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# Advancements in Bone Tissue Regeneration: A Review of Common Scaffolds in Tissue Engineering

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## Abstract

Regenerative medicine offers innovative solutions through cell therapy and tissue engineering techniques to address irreparable bone damage. Engineered structures play an important role in enhancing the body's natural healing process, especially in cases where extensive bone loss prevents natural recovery. This article provides an overview of the most commonly used scaffolds in tissue engineering for bone regeneration. Given that bone is a rigid and inflexible tissue, scaffolds designed for bone repair must be made from materials that possess similar hardness. For example, bioactive glasses are an ideal material, as they form a crystal layer of hydroxyapatite when exposed to the body's physiological fluids. The choice of manufacturing method depends on the structure of the tissue being studied. Scaffolds are crucial in tissue engineering, and various methods have been developed to create effective scaffolds. One of these methods is electrospinning, which allows the creation of fibers ranging from several microns to nanometers in size by altering specific conditions. The high surface area-to-volume ratio of electrospun fibers increases cell adhesion and proliferation on the scaffold. Consequently, scaffolds made by electrospinning, combining bioactive glass and polymer materials, provide a promising foundation for the treatment of bone diseases.

**Keywords:** Tissue engineering, Scaffolds, Bone tissue, Regeneration

## Introduction

Bone tissue is crucial for the body's functionality, and any damage to its structure, whether from injury, disease, or lesions, can disrupt the body's equilibrium and significantly affect a person's quality of life [1, 2]. While bone tissue has a natural ability to heal after injury [3], it is only effective in minor fractures. In these cases, the body's natural healing processes, involving stromal cells, stem cells, macrophages, osteoblasts, and osteoclasts, work together to repair the damage [4, 5]. However, in severe cases such as major fractures, defects like displaced bone fractures, traumatic injuries, periodontal disorders, or congenital issues like cleft palates, the body's natural repair mechanisms fall short, and medical intervention becomes necessary [6, 7].

Bone grafting is the most common surgical procedure used today to repair and strengthen bones in orthopedic practices [8-10]. There are several types of bone grafts: Xenograft, Allograft, and Autograft. Xenografts involve taking tissue from another species, such as animals and carry risks of immune rejection and infection transmission. Allografts are human-derived grafts typically taken from deceased individuals, though they require sterilization to avoid immune responses and

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disease transmission. The challenges with allografts include limited availability and potential transmission of diseases like AIDS, hepatitis, and cancer [11, 12]. Autografts involve transplanting tissue from one part of a person's body to another. Although this avoids immune rejection, the extensive surgery required can result in long-term pain and discomfort [13, 14].

Despite the widespread use of bone grafting, several obstacles remain. These include challenges in finding suitable tissue for transplantation, poor bone quality in conditions like osteoporosis [15-17], risks of disease transmission, the need for re-surgery, and difficulties with tissue integration [18]. In contrast, tissue engineering, which uses cell-based or autogenous tissue transplantation, has emerged as a solution to many of these challenges. The concept of tissue engineering builds on the principles of autograft transplantation [19, 20].

Regenerative medicine, using tissue engineering and cell therapy, offers innovative approaches to repairing irreparable bone damage. Engineered structures play a critical role in accelerating the healing process, especially when extensive tissue loss makes natural recovery impossible. This article explores the different scaffolds used in tissue engineering for bone regeneration.

## Results and Discussion

### *Tissue engineering scaffolds*

Cells in the body secrete proteins and other macromolecules that form a complex, porous network known as the extracellular matrix. This matrix provides support for cells, allowing them to grow and multiply. The combination of these cells and the matrix is referred to as tissue. Most cells in the body, with a few exceptions such as blood cells and certain embryonic tissues, grow on this extracellular matrix [21, 22]. Artificially created extracellular matrices, called scaffolds, serve as temporary structures that provide support for cells to connect, proliferate, and differentiate into the desired tissues or organs. Over time, these scaffolds degrade at a controlled rate, and new tissue gradually replaces them. Today, scaffolds are widely used in regenerative medicine, tissue engineering, gene therapy, and drug delivery [23, 24].

### *Bone tissue overview*

Bone is a dynamic, highly vascularized tissue that is vital for several functions in the body [25]. As a core component of the skeletal system, bones offer protection to critical organs like the brain, lungs, and heart. Additionally, bones provide structural strength and support for movement. They also help regulate various bodily functions, such as metabolism, glucose levels, and testosterone, and act as a reservoir for important minerals including calcium, magnesium, and phosphorus [26].

The structure of bone tissue is composed of both cells and an extracellular matrix. The extracellular matrix consists of two components: an organic phase and an inorganic phase. Bone tissue contains approximately 8% water, 22% protein, and 70% minerals. The mineral content consists primarily of calcium ions, calcium carbonate, and phosphate, forming a substance known as hydroxyapatite. Hydroxyapatite accounts for about 65% of the bone's weight and contributes to its strength and rigidity. The organic component of bone is mainly made up of type I collagen fibers, along with osteopontin and osteocalcin [27]. Type I collagen is crucial for providing flexibility and tensile strength to the bone matrix. These collagen fibers are made up of three helical chains that form fibrils [28].

The combined presence of collagen and hydroxyapatite determines the bone's mechanical strength. There are three primary cell types within bone tissue: osteoblasts, osteocytes, and osteoclasts. Osteoblasts, which are derived from mesenchymal stem cells, are responsible for synthesizing and secreting the bone matrix. They play a role in repairing minor cracks or damage within the bone [26]. Osteoblasts represent about 4-6% of bone cells. When active, they secrete the bone matrix, containing numerous vesicles, an advanced Golgi apparatus, and a rough endoplasmic reticulum, giving the cells a cubic appearance [29].

Osteoblasts also contain various growth factors, such as bone morphogenetic proteins, platelet-derived growth factor, fibroblast growth factor, and insulin-like growth factor. They also have receptors for hormones such as prolactin, progesterone, insulin, thyroid hormone, and growth hormones. Osteoblasts either remain in the bone matrix, where they continue to form bone or undergo apoptosis (programmed cell death), transforming into osteocytes once the matrix is calcified [30]. Osteocytes, which make up 90-95% of bone cells, have an extended lifespan, often exceeding 25 years [29]. Osteoclasts, large multinucleated cells originating from monocyte progenitors, are responsible for resorbing bone tissue and play a critical role in bone remodeling [31].

*Bone tissue engineering scaffold design*

The design of scaffolds for bone tissue engineering is essential, as it involves selecting materials that are biocompatible, biodegradable, and non-toxic for cells [32]. Since bone tissue is composed of both a mineral phase and a polymer phase [33], scaffolds must replicate these components to effectively facilitate bone regeneration. Bioceramics are commonly used to represent the mineral phase, while a variety of natural, synthetic, or hybrid polymers are used to create the polymer phase. Successful scaffold design requires a deep understanding of bone biology, including its development and repair processes, as the goal is to regenerate functional bone tissue [34].

*Materials for bone tissue engineering scaffolds*

Bone tissue engineering scaffolds can be made from a wide range of materials, which can be classified into three primary categories: natural polymers, synthetic polymers, and ceramics [35]. These materials can either be biodegradable or non-biodegradable, depending on the needs of the tissue engineering process.

*Natural polymers*

Natural polymers are derived from organic sources such as plants, animals, and insects. These materials offer several advantages, including biocompatibility, mechanical properties that closely resemble those of natural tissues, and minimal inflammatory responses. However, they also have the downside of lower mechanical strength. Natural polymers are beneficial for supporting cell attachment, proliferation, and differentiation, and are biologically active by nature [36]. These polymers can be categorized into three main types:

1. *Protein-based polymers:* Examples include silk, gelatin, and collagen.
2. *Polysaccharide-based polymers:* Sourced from plants, animals, or microbes, these materials are non-toxic, biocompatible, and cost-effective. Notable examples are alginate, chitosan, and hyaluronan.
3. *Polyhydroxyalkanoates:* These are biodegradable polymers produced by bacteria. They are notable for their high biodegradability, elasticity, and biocompatibility, and have gained attention due to their production from renewable resources [37].

Overall, natural polymers are excellent for promoting cell adhesion and growth [37].

*Synthetic polymers*

Synthetic polymers are manufactured under controlled conditions, allowing for precise manipulation of their mechanical properties and degradation rates. These materials generally have lower biological properties and flexibility compared to natural polymers. Examples of synthetic polymers include polyvinyl alcohol, polyhydroxybutyrate, polylactic acid, polyglycolic acid, and polycaprolactone [38].

*Bioceramics*

Bioceramics are widely used in orthopedic and dental applications for repairing damaged bones and tissues. Materials like cobalt-based alloys, titanium alloys, and 316L stainless steel are commonly used in implants. While metal implants help with tissue regeneration, they can also cause issues such as the formation of fibrous tissue, which reduces mechanical strength and can lead to immune reactions. Additionally, the release of toxic metal ions into the body can pose long-term health risks, including cancer [39]. As a result, there is growing interest in biodegradable alternatives to metal implants.

Bioceramics are ceramic materials applied to repair or replace defective tissues and organs. They are divided into two categories based on their origin: natural bioceramics (e.g., coral and hydroxyapatite) and synthetic bioceramics (e.g., bioactive glasses, calcium triphosphate, and synthetic hydroxyapatite) [40].

Bioceramics can also be classified based on their chemical interactions with body tissues, categorized into three groups:

1. *Inactive bioceramics:* These materials (e.g., alumina, zirconia) do not interact with the body and have high abrasion resistance.
2. *Non-absorbable bioceramics:* Materials like calcium phosphate and calcium triphosphate, which do not degrade in the body but are eventually replaced by natural tissue.
3. *Bioactive bioceramics:* These, including hydroxyapatite ceramics and bioactive glass, can stimulate cellular reactions that promote bone formation and regeneration.

Among synthetic bioceramics, bioactive glasses exhibit the best bioactivity. These glasses can bond with both soft and hard tissues, stimulating growth factors and promoting osteoblast activity, cell growth, and angiogenesis. Smaller bioactive glass particles tend to exhibit higher biological activity, which is beneficial when used as carriers for gene or drug delivery. The

nanometer scale plays a significant role in this increased activity [41, 42].

To enhance their mechanical or biological properties, various oxides, such as zinc, magnesium, zirconia, titanium, silver, and boron, can be added to bioactive glasses. For instance, adding zinc enhances their mechanical properties and supports bone formation both in vitro and in vivo. Furthermore, bioactive glasses containing silver can serve as antimicrobial coatings, offering a controlled release of antimicrobial agents to combat bacterial growth [43]. Bioactive glasses create a strong chemical bond with bone tissue, making them valuable as bioactive materials in bone regeneration applications [44].

*methods of making tissue engineering scaffolds*

The choice of scaffold construction method is crucial, as it directly impacts the tissue structure and the scaffold's ability to support cell attachment, differentiation, and proliferation. Several fabrication methods are employed in tissue engineering, each suited to different scaffold properties. Some of the most common methods include phase separation, gas foaming, freeze-drying emulsion, solvent casting particulate leaching, and electrospinning [45].

*Phase separation*

In this method, a polymer is dissolved in a solvent with a low melting point and then mixed with a water solution to form two distinct phases—one rich in polymer and the other with less polymer. As the temperature drops below the solvent's melting point, two solid phases form. By drying the mixture in a vacuum, the solvent sublimates, leaving behind a porous scaffold structure [46].

*Gas foaming method*

In the gas foaming method, carbon dioxide gas is applied at high pressure to a polymer for several days on mesh plates. Once the pressure is released to atmospheric levels, the gas escapes, leaving behind pores in the scaffold. The porosity depends on the amount of gas dissolved in the polymer, which can be controlled by adjusting temperature and pressure. This method is particularly advantageous because it doesn't require organic solvents, making it an environmentally clean process [47, 48]. Additionally, adding salt particles like ammonium bicarbonate enhances the method's efficiency by creating more pores as the salt releases gas during its interaction with water [48, 49].

*Freeze drying emulsion*

In the freeze-drying emulsion method, a polymer is dissolved in a solvent and then mixed with water to create an emulsion. The mixture is stirred to prevent phase separation before being poured into a mold. The mold is then placed in liquid nitrogen to freeze the mixture. Subsequently, a freeze-dryer removes the solvent and water, creating porosity in the structure. The porosity is controlled by adjusting factors like the percentage of solvent, polymer concentration, water content, and freezing temperature. This technique is primarily used for creating scaffolds for hard tissue [50].

*Solvent casting particulate leaching*

For this method, salt crystals (e.g., sodium chloride) are placed in a mold. A polymer and solvent mixture is then added to the mold, and the polymer is allowed to harden. The salt is later removed using a second solvent, usually distilled water. The removal of the salt creates a porous scaffold structure that matches the shape of the mold. The size of the pores can be controlled by adjusting the size and amount of salt crystals used [51].

*Electrospinning*

Electrospinning is a simple and cost-effective technique used to produce fibers with diameters ranging from microns to nanometers. The process uses a high-voltage electric field to draw fibers from a polymer solution. The electric field overcomes the surface tension of the polymer droplet, causing it to elongate and form fibers as it travels toward the collecting plate. Electrospinning is beneficial for creating scaffolds that mimic the extracellular matrix, as the high surface area-to-volume ratio of nanofibers promotes cell adhesion and proliferation. This method also allows the incorporation of various compounds, including bioglass, into the polymer solution to produce composite scaffolds [52-54].

## Conclusion

Bone tissue has the remarkable ability to repair minor damage on its own, but when the damage is extensive, it may not be able to heal completely. In such cases, bone tissue engineering offers a promising solution. This field combines growth factors and cell scaffolding to promote bone regeneration, with scaffold design being the most crucial component for success. Understanding the target tissue is essential when designing scaffolds, as bone is a hard and inflexible tissue. Therefore, scaffolds should be made from similarly rigid biological materials.

One such material is bioactive glass, which, when placed in a body-simulated environment, forms a hydroxyapatite crystal layer. This layer closely resembles the mineral phase of bone, making bioactive glass an ideal choice for the hard phase of bone scaffolds. The manufacturing method for the scaffold is another critical factor and depends on the specific tissue structure required.

Among the various scaffold fabrication methods, electrospinning is a widely used technique due to its ability to produce fibers ranging from several microns to nanometers. The high surface area-to-volume ratio of these electrospun fibers promotes better cell adhesion and proliferation. When combined with bioactive glass, electrospun scaffolds can create an effective foundation for treating bone-related diseases and injuries.

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**References**

1. Alshaer N, Bakhaider R, Elias AY, Yamany I, Alshouibi E, Elias W. Dental misconceptions in social media accounts: Youtube and Instagram applications among fluoride toxicity, bleaching and, waterjet. Ann Dent Spec. 2022;10(2):19-24.
2. Singh GP, Attavar SH, Kavuri S. Amnion membrane matrix and bio dentine in the management of an external apical root resorption. Ann Dent Spec. 2022;10(2):11-4.
3. Makurina ON, Mal GS, Dorontsev AV, Komarov MN, Romanova AV, Eremin MV, et al. Possibilities of handball practice in strengthening heart function in university students. J Biochem Technol. 2022;13(1):29-33.
4. Raggatt LJ, Wullschleger ME, Alexander KA, Wu AC, Millard SM, Kaur S, et al. Fracture healing via periosteal callus formation requires macrophages for both initiation and progression of early endochondral ossification. Am J Pathol. 2014;184(12):3192-204.
5. Urusov E, Li A, Davtyan A, Mikhaylova M, Diachkova E, Makarov A. Optimization of prosthetic treatment of patients with dental tissue using metal-free restorations. Ann Dent Spec. 2021;9(4):48.
6. Csaki C, Schneider PR, Shakibaei M. Mesenchymal stem cells as a potential pool for cartilage tissue engineering. Ann Anat. 2008;190(5):395-412.
7. Oleksandrivna CM, Vitaliivna SO, Petrivna SL, Borisivna YO, Prystupiuk M, Prystupiuk L, et al. Markers of undifferentiated connective tissue dysplasia in female patients with acute q-myocardial infarction. Arch Pharm Pract. 2021;12(2):80-5.
8. Liu Y, Chan JK, Teoh SH. Review of vascularised bone tissue-engineering strategies with a focus on co-culture systems. J Tissue Eng Regen Med. 2015;9(2):85-105.
9. Muth Lakshmi K, Lakshmi K, Kannan A, Aniyan Y. Evaluation of novel microRNA profile-21 and 191 in oral leukoplakia and oral squamous cell carcinoma in comparison with healthy tissues–A cross-sectional study. Clin Cancer Investig J. 2021;10(6):275-82.
10. Basher NS, Alsubeie MS, Rudayni HA. Investigation the lethal effect of *Colotropis procera* ait leaves extracts against aedes aegypti (l) larvae. Entomol Appl Sci Lett. 2022;9(4):19-27.
11. Verrier S, Alini M, Alsberg E, Buchman SR, Kelly D, Laschke MW, et al. Tissue engineering and regenerative approaches to improving the healing of large bone defects. Eur Cell Mater. 2016;32:87-110.
12. Alobaidi A, Abuhaimed B, Alhomrani M, Alshahrani S. Knowledge and practice on post-endodontic restorations among dental practitioners; a survey-based study in Riyadh, Saudi Arabia. Ann Dent Spec. 2021;9(3):20-4.
13. Chiara G, Letizia F, Lorenzo F, Edoardo S, Diego S, Stefano S, et al. Nanostructured biomaterials for tissue engineered bone tissue reconstruction. Int J Mol Sci. 2012;13(1):737-57.
14. Solyeyko O, Tsarenko S, Chernykh M, Berezovskiy A, Soleyko L, Fedorchenko O, et al. Integrative art-therapeutic correction of psychosomatic disorders in children with undifferentiated connective tissue dysplasia. Arch Pharm Pract. 2023;14(1):63.
15. Wattanutchariya W, Changkowchai W. Characterization of porous scaffold from chitosan-gelatin/hydroxyapatite for bone grafting. In Proceedings of the International Multiconference of Engineers and Computer Scientists 2014 Jan 1 (Vol. 2, pp. 12-14).

16. Grayson WL, Bunnell BA, Martin E, Frazier T, Hung BP, Gimble JM. Stromal cells and stem cells in clinical bone regeneration. Nat Rev Endocrinol. 2015;11(3):140-50.
17. Ingale Y, Bavikar R, Kulkarni S, Kale N. Histological spectrum of benign soft-tissue neoplasm in a tertiary care center. Clin Cancer Investig J. 2021;10(3):108-11.
18. Yunus Basha R, Sampath Kumar TS, Doble M. Design of biocomposite materials for bone tissue regeneration. Mater Sci Eng C Mater Biol Appl. 2015;57:452-63.
19. Liu X, Ma PX. Polymeric scaffolds for bone tissue engineering. Ann Biomed Eng. 2004;32(3):477-86.
20. Belachew ZG, Jenber AJ. Status, Importance, and Management of the White Mango Scale (Aulacaspis Tubercularis Newstead) In Ethiopia: a Review. Entomol Appl Sci Lett. 2022;9(3):50-9.
21. Boal DH. Mechanics of the Cell. Cambridge University Press; 2012.
22. Rajamanickam P, Babu H, Jain RK, Balasubramaniam A. Evaluation of Dentoalveolar and soft tissue changes in adult class ii malocclusions treated with different modalities. Ann Dent Spec. 2022;10(4):22-8.
23. Fischer KM, Morgan KY, Hearon K, Sklaviadis D, Tochka ZL, Fenton OS, et al. Poly(Limonene Thioether) Scaffold for Tissue Engineering. Adv Healthc Mater. 2016;5(7):813-21.
24. Chernykh M, Solyeyko O, Soleyko L, Mironov Y, Terekhovska O, Berezovskiy A, et al. Q-myocardial infarction on the background of undifferentiated connective tissue dysplasia: pathogenetic “paradoxes” and “crossovers”. Arch Pharm Pract. 2022;13(4):40-4.
25. Safadi FF, Barbe MF, Abdelmagid SM, Rico MC, Aswad RA, Litvin J, et al. Bone structure, development and bone biology. Bone Pathol. 2009:1-50.
26. Kini U, Nandeesh BN. Physiology of bone formation, remodeling, and metabolism. Inradionuclide and Hybrid Bone Imaging. Berlin, Heidelberg: Springer; 2012. p. 29-57.
27. Kheirallah M, Almeshaly H. Bone graft substitutes for bone defect regeneration. A collective review. Int J Dentistry Oral Sci. 2016;3(5):247-57.
28. Kenkre J, Basset TJ. The bone remodelling cycle. Ann Clin Biochem. 2018;55(3):308-27.
29. Florencio-Silva R, Sasso GR, Sasso-Cerri E, Simões MJ, Cerri PS. Biology of bone tissue: structure, function, and factors that influence bone cells. Biomed Res Int. 2015;2015:421746.
30. Porter JR, Ruckh TT, Popat KC. Bone tissue engineering: a review in bone biomimetics and drug delivery strategies. Biotechnol Prog. 2009;25(6):1539-60.
31. Boyle WJ, Simonet WS, Lacey DL. Osteoclast differentiation and activation. Nature. 2003;423(6937):337-42.
32. Shalumon KT, Lai GJ, Chen CH, Chen JP. Modulation of bone-specific tissue regeneration by incorporating bone morphogenetic protein and controlling the shell thickness of Silk Fibroin/Chitosan/Nanohydroxyapatite Core-Shell Nanofibrous membranes. ACS Appl Mater Interfaces. 2015;7(38):21170-81.
33. Miao X, Tan D, Li J, Xiao Y, Crawford R. Mechanical and biological properties of Hydroxyapatite/Tricalcium phosphate scaffolds coated with poly (Lactic-Co-Glycolic Acid). Acta Biomater. 2008;4(3):638-45.
34. Amini AR, Laurencin CT, Nukavarapu SP. Bone tissue engineering: recent advances and challenges. Crit Rev Biomed Eng. 2012;40(5):363-408.
35. Bose S, Roy M, Bandyopadhyay A. Recent advances in bone tissue engineering scaffolds. Trend Biotechnol. 2012;30(10):546-54.
36. Chen FM, Liu X. Advancing biomaterials of human origin for tissue engineering. Prog Polym Sci. 2016;5(3):86-168.
37. Sharma S, Srivastava D, Grover S, Sharma V. Biomaterials in tooth tissue engineering: a review. J Clin Diagn Res. 2014;8(1):309-15.
38. Mi HY, Jing X, Turng LS. Fabrication of porous synthetic polymer scaffolds for tissue engineering. J Cell Plast. 2015;51(2):165-96.
39. Brown R, Fowler B, Fustinoni S, Nordberg M. Toxicity of metals released from implanted medical devices. Handbook on the Toxicology of Metals. 2015;1:113-22.
40. Meyer U, Wiesmann HP. Bone and Cartilage Engineering. Springer Science & Business Media; 2006.
41. Schrooten J, Helsen JA. Adhesion of bioactive glass coating to Ti6A14V oral implant. Biomaterials. 2000;21(14):1461-9.

42. Boccaccini AR, Erol M, Stark WJ, Mohn D, Hong Z, Mano JF. Polymer/bioactive glass nanocomposites for biomedical applications: a review. Compos Sci Technol. 2010;70(13):1764-76.
43. Baino F, Hamzehlou S, Kargozar S. Bioactive glasses: Where are we and where are we going? J Funct Biomater. 2018;9(1):25.
44. Hench LL. The story of Bioglass. J Mater Sci Mater Med. 2006;17(11):967-78.
45. Eltom A, Zhong G, Muhammad A. Scaffold techniques and designs in tissue engineering functions and purposes: a review. Adv Mater Sci Eng. 2019;2019:1-13.
46. Abedalwafa M, Wang F, Wang L, Li C. Biodegradable poly-epsilon-caprolactone (PCL) for tissue engineering applications: a review. Rev Adv Mater Sci. 2013;34(2):123-40.
47. Mooney DJ, Baldwin DF, Suh NP, Vacanti JP, Langer R. Novel approach to fabricate porous sponges of poly(D,L-lactic-co-glycolic acid) without the use of organic solvents. Biomaterials. 1996;17(14):1417-22.
48. Janik H, Marzec M. A review: fabrication of porous polyurethane scaffolds. Mater Sci Eng C Mater Biol Appl. 2015;48:586-91.
49. Costantini M, Barbetta A. Gas foaming technologies for 3D scaffold engineering. InFunctional 3D tissue engineering scaffolds 2018 Jan 1 (pp. 127-149). Woodhead Publishing.
50. Stamatialis DF, Papenburg BJ, Gironés M, Saiful S, Bettahalli SN, Schmitmeier S, et al. Medical applications of membranes: drug delivery, artificial organs and tissue engineering. J Membr Sci. 2008;308(1-2):1-34.
51. Loh QL, Choong C. Three-dimensional scaffolds for tissue engineering applications: role of porosity and pore size. Tissue Eng Part B Rev. 2013;19(6):485-502.
52. Xin BJ, Chen W. Morphology, structure and properties of electrospun multi-walled carbon nanotube/polysulfonamide composite nanofibers. J Eng Fibers Fabr. 2015;10(1):155892501501000105.
53. Meng ZX, Zheng W, Li L, Zheng YF. Fabrication, characterization and in vitro drug release behavior of electrospun PLGA/chitosan nanofibrous scaffold. Mater Chem Phys. 2011;125(3):606-11.
54. Bulzan M, Cavalu S, Voita-Mekeres F, Bulzan M. Relevant predictors in the association between patients' functional status and scar outcomes after total hip arthroplasty. Cureus. 2023;15(12).