EC ORTHOPAEDICS
Editorial

Nanocellulose-Based Scaffolds in Bone Tissue Engineering

Esmat Alemzadeh[1,2] and Ahmad Oryan[3]*

[1]Infectious Diseases Research Center, Birjand University of Medical Sciences, Birjand, Iran

[2]Department of Medical Biotechnology, Faculty of medicine, Birjand University of Medical Sciences, Birjand, Iran

[3]Department of Pathology, School of Veterinary Medicine, Shiraz University, Shiraz, Iran

***Corresponding Author:** Ahmad Oryan, Professor of Comparative Pathology, School of Veterinary Medicine, Shiraz University, Shiraz, Iran.

Received: October 25, 2023; **Published:** November 06, 2023

Bone grafts are used in various medical situations to enhance the healing and regrowth of bones [1]. The current clinical treatments for bone repair and regeneration, such as autografts and allografts, have been found to have significant drawbacks, limitations, and complications. Autografts are currently considered the best option for bone grafts due to their compatibility with the patient's own tissue and lack of immune response, as well as their ability to provide all the necessary properties for bone regeneration [2,3]. Nevertheless, autografts necessitate the extraction of bone from the patient's iliac crest, which entails an additional surgical procedure. Moreover, these autologous bone transplants are associated with high costs [4,5].

Tissue engineering and regenerative medicine is a novel approach that utilizes various biomaterials and treatment methods to overcome the significant limitations of traditional grafts and promote a healing response that enhances the speed and quality of healing. These technologies are employed to generate new bone in the damaged area, ensuring it is fully functional and normal with minimal complications during the healing process. Utilizing the tissue engineering method for repairing bone defects is considered as a superior approach [6] with the aim to find alternative treatment strategies that can address the problems associated with current treatments, such as the need for additional surgery to extract bone from the patient's iliac crest and the high cost of using the patient's own tissue for bone transplants. Bone tissue engineering (BTE) aims to eliminate issues like donor site morbidity, limited availability, immune rejection, and pathogen transfer that are commonly encountered in current clinical treatments. As a result, modern bone engineering strategies based on osteogenic cells, osteoinductive factors, and osteoconductive scaffolds have emerged as potential methods to create biological tissue substitutes to reconstruct large bone defects [7,8].

Scaffolds must be highly porous to allow cell ingrowth and facilitate neovascularization of the construct. An ideal bone scaffold should provide a desirable environment for cell attachment, growth, and differentiation without inducing any toxic or immunological side effects [3]. Additionally, a bone-mimicking scaffold with an interconnected porous network, suitable mechanical properties, and appropriate biodegradability is required to construct a functional bone similar to the native structure. A pore size of 300 µm or larger has been recommended to allow acceptable mass transfer and vascularization for guiding cellular behavior in the direction of new bone formation. Additionally, scaffolds should tolerate compressive loads between 5 and 224 MPa [9].

In bone tissue engineering, several types of polymeric materials have been used to provide structural support and tissue regeneration. Proteins such as collagen and gelatin offer a number of advantages, such as high biocompatibility, low toxicity, and enhanced cell responses. However, they fail to provide sufficient mechanical strength and stability in physiological conditions. Polysaccharides such as chitosan, alginate, and starch have a number of advantages, including biodegradability and biocompatibility but are fragile and typically do not contain cell-binding moieties that promote cell attachment and infiltration. In contrast, synthetic polymers (e.g. PLA, PCL, PHB, and PVA) exhibit strong mechanical properties and tunable mechanical properties and stability *in vivo*. However, their bioactivity and cell attachment are insufficient for bone tissue engineering. Among these polymers, cellulose is a linear polysaccharide abundantly found in natural sources from several plants (cotton, bast plants, wood, and bamboo) to some organisms such as bacteria, fungi, algae. Notably, cellulose in the pristine or chemically modified form is one of the most common polymers used in bone tissue engineering due to its remarkable advantages such as high specific mechanical properties, non-immunogenicity, nontoxicity, source abundance, and low production cost [10,11].

Cellulose is a natural organic compound that is a key structural component of the primary cell wall of green plants, many forms of algae, and the oomycetes. It is also secreted by some bacteria to form biofilms. Cellulose is the most abundant organic polymer on Earth. In bone tissue engineering, cellulose is used to create hydrophilic and highly absorbent sponges that can be combined with other materials. Recently, a micro-/nanostructured scaffold made from cellulose and collagen was applied in tissue engineering. After culturing human osteoblasts on this scaffold, it was found that the scaffold supported optimal adhesion and phenotype maintenance of cultured cells. This was reflected by higher levels of osteogenic enzyme alkaline phosphatase and mineral deposition compared to the control polyester micro-/nanostructured scaffolds with identical pore properties [12,13].

Nanocellulose is a substance derived from cellulose, which is the major component of plants and a smaller quantity in animals and bacteria. It has nano dimensions structurally. Nanocellulose can be divided into three types based on its creation and technique of production: cellulose nanocrystals (CNCs), cellulose nanofibrils (CNFs), and bacterial cellulose (BC) [14]. Nanocellulose is highly compatible with tissues, durable, and results in lower levels of calcification. It is a promising choice for the replacement of cartilages. Bacterial cellulose/polyacrylamide gels are used as a crosslinker. These gels are able to furnish longitudinally and their tensile strength are similar to ligaments and tendons. Nanocellulose is also a promising scaffold for osteoblast and chondroblasts and it can be used for regeneration and repair of osteoblast cells. Bacterial cellulose and hydroxyapatite containing membrane is potential for bone regeneration. It facilitates development and growth of bone cells, it causes enhanced alkaline phosphatase enzyme activity, which is essential for osteoblast functioning and also enhance bone growth and is effective in bone healing [15-17].

Nanocellulosic materials offer significant benefits in terms of their ability to withstand localized forces. Additionally, numerous studies have focused on enhancing the biological properties of BC. For this purpose, BC-collagen (BC-COL) composites have been created for potential use in tissue engineering. Collagen serves as a physical material that aids in cell proliferation and also improves cell adhesion, differentiation, and function [18]. Because of the presence of hydrogen bonds, nanocellulose has the ability to self-assemble and can also be combined and assembled with other polymer materials. However, aerogels made solely from cellulose have been found to have drawbacks such as hydrophilicity and poor osteoconduction. To address these limitations and maintain the inherent advantages of nanocellulose, there has been increasing interest in the development of composite nanocellulose aerogels. These fabrication methods involve combining cellulose with various organic and inorganic compounds to adjust the mechanical properties, biodegradability, bioactivity, and biological properties of bone scaffolds [19]. The sustained release of bioactive molecules through nanocellulose-based aerogels shows promising potential to be used for bone regeneration [20]. Qin and colleagues conducted a study in which they created the cellulose aerogels loaded with resveratrol, using a freeze-drying method. They found that the resveratrol-loaded cellulose aerogels exhibited excellent stability in PBS and simulated gastric fluid, and they were able to release resveratrol steadily. These findings suggest that these aerogels have an appropriate potential in treatment of osteoarthritis [21].

Taken together, nanocellulose is a promising material for tissue engineering and bioremediation. It has several features that contribute to its beneficial effects in these fields to be applied in tissue regeneration. However, the energy consumption during its production process and the mild toxicity reported from its end products are becoming a hindrance for the further exploration and application of this amazing compound in humans and in the environment. The future perspective of nanocellulose research should focus mainly on minimizing or nullifying its toxic manifestations in the human population. In environmental remediation methods, the actual utility and all possible efficacy of nanocellulose in purifying the surroundings should be studied in detail and implemented on a large scale worldwide [14].

Bibliography

1. Amini Ami R., *et al*. "Bone tissue engineering: recent advances and challenges". *Critical Reviews in Biomedical Engineering* 40.5 (2012): 363-408.
2. Dimitriou R., *et al*. "Bone regeneration: current concepts and future directions". *BMC Medicine* 9.66 (2011).
3. Oryan A., *et al*. "Bone regenerative medicine: classic options, novel strategies, and future directions". *Journal of Orthopaedic Surgery and Research* 9.18 (2014).
4. Oryan A., *et al*. "Bone injury and fracture healing biology". *Biomedical and Environmental Sciences* 28.1 (2015): 57-71.
5. Oryan A., *et al*. "Platelet-rich plasma for bone healing and regeneration". *Expert Opinion on Biological Therapy* 16.2 (2016): 213-232.
6. Moshiri A., *et al*. "An overview on bone tissue engineering and regenerative medicine: current challenges, future directions and strategies". *Journal of Sports Medicine and Doping Studies* 5.2 (2015).
7. Bigham-Sadegh A., *et al*. "Bone tissue engineering with periosteal-free graft and pedicle omentum". *ANZ Journal of Surgery* 83.4 (2013): 255-261.
8. Oryan A., *et al*. "Current concerns regarding healing of bone defects". *Hard Tissue* 2.2 (2013): 13.
9. Janmohammadi M., *et al*. "Cellulose-based composite scaffolds for bone tissue engineering and localized drug delivery". *Bioactive Materials* 20 (2023): 137-163.
10. Moghadam ET., *et al*. "Current natural bioactive materials in bone and tooth regeneration in dentistry: a comprehensive overview". *Journal of Materials Research and Technology* 13 (2021): 2078-2114.
11. Reddy MSB., *et al*. "A comparative review of natural and synthetic biopolymer composite scaffolds". *Polymers* 13.7 (2021): 1105.
12. Aravamudhan A., *et al*. "Cellulose and collagen derived micro-nano structured scaffolds for bone tissue engineering". *Journal of Biomedical Nanotechnology* 9.4 (2013): 719-731.
13. Nishiyama Y., *et al*. "Crystal structure and hydrogen-bonding system in cellulose Ibeta from synchrotron X-ray and neutron fiber diffraction". *Journal of the American Chemical Society* 124.31 (2002): 9074-9082.
14. Jacob S., *et al*. "Nanocellulose in tissue engineering and bioremediation: mechanism of action". *Bioengineered* 13.5 (2022): 12823-12833.
15. Huang C., *et al*. "Bio-inspired nanocomposite by layer-by-layer coating of chitosan/hyaluronic acid multilayers on a hard nanocellulose-hydroxyapatite matrix". *Carbohydrate Polymers* 222 (2019): 115036.
16. Reshmy R., *et al*. "Nanocellulose as green material for remediation of hazardous heavy metal contaminants". *Journal of Hazardous Materials* 424.PtB (2022): 127516.

17. Luo H., *et al*. "Advances in tissue engineering of nanocellulose-based scaffolds: A review". *Carbohydrate Polymers* 224 (2019): 115144.

18. Saska S., *et al*. "Bacterial cellulose-collagen nanocomposite for bone tissue engineering". *Journal of Materials Chemistry* 22 (2012): 22102-22112.

19. Zhang Y., *et al*. "Application of nanocellulose-based aerogels in bone tissue engineering: current trends and outlooks". *Polymers* 15.10 (2023): 2323.

20. Seyedi Z., *et al*. "Icariin: a promising natural product in biomedicine and tissue engineering". *Journal of Functional Biomaterials* 14.1 (2023): 44.

21. Qin L., *et al*. "Preparation, characterization, and *in vitro* evaluation of resveratrol-loaded cellulose aerogel". *Materials* 13.7 (2020): 1624.

Volume 14 Issue 9 September 2023