degrad Stab*, vol. 95, no. 11, pp. 2126–2146, Nov. 2010, doi: 10.1016/J.POLYMDEGRADSTAB.2010.06.007.

[23] P. V. Giannoudis, H. Dinopoulos, and E. Tsiridis, "Bone substitutes: an update*.," Injury, vol. 36 Suppl 3, 2005,* doi: 10.1016/J.INJURY.2005.07.029.

[24] Witte, F., Hort, N., Vogt, C., Cohen, S., Kainer, K. U., Willumeit, R., & Feyerabend, F. (2008). Degradable biomaterials based on magnesium corrosion. *Current Opinion in Solid State and Materials Science*, 12(5–6), 63–72. https://doi.org/10.1016/j.cossms.2009.04.001

[25] F. Khoury, "Augmentation of the sinus floor with mandibular bone block and simultaneous implantation: A 6-year clinical investigation," *International Journal of Oral and Maxillofacial Implants*, vol. 14, no. 4, pp. 557–564, 1999. [

[26] M. S. Block and M. Degen, "Horizontal ridge augmentation using human mineralized particulate bone: Preliminary results," *Journal of Oral and Maxillofacial Surgery*, vol. 62, no. SUPPL. 2, pp. 67–72, Sep. 2004, doi: 10.1016/J.JOMS.2004.05.209.

[27] M. Bolander and G. Balian, "The use of demineralized bone matrix in the repair of segmental defects. Augmentation with extracted matrix proteins compared with autologous grafts," *Journal of Bone and Joint Surgery*, vol. 68, no. 8, pp. 1264–1274, 1986.

[28] P. P. T. Araújo, K. P. Oliveira, S. C. L. Montenegro, A. F. P. Carreiro, J. S. P. Silva, and A. R. Germano, "Block allograft for reconstruction of alveolar bone ridge in implantology: A systematic review," *Implant Dent*, vol. 22, no. 3, pp. 304–308, Jun. 2013, doi: 10.1097/ID.0B013E318289E311.

[29] T. W. Sterio, J. A. Katancik, S. B. Blanchard, P. Xenoudi, and B. L. Mealey, "A Prospective, Multicenter Study of Bovine Pericardium Membrane with Cancellous Particulate Allograft for Localized Alveolar Ridge Augmentation," *Int J* Periodontics Restorative Dent, vol. 33, no. 4, pp. 499–507, Jul. 2013, doi: 10.11607/PRD.1704.

[30] J. M. Whittaker, R. A. James, and J. L. Lozada, "Histologic response and clinical evaluation of heterograft and allograft materials in the elevation of the maxillary sinus for the placement of endosteal implants," *Journal of Oral Implantology*, vol. 15, no. 3, pp. 141–146, 1989.

[31] P. Valentini and D. Abensur, "Maxillary sinus floor elevation for implant placement with demineralized freeze-dried bone and bovine bone (Bio-Oss): A clinical study of 20 patients," *International Journal of Periodontics & Restorative Dentistry, vol. 17, no. 3, pp. 232–241, 1997.*

[32] J. S. Guerrero and B. A. Al-Jandan, "Allograft for maxillary sinus floor augmentation: A retrospective study of 90 cases," Implant Dent, vol. 21, no. 2, pp. 136–140, 2012, doi: 10.1097/ID.0B013E31824A023B.

[33] G. Avila et al., "Clinical and histologic outcomes after the use of a novel allograft for maxillary sinus augmentation: A case series," Implant Dent, vol. 19, no. 4, pp. 330–341, Aug. 2010, doi: 10.1097/ID.0B013E3181E59B32.

[34] D. S. Sohn, J. K. Lee, K. M. An, and H. I. Shin, "Histomorphometric evaluation of mineralized cancellous allograft in the maxillary sinus augmentation: A 4-case report," *Implant Dent*, vol. 18, no. 2, pp. 172–181, Apr. 2009, doi: 10.1097/ID.0B013E318199045D.

[35] X. Niu, Q. Feng, M. Wang, X. Guo, and Q. Zheng, "Porous nano-HA/collagen/PLLA scaffold containing chitosan microspheres for controlled delivery of synthetic peptide derived from BMP-2," *Journal of Controlled Release*, vol. 134, no. 2, pp. 111–117, Mar. 2009, doi: 10.1016/J.JCONREL.2008.11.020.

[36] Z. Xiong, Y. Yan, R. Zhang, and L. Sun, "Fabrication of porous poly (L-lactic acid) scaffolds for bone tissue engineering via precise extrusion," *Scr Mater*, vol. 45, no. 7, pp. 773–779, Oct. 2001, doi: 10.1016/S1359-6462(01)01094-6.

[37] S. Higashi, T. Yamamuro, T. Nakamura, Y. Ikada, S. H. Hyon, and K. Jamshidi, "Polymer-hydroxyapatite composites for biodegradable bone fillers," Biomaterials, vol. 7, no. 3, pp. 183–187, 1986, doi: 10.1016/0142-9612(86)90099-2.

[38] M. Vert, "Aliphatic polyesters: Great degradable polymers that cannot do everything," *Biomacromolecules*, vol. 6, no. 2, pp. 538–546, Mar. 2005, doi: 10.1021/bm0494702.

[39] E. Nejati, H. Mirzadeh, and M. Zandi, "Synthesis and characterization of nano-hydroxyapatite rods/poly (l-lactide acid) composite scaffolds for bone tissue engineering," *Compos Part A Appl Sci Manuf*, vol. 39, no. 10, pp. 1589–1596, Oct. 2008, doi: 10.1016/J.COMPOSITESA.2008.05.018.

[40] A. L. C. Lagoa, C. Wedemeyer, M. Von Knoch, F. Löer, and M. Epple, "A strut graft substitute consisting of a metal core and a polymer surface," J Mater Sci Mater Med, vol. 19, no. 1, pp. 417–424, Jan. 2008, doi: 10.1007/S10856-006-0022-0.

[41] W. H. Warden, R. Friedman, L. M. Teresi, and D. W. Jackson, "Magnetic resonance imaging of bioabsorbable polylactic acid interference screws during the first 2 years after anterior cruciate ligament reconstruction," *Arthroscopy - Journal of Arthroscopic and Related Surgery*, vol. 15, no. 5, pp. 474–480, 1999, doi: 10.1053/AR.1999.V15.015047.

[42] K. J. Bozic, L. E. Perez, D. R. Wilson, P. G. Fitzgibbons, and J. B. Jupiter, "Mechanical testing of bioresorbable implants for use in metacarpal fracture fixation," *Journal of Hand Surgery*, vol. 26, no. 4, pp. 755–761, 2001, doi: 10.1053/JHSU.2001.24145.

[43] A. A. Ignatius and L. E. Claes, "In vitro biocompatibility of bioresorbable polymers: Poly (L, DL-lactide) and poly(L-lactide-co-glycolide)," Biomaterials, vol. 17, no. 8, pp. 831–839, 1996, doi: 10.1016/0142-9612(96)81421-9.

[44] L. Nie, D. Chen, J. Fu, S. Yang, R. Hou, and J. Suo, "Macroporous biphasic calcium phosphate scaffolds reinforced by poly-L-lactic acid/hydroxyapatite nanocomposite coatings for bone regeneration," *Biochem Eng J*, vol. 98, pp. 29–37, Jun. 2015, doi: 10.1016/J.BEJ.2015.02.026.

[45] Y. S. Nam and T. G. Park, "Porous biodegradable polymeric scaffolds prepared by thermally induced phase separation," *Journal of Biomedical Materials Research*, vol. 47, no. 1, pp. 8–17, Oct. 1999, doi: 10.1002/(SICI)1097-4636(199910)47:1<8: AID-JBM2>3.0.CO;2-L.

[46] S. Vainionpää, J. Kilpikari, J. Laiho, P. Helevirta, P. Rokkanen, and P. Törmälä, "Strength and strength retention vitro, of absorbable, self-reinforced polyglycolide (PGA) rods for fracture fixation," Biomaterials, vol. 8, no. 1, pp. 46–48, 1987, doi: 10.1016/0142-9612(87)90028-7.

[47] J. W. Leenslag, A. J. Pennings, R. R. M. Bos, F. R. Rozema, and G. Boering, "Resorbable materials of poly(l-lactide). VII. In vivo and in vitro degradation," *Biomaterials*, vol. 8, no. 4, pp. 311–314, 1987, doi: 10.1016/0142-9612(87)90121-9.

[48] P. C.- Biomaterials and undefined 1980, "Biodegradable composites for internal fixation," *cir.nii.ac.jp*, Accessed: Jan. 26, 2024.

[49] S. Yang, K. F. Leong, Z. Du, and C. K. Chua, "The design of scaffolds for use in tissue engineering. Part I. Traditional factors," *Tissue Engineering*, vol. 7, no. 6. 2001. doi: 10.1089/107632701753337645.

[50] K. J. L. Burg, S. Porter, and J. F. Kellam, "Biomaterial developments for bone tissue engineering," *Biomaterials,* vol. 21, no. 23, pp. 2347–2359, Dec. 2000, doi: 10.1016/S0142-9612(00)00102-2.

[51] H. Zhang, X. Mao, D. Zhao, W. Jiang, Z. Du, and Q. Li, "Three-dimensional printed polylactic acid–hydroxyapatite composite scaffolds for prefabricating vascularized tissue-engineered bone: An in vivo bioreactor model," *Scientific Reports*, vol. 7, no. 1, 2017.

[52] N. Top, İ. Şahin, H. Gökçe, and H. Gökçe, "Computer-aided design and additive manufacturing of bone scaffolds for tissue engineering: state of the art," *Journal of Materials Research 2021 36:19*, vol. 36, no. 19, pp. 3725–3745, Mar. 2021, doi: 10.1557/S43578-021-00156-Y.

[53] Y. Wu, Y. Lu, M. Zhao, S. Bosiakov, and L. Li, "A Critical Review of Additive Manufacturing Techniques and Associated Biomaterials Used in Bone Tissue Engineering," *Polymers 2022, Vol. 14, Page* 2117, vol. 14, no. 10, p. 2117, May 2022, doi: 10.3390/POLYM14102117.

[54] J. Babak, wang Xinnan, and B. Amanda, "Additive Manufacturing Techniques for Fabrication of Bone Scaffolds for Tissue Engineering Applications," *Recent Progress in Materials 2020, Vol. 2, 021*, vol. 2, no. 3, pp. 1–41, Sep. 2020, doi: 10.21926/RPM.2003021.

[55] M. Subramaniyan, S. Karuppan, S. Helaili, I. Ahmad, "Structural, mechanical, and in-vitro characterization of hydroxyapatite loaded PLA composites", *Journal of Molecular Structure., vol.1306,* Jun 2024, doi: 10.1016 /j.molstruc.2024.137862

[56] D. Qin, N. Wang, X. You, A. Zhang, X. Chen, Y. Liu "Collagen-based biocomposites inspired by bone hierarchical structures for advanced bone regeneration: ongoing research and perspectives", *Journal of Biomaterials Science., Issue 2, 2022*, doi: https://doi.org/10.1039/D1BM01294K

[57] Zarei, M., Shabani Dargah, M., Hasanzadeh Azar, M. et al. Enhanced bone tissue regeneration using a 3D-printed poly(lactic acid)/Ti6Al4V composite scaffold with plasma treatment modification. Sci Rep 13, 3139 (2023). https://doi.org/10.1038/s41598-023-30300-z

[58] Dai, Jiamu, et al. "Electrospinning of PLA/pearl powder nanofibrous scaffold for bone tissue engineering." RSC advances 6.108 (2016): 106798-106805.

[59] A. Nadi, M. Khodaei, M. Javdani, A. Mirzaei, M. Soleimannejad, L. Tayebi, S. Asadpour "Fabrication of functional and nano-biocomposite scaffolds using strontium-doped bredigite nanoparticles/polycaprolactone/poly lactic acid via 3D printing for bone regeneration.", *International Journal of Biological Macromolecules.,* vol. 219, pp. 1319-1336, Oct .2022, doi: 10.1016/ POLYM14102117