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COMMON SCAFFOLDS IN TISSUE ENGINEERING FOR BONE TISSUE REGENERATION: A REVIEW ARTICLE

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ABSTRACT

Regenerative medicine offers a new solution by cell therapy and tissue engineering methods to improve irreparable bone damage. Engineered structures help to accelerate the natural recovery of the tissue because in some bone injuries, the lost tissue is extensive and it is not possible to recover naturally. This article provides an overview of common scaffolds in tissue engineering for bone tissue regeneration. Because bone is a hard and inflexible tissue, therefore, biological materials that are hard like bone should be used for scaffold design. From this category of materials, we can mention bioactive glasses, which when these glasses are placed in the simulated environment of the body, form a crystal layer of hydroxyapatite in contact with the body's physiological fluid. Choosing the right manufacturing method depends on the desired tissue structure. Considering the vital role of scaffolds in tissue engineering, several methods have been used to design and build good scaffolds for tissue engineering. Electrospinning is a common method for making scaffolding. In this technique, by changing the conditions, fibers from several microns to several nanometers can be created. Because the area ratio to the regional volume of the fibers obtained from electrospinning is high, this characteristic increases the connection and proliferation of cells on the scaffold. Therefore, the electrospun scaffold, which is a combination of bioactive glass and polymer, can provide the basis for the treatment of bone diseases.

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Introduction

Because of the various and numerous functions of bone tissue, any change that occurs in its structure after an injury, disease, or lesion affects the body's balance and the person's life [1, 2]. Bone has an innate ability to repair itself after injury [3]. In small and fractured bone injuries, the healing process is done by the body. Thus, following bone injury, the stromal and stem cells in the bone tissue, along with the macrophages and other cells, including osteoclasts and osteoblasts, work in concert to initiate a reparative functions cascade to improve bone damage [4, 5]. However these abilities have limitations so in major fractures and defects including misplaced bone fusion, accidents, periodontal disorders, congenital cleft palate, and bone loss because of trauma, the healing process using the body does not require an effective treatment by a doctor [6, 7].

Today, bone grafting is the most popular surgical procedure to reconstruct and strengthen bones in orthopedics [8-10]. Common transplants include Xenograft, Allograft, and Autograft. Gene graft is a transplant taken from another species such as animal species. The risks of this transplant are immune reactions and infections that may cause rejection of the transplant. An allograft is a transplant that is usually taken from humans with various genotypes after their death. Thus, to avoid immune reactions and transmission of infection, and to use this transplant, the desired tissue should be completely sterilized, and many tissue components should be destroyed during sterilization. One of the limitations of this transplant type is the lack of donors and subsequent infections [11, 12]. Also, this transplant has the transmission of diseases such as AIDS, hepatitis, and cancer from the donor to the transplant recipient. Autograft is a transplant in which a part of a person's body tissue is transferred to another part of the same person's body [13, 14]. Although this graft does not stimulate the inflammatory reactions of the host, the large area of surgery may cause long-term pain and discomfort for the patient [15].

Therefore, although bone grafting has been a standard procedure until today and is the second most common graft after blood transplantation, this treatment procedure faces many obstacles. Among these problems, the following can be mentioned:

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limitations in finding suitable transplant tissue, inappropriate bone quality for transplant in some bone diseases such as osteoporosis [16, 17], the possibility of transmission and infection of diseases, the re-surgery need, and lack of fusion with host tissue [18]. Compared to allograft, Autograft, and traditional methods, tissue engineering that is based on cell or autogenous tissue transplant eliminates the mentioned transplant problems. The main tissue engineering idea is taken from Autograft engineering [19, 20].
Regenerative medicine with the help of tissue engineering methods and cell therapy creates a new method for healing irreparable bone damage. Engineered structures help to accelerate the natural recovery of the tissue because in some bone injuries, the lost tissue is extensive and it is not possible to recover naturally. This article provides an overview of common scaffolds in tissue engineering for bone tissue regeneration.

Tissue Engineering Scaffolds

Cells in various tissues of the body, according to the type of tissue, secrete certain types of macromolecules such as proteins. These substances form a complex and porous network around the cell, which is called the extracellular matrix, and cells grow and multiply on it. The sum of cells and extracellular matrix is called tissue. All the cells of the body, except the cells of the blood supply system and some special embryonic tissues, grow on the extracellular matrix [21, 22]. The artificially constructed extracellular matrix is called a scaffold. Scaffolding is a temporary structure for cell support, connection, proliferation, and differentiation of cells to expected tissues and organs. Finally, this structure is decomposed over time with different and adjustable percentages, new tissue grows and replaces it. Today, these scaffolds are applied in different fields including cell therapy, gene therapy, and drug delivery. Their main application is in regenerative medicine and tissue engineering [23, 24].

Bone Tissue

Bone is a dynamic and very vascular tissue [25]. Bones are components of the skeletal system that are responsible for protecting important organs such as the brain, lungs, and heart. They are also responsible for creating mechanical strength and facilitating the movement of living things. Bones play a role in regulating the body's homeostasis by regulating the body's endocrine glands, such as metabolism, glucose, and testosterone, and are a source of minerals such as calcium, magnesium, and phosphorus [26].
Bone tissue is composed of bone cells and extracellular matrix. The extracellular matrix includes two parts, organic and inorganic. About 8% of bone is made of water, 22% of protein, and 70% of minerals. The mineral part includes calcium ions, calcium carbonate, and phosphate. This part of the bone is known as hydroxyapatite and its structure is in the form of hexagonal and needle-shaped crystals with a length of 60 nm and a width of 5-20 nm. This substance makes up about 65% of the weight of the bone and the hardness and strength of the bone depend on its existence. The organic part of bone includes type I collagen fibers, osteopentin, and osteocalcin [27]. Type I collagen fibers provide elasticity, flexibility, and tensile strength to the bone matrix. Collagen fibrils are in turn a collection of collagen fibrils consisting of three alpha-helical chains and their combination is formed with each other [28].
The strength of bone tissue depends on the presence of collagen and hydroxyapatite together. Bone tissue cells include osteoblast, osteocyte, and osteoclast. Osteoblasts are cells that are differentiated from mesenchymal stem cells and their primary function is the production and secretion of bone extracellular matrix. These cells play a role in the transformation of bone tissue in the form of eliminating small cracks and small tissue damage [26]. These cells make up about 4-6% of all bone cells. Osteoblasts in their active state build bone. In this case, their cytoplasm has numerous secretory vesicles, developed Golgi apparatus, and rough endoplasmic reticulum. In this case, they are defined as open and closed with a cubic appearance [29].
Osteoblasts contain a wide range of growth factors including bone morphogenetic proteins, beta growth factor, platelet-derived growth factor, fibroblast growth factor, and insulin growth factor. In addition, prolactin, progesterone, insulin, thyroid, parathyroid, and receptors for growth hormones are located in osteoblasts. Osteoblasts have two fates, either they are actively located in their bone matrix and in this case, they form bone, or they undergo apoptosis (programmed cell death) and become inactive, the secreted matrix is calcified, and they are called osteocyte state [30]. Osteocytes make up 90-95% of bone cells and their lifespan is over 25 years [29]. Osteoclasts are giant multinucleated cells that are irregularly formed from monocyte progenitor cells. The diameter of osteoclasts reaches up to 200 micrometers. These cells contain lysosomal enzymes, a Golgi network, and mitochondria [30]. These cells are responsible for reabsorption (swallowing) and bone formation, and their location is on the bone surface, in damaged bones [31].

Design of Bone Tissue Engineering Scaffolds

The design of tissue engineering scaffold is of particular importance, which includes the selection of suitable biocompatible, biodegradable, and non-toxic materials for cells [32]. Considering that two-phase composite bone includes a mineral phase and polymer phase [33], it is essential to provide the necessary conditions for the creation of both phases for the design of bone tissue engineering scaffolds. Usually in the mineral phase of bioceramics and the polymer phase, natural synthetic or mixed polymers including natural-synthetic polymer and natural-natural polymer are applied. To design bone tissue engineering scaffolds, knowledge of bone biology, development, construction, and repair is necessary. Because the main aim is to create new bone tissue for bone repair and reconstruction [34].

Compositions of Bone Tissue Engineering Scaffolds

Biopolymers used in the construction of scaffolds can be natural or synthetic, as well as biodegradable or non-biodegradable. These materials can be divided into three categories: natural, synthetic, and ceramics [35].

Natural Polymers

Natural polymers are obtained from materials found in nature such as plants, insects, or animals. Their advantages include biocompatibility, mechanical properties similar to natural tissue, and low inflammatory reactions, and the disadvantages of this category of polymers include low mechanical strength. Also, these polymers support cell attachment, proliferation, and differentiation [36]. They are inherently biologically active.

These polymers are classified into three groups, which are: 1) Polymers whose origin is protein, for example, silk, gelatin, and collagen; 2) Polysaccharide-based polymers, which are obtained from different sources including microbial, animal, and plant. These polymers are non-toxic, react with living cells, have good biocompatibility, and are usually less expensive than other restorative materials. Alginate, Chitosan, and hyaluronan can be mentioned in this category; 3) The third category includes polyhydroxyalkanoates that are synthesized by bacteria. This category of polymers has attracted a lot of attention due to their production from different renewable sources. These polymers have high biodegradability, elasticity, and biocompatibility [37]. In general, natural polymers create good cell adhesion [37].

Synthetic Polymers

These polymers are made under controlled conditions, so their mechanical and degradability properties can be controlled. This class of materials has low flexibility and biological properties. Among these polymers, polyvinyl alcohol, polyhydroxybutyrate, polylactic acid, polyglycolic acid, and polycaprolactone can be mentioned [38].

Bioceramics

Alloys and Metals are widely applied in orthopedics and dentistry to repair broken bones as implant materials. Cobalt-based alloys, Titanium alloys, and 316L stainless steel are among the most attractive alloys used in the manufacture of implants. Metal implants are similar to a double-edged blade. On the one hand, they assist in tissue regeneration after being placed in the environment of body, they are surrounded using fibrous tissue, which leads to undesirable properties including reducing the mechanical properties of the implant and causing reactions. Immunity is established at the junction of tissue and implant. In addition, the metal implants used to repair bone damage cause the harmful release, of toxic ions and their accumulation in different body parts, which increases the possible risk of cancer [39]. For this reason, researchers have directed their efforts to receive biodegradable and new materials to prevent the occurrence of the mentioned problems.

Bioceramics are a group of ceramic materials that are applied to strengthen and repair parts of defective or disabled tissues and organs of the human body. Based on their origin, bioceramics are divided into two groups: natural (such as coral and hydroxyapatite) and synthetic (such as bioactive glasses, calcium triphosphate, and synthetic hydroxyapatite) [40]. The other classification of bioceramics is based on their chemical bond with body tissues, which are divided into three categories: inactive, non-absorbable, and bioactive. Inert bioceramics (such as alumina, zirconia, and calcium nitride) have good abrasion resistance due to their inactivity in the body environment. Non-absorbable bioceramics (such as calcium phosphate, aluminum phosphate, calcium, and calcium triphosphate) decompose after being placed in the body environment and are replaced by natural tissue. Among bioactive bioceramics, we can mention hydroxyapatite ceramics and bioactive glass. This group of biomaterials induces intracellular and extracellular reactions by emitting ions released from the surface, which lead to the acceleration of bone formation.

Among synthetic bioceramics, the best bioactivity behavior is related to bioactive glasses [41]. These glasses can connect to soft and hard tissue. The products resulting from their degradation stimulate growth factors, osteoblast gene expression, cell growth, and proliferation and lead to angiogenesis. The smaller the size of the bioglass, the higher its biological activity. In other words, the proliferation of bone cells increases in the vicinity of small glass particles. Especially when these glasses are used as a carrier, a means to transfer genes or drugs into cells. Nanometer dimensions are very important [42].

Bioactive glasses have limited mechanical properties and to improve mechanical or biological properties, various oxides such as zinc, magnesium, zirconia, titanium, silver, and boron are added to these glasses. For example, by adding zinc to these glasses, they expand their mechanical properties and promote bone formation in the laboratory environment and in the body environment, or glasses that contain silver can be used as coatings for hundreds of bacteria. The controlled release rate was used against Gram-negative and positive bacteria [43]. By creating a strong chemical bond, bioglass creates a suitable biological response at the junction of bone and tissue, and for this reason, it is considered a bioactive material [44].

Methods of Making Tissue Engineering Scaffolds

Choosing the right scaffold construction method depends on the desired tissue structure. Choosing the method of scaffold construction is vital because by providing the appropriate construction method, an appropriate contact surface is provided for cell attachment, differentiation, and proliferation [33]. Considering the vital role of scaffolds in tissue engineering, multiple methods have been used to design and build appropriate scaffolds. Phase separation, foam gas, dry ice emulsion, electrospinning, and solvent casting are the most attractive methods of fabricating tissue engineering scaffolds [45].

Phase Separation

In this method, the desired polymer is dissolved in an appropriate solvent with a low melting point, and then it is added to the water solution to make two phases. One of the phases is rich in polymer and the other has a smaller amount of polymer. In the next step, the mixture temperature is brought under the solvent melting temperature, and two solid phases are created, by drying them in a vacuum, the solvent is sublimated and a porous scaffold is built [46].

Gas Foaming Method

In this method, to make a scaffold, the polymer is exposed to carbon dioxide gas at high pressure for several days on mesh plates. Then, the gas pressure is reduced and brought to atmospheric pressure, which creates holes in the scaffold when the gas leaves the polymer. The structure porosity depends on the gas solubility amount in the polymer, which is controlled by changing the gas temperature and pressure. Due to the non-use of any organic solvent in scaffold construction, this construction method is clean [47, 48]. To make this method more efficient, salt particles are used. Ammonium bicarbonate salt is added to the polymer paste or gel, then the polymer is immersed in water, and the salt turns into ammonia and carbon dioxide gas. Ammonia is washed with water carbon dioxide is removed and a porous scaffold is created [48, 49].

Freeze Drying Emulsion

In this method, the desired polymer is dissolved in a suitable solvent, then it is added to the water solution and an emulsion solution is created. Here, the mixture should be stirred regularly so that the two phases do not separate. Then the mixture is poured into the mold and the mold is placed in liquid nitrogen to freeze. Then, the solvent and water are removed from the environment with the freeze dryer method, which creates porosity with the removal of these materials [50]. The porosity of the structure is controlled by changing parameters such as solvent percentage, polymer solution concentration, water percentage, and freezing temperature. This technique is used to make hard tissue scaffolds [26].

Solvent Casting Particulate Leaching

In this method, progen or salt crystals (sodium chloride) are poured into the mold, then the mixture of polymer and solvent is added to the mold and the polymer is allowed to harden. The next step is to use another solvent to remove the salt crystals, which is usually the second solvent of distilled water, and by removing the protrusion particles, a polymer scaffold with a porous structure, suitable for the shape of the container is created. The size of the pores depends on the size of the progeny particles. The porosity and pore size of the scaffold is controlled by changing the amount and size of salt particles [51].

Electrospinning

Electrospinning is an easy and economical method to produce fibers. The diameter of the fibers produced in this technique varies from a few microns to a few nanometers. The fibers obtained from this process are used for drug release, tissue engineering scaffolds, protective coatings, sensors, filtration, catalyst carriers, and fluorescent materials [52].

With the electrospinning technique, a structure similar to the extracellular matrix can be prepared. Because the ratio of the area to the area volume of nanofibers is high, this feature increases the connection and proliferation of cells on the nanofibers. A high-voltage electric field is used to make fibers. So that a potential difference is created between the polymer solution inside the syringe and the fiber collecting plate, the electric field overcomes the surface tension of the drop of the polymer solution, and the pregnancy current exits from the drop located at the tip of the needle. Due to the presence of repulsive forces between the available charges, the drop becomes unstable, becomes thin and elongated, and reaches the size of nanometers. Then these fibers are placed on the collector plate and the solvent evaporates from its surface. One of the benefits of this method is the possibility of adding various organic and inorganic compounds, including bioglass, to the polymer solution and producing a composite scaffold [53, 54].

Conclusion

Considering that bone is a tissue that can repair its small damages, sometimes the damage done to the bone is big and the bone is not able to repair it. In these cases, the best treatment method is bone tissue engineering. Bone tissue engineering is a combination of growth factors and cell scaffolding, and it can be safely said that the most important part of it is designing the scaffolding according to the desired strength. To design scaffolding, it is necessary to know enough about the target tissue. Because bone is a hard and inflexible tissue, therefore, biological materials that are hard like bone should be used for scaffold design. From this category of materials, we can mention bioactive glasses, which when these glasses are placed in the simulated environment of the body, form a crystal layer of hydroxyapatite in contact with the body's physiological fluid. This layer is very similar to the mineral phase of bone. Therefore, it is appropriate to choose this material as the hard phase of bone. Choosing the right manufacturing method depends on the desired tissue structure. Considering the vital role of scaffolds in tissue engineering, multiple methods have been used to design and build suitable scaffolds for tissue engineering. Electrospinning is a common method for making scaffolding. In this technique, by changing the conditions, fibers from several microns to several nanometers can be created. Because the area ratio to the regional volume of the fibers obtained from electrospinning is high, this characteristic increases the connection and proliferation of cells on the scaffold. Therefore, the electrospun scaffold, which is a combination of bioactive glass and polymer, can provide the basis for the treatment of bone diseases.

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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. pp. 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).