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Nano bacterial cellulose for biomedical applications: A mini review focus on tissue engineering

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Abstract

Cellulose is one of the main constituents of natural biopolymer. Its properties like renewable, eco-friendly, sustainable biomaterial, and biocompatibility, biodegradable, cost-effectiveness, lightweight, and high mechanical strength, make it very useful in many fields. Nanocellulose is an ideal material to be used in the production of biopolymer composite, because of its properties such as low density, non-abrasiveness, combustibility, nontoxicity, and inexpensiveness. We can extract nanocellulose from both Bactria and plants. There are some reasons that bacterial cellulose is better than plant cellulose, which are given below. Bacterial nanocellulose has been used in various applications like medical products, food packaging, etc. This mini-review talks about the significant role of bacterial nanocellulose in the medical application including tissue engineering, drug delivery agents, wound healing, dental implant, bone tissue, and neural implants, cardiovascular implants, artificial cornea, etc. some studies have shown that some body`s cells such as endothelial, chondrocytes, and smooth muscle cells have good adhesion to BC.

Keywords: Bacterial nanocellulose, Biomedical applications, nanocomposites, wound healing, tissue engineering.

1 Introduction

Nanocellulose can be produced by various methods: electrospinning, enzymatic hydrolysis, and mechanical treatments [6]. But after produced NC, it needs to be checked that all the additional products like lignin and hemicelluloses have been removed [7, 8]. So it needs additional costs. Although in terms of chemical structure bacterial cellulose is the same as plant-based cellulose, some properties make bacterial cellulose more useful than them [8, 9]. One of them is that BC is pure, it has no pectin, lignin, and hemicellulose [8-12]. So, it doesn`t need purification reactions and because of that no extra energy is wasted, and also the cost is reduced [3, 4, 9, 13, 14]. And the process of separating the product's harmful compounds for the environment [3, 9, 11, 15, 16]. Second, some of its properties include biocompatibility, mechanical strength, porosity, hydrophilicity, and crystallinity, ultrafine network, high surface area per unit mass, transparency, and non-toxicity, makes it a better choice [3, 11, 17-19]. In addition, the BC production process is easy and also the remaining bacteria can be easily removed with simple technology. Besides all these properties BNC belongs to the class of generally recognized as safe (GRAS) products [20]. It is also very simple to convert it to any desired shape during and after synthesis, the morphology of BNC can differ based on cultivation mode and cultural parameters.

BC is the extracellular metabolic product of rod-shaped Gram-negative bacteria. Bacterial nanocellulose (BNC) is secreted by some types of bacterial strains such as Acetobacter, Agrobacterium, Alcaligenes, Azotobacter, Pseudomonas, Rhizobium, Rhodobacter, Achromobacter, or Sarcina. [4, 8, 19, 21-25] However, the most efficient producer is Acetobacter xylinum, which is reclassified within the genus Gluconacetobacter xylinus as G. xylinus. You can see the pathway for the biosynthesis of cellulose by G. xylinus in the figure 1. Acetobacter xylinum is a non-pathogenic mesophile identified by A.J Brown in 1886 [26] and is known as the source of bacterial cellulose. [9, 25, 27-31] G. xylinus bacteria are immobile on solid surfaces and this property suggests a simple approach for creating BC. [29, 32, 33]

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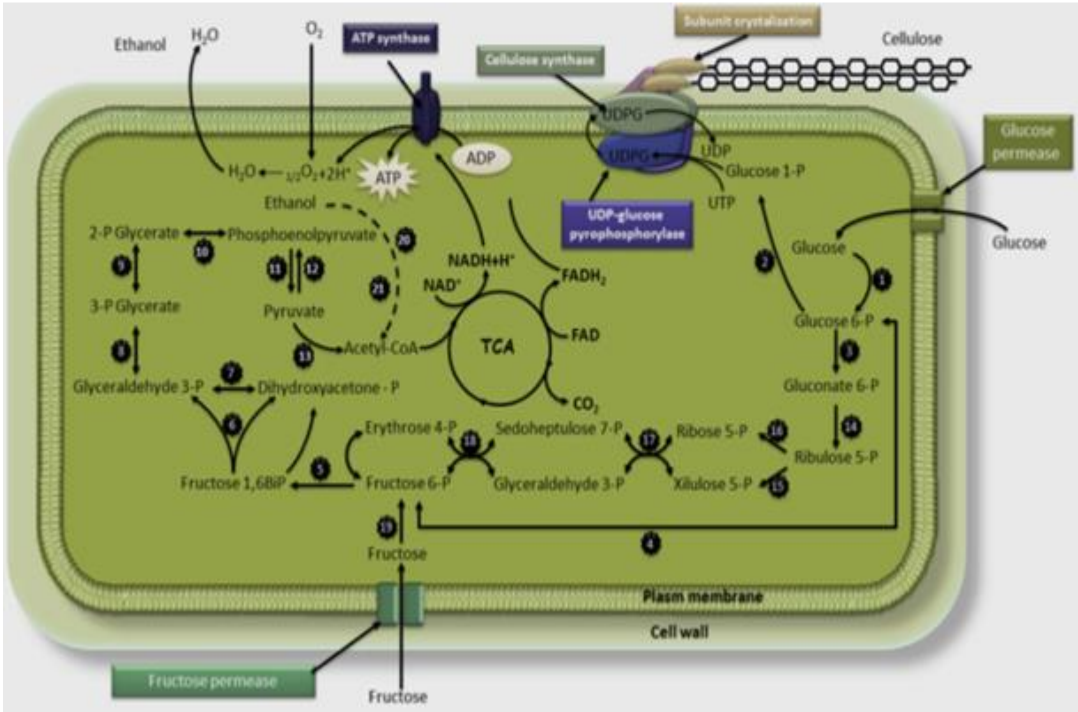

Figure 1. Hypothetical model of the pathway for the biosynthesis of cellulose by G. xylinus. (Adapted from[24]).

Bacterial cellulose production is divided into the static culture, agitation culture, and bioreactor [3, 25, 30, 34]. The overall yield of BC in static culture depends on the surface area of the gas-liquid interface because BC film is produced at the gas-liquid interface. In static culture, the methods are simple; Cultivated BC sheets are purified with hot water and sodium hydroxide [24, 25, 30, 32]; after that to achieve a neutral pH they are washed with water. Due to the high cost in static culture, you get little product [3, 25, 35]. To reduce this problem, we can use agitation culture. But there are still a few problems with this method too. Although, in agitation culture, productivity increases, but polymerization, mechanical properties, and crystallinity are reduced in contrast to static culture [3, 25]. Therefore, bioreactor culture was used to increase the yield of BC [25, 30]. But the result was not very satisfactory, even though static culture is expensive and time-consuming with low products, it is still the most common method for preparing BC [3].

Figure 2. Some properties of BNC.

BC has wide applications in many fields due to its unbelievable physicochemical and biological characteristics, in the arenas of a lot of application mainly in health care, food industry, sanitary products, electronics, etc. [3, 10, 18, 32, 34]. Out of its useful applications, the most amazing application exists in the biomedical field, which is discussed in the following.[36] It is worthy to mention here some points, first of all, modification of BC during the fermentation process is caused a lot of benefits and improves the BC in terms of its characteristics [3, 23, 37, 38]. Pure BNC (you can see a picture of it in figure 3) State is not a bioactive material, these properties in biomedical application make some limitations. On the other hand, BNC in the human body has a comparatively low degradation rate that makes some challenges. So these points make us incorporate some chemicals into BC culture [39].

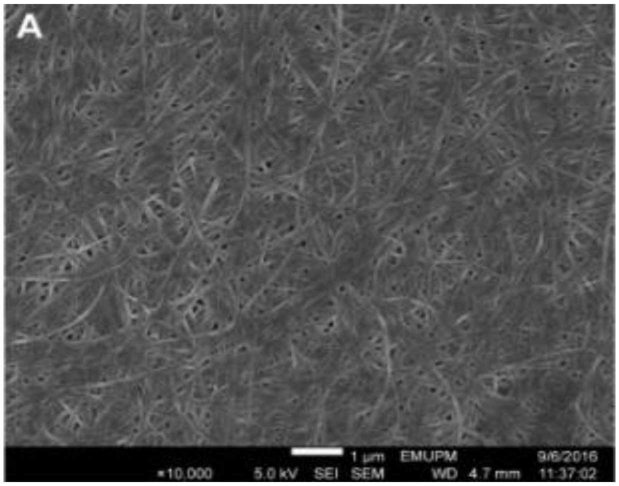

Figure 3. Image of pure BNC. (Adapted from [40])

2 BNC in medical application

At first in the 1990 [41] BNC was used for skin tissue repair, and then in 2001 was used for artificial blood vessel for microsurgery. Previous studies show that BC can be used in tissue engineering, including vascular, bone, cartilage, and adipose tissue engineering, neural tissue engineering, biosensing and controlled drug delivery and cell transfection, and engineering of blood vessels [18, 22, 30, 32, 42]. Other important applications are connective tissue repair, repair of congenital heart defects, skin therapy, wound dressings, repair, and wound healing, due to their ability to enhance the healing process of chronic injuries and burn injuries, and other deep wounds [34, 39, 43]. Here in this mini-review, we have collected some of the most recent studies in various areas of biomedical application (figures 4, 5), which on the following part of this mini-review is focused more deeply on each part.

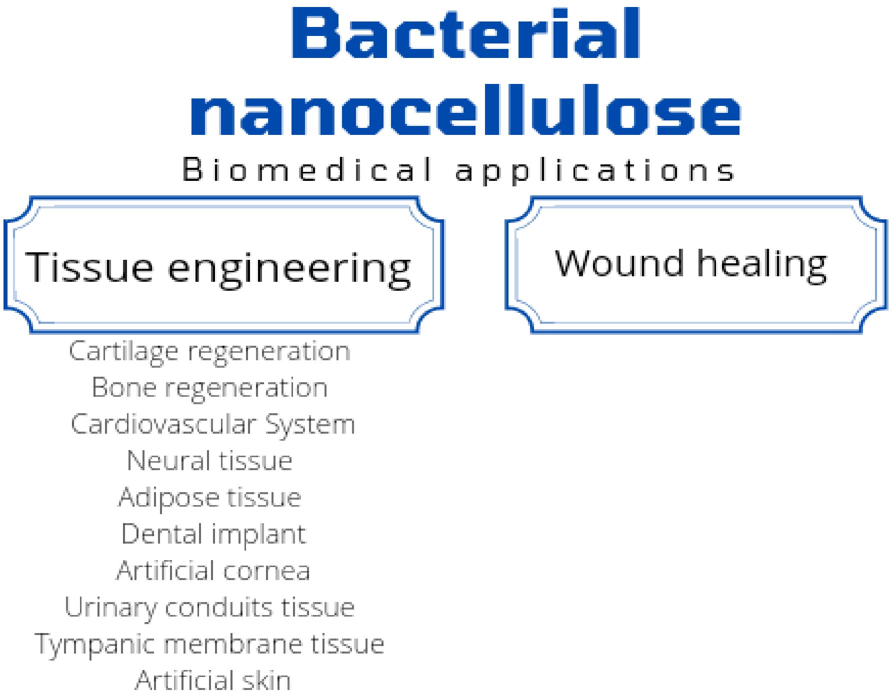

Figure 4. Some applications of bacterial nanocellulose in medicine.

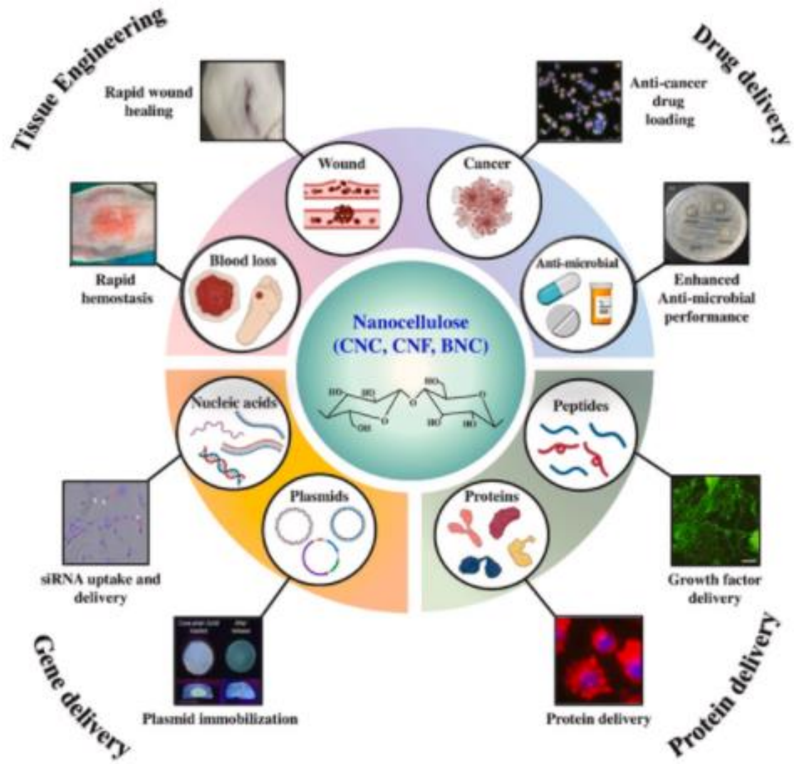

Figure 5. Some applications of different type of Nanocellulose (adopted from [44]).

3 Tissue engineering

Due to the existence of BNC and its significant application in tissue engineering in recent years, great progress has been made in this science [1, 22]. Tissue engineering helps us to repair or replacement of damaged tissues or organs. In tissue engineering, we need a 3D cell-culture system to provide the basis for cell attachment. BNC is also an excellent scaffold for cell cultures. In recent studies, BNC has been used as a scaffold for various types of cell growth. The next components of tissue engineering are cells and signaling molecules like growth factors. The porosity, Biodegradability, biocompatibility, mechanical strength, and hydrophilicity of BNC are positive points for tissue engineering [1, 9, 30, 39, 45] (figure 2). It is also important to point out that BNC has the same situation as the extracellular matrix (ECM) in terms of structure and morphology [45, 46]. Tissue engineering consists of several parts, each of which is described below.

3.1 Cartilage tissue

In vivo cartilage mostly contains elastic cartilage, for example, cartilage of outer ear; fibrocartilage which is present in the joint capsule, intervertebral disc, and ligament; and the most plentiful cartilage, hyaline cartilage which is included joint surface. In the field of cartilage engineering, the numerous properties of BNC are caused that it is used not only as a scaffold for substituting cartilages and also, stimulating the formation of new tissues and support cellular proliferation and growth [9]. The chondrocyte is the most particle that constituent cartilage, that one of their properties is that they don`t divide therefore repair of cartilage tissue is so slow because there's not enough vessel and nerve to operate metabolism required, therefore this is a great challenge in tissue engineering [18].

Researchers use BNC as a scaffold and were observed chondrocyte growth rapidly, and no sign of interference was observed for chondrocyte proliferation [9]. It was found that

The porous construct of BNC let chondrocyte increase onto both the inside and outside pore surfaces of the scaffold [9, 34]. Using BNC as scaffolds can avoid the problems of autografting. Another advantage of BNC is the low rate of degradation of BC in the human body, this leads to the suitability of cartilage repair time [3, 18, 39, 47]. Because of its special properties, can use as a bio-ink in 3D bio-printing technology, to replace nasal cartilage too.

We also can use BNC for cartilage repair with the meniscus, which has approximately similar mechanical strength. Studies were shown pig meniscus in comparison with artificial meniscus made by BC gel, that Young's modulus of them are same [18, 32]. And also other studies on the knee meniscus showed that the microchannels are suitable for replacing knee meniscus and tendons because they can align cells and collagen fibers. Recently studies tell that BC product can be used as an implant for auricular cartilage, because of the host tissue response of human auricular cartilage and also in terms of the mechanical strength it matches with auricular cartilage.

3.2 Bone tissue

Using BNC for damaged bone tissues is an emerging bone repair method since the use of common methods such as bone grafting has its own drawbacks including, immune rejection, and disease transmission, etc. [9, 37]. Bone is a mineralized connective tissue, in fact, it can be said bone constituted organic material like collagen and noncollagenous proteins and mineral material like calcium hydroxyapatite [3, 18]. Bone tissue involves collagen that surrounds osteoblasts, osteocytes, and lining cells and, a solid matrix of inorganic calcium phosphates [18, 48]. Recent studies on rat calvarial osteoblasts, describe that we can enhance the performance of MSCs and other bone-forming cells, with nanocellulose-based scaffolds, by biomimetic mineralization with calcium phosphates, such as hydroxyapatite and tricalcium phosphate. New reports show BNC is an operative scaffold that is synthesized by Glucoacetobacter xylinus, simplifies bone regeneration [48].
BNC supports cells growth and also preserves their morphology and because of its nano-scale pore characteristics prevent inflammatory responses. For bone implant, a type of BC composite is used in which Calcium chloride or Calcium phosphate has been deposited, Calcium carbonate increased the biocompatibility of BC. To enhance calcium carbonate deposition on BC membranes, calcium chloride (CaCl2) and sodium carbonate (Na2CO3) are used as starting reactants [8, 9, 18]. Some studies are shown that BNC-HAP composites enhance BC composite`s mechanical properties because bone tissue generally consists of collagen and hydroxyapatite (HAP) and one of HAP`s properties is bioactivity and osteoconductivity [9, 18, 49]. BC-Hap biomaterials increase the speed of regeneration of bone tissue. Researchers also found that the Hap crystals can be replaced by carbonate, resembling natural bones. Since BC-Hap nanocomposites improve osteoblasts properties such as adhesion, proliferation, and mineralization, they can regenerate bone tissue more quickly [3, 8, 9, 18, 29]. And also in terms of BC-Hap nanocomposites are close to the biological apatites, make it the best choice for artificial bones for bone tissue engineering. In order to enhance BC`s properties for regenerate bone tissue, it can be impregnated some materials to BC cultures such as growth factors, bone marrow mesenchymal stem cells (BMSC), extracellular matrix protein, and estrogen [3].

3.3 Vascular tissue engineering

The vessels can be clogged or harshly damaged in different situations [28, 32, 34]. Instead of using vessels drawn from the patient's body/donor, that have some drawbacks as previously explained at bone tissue part. We can get help from tissue engineering. For vascular tissue engineering, BNC can be used to create tubular structures. The advantage of using BC as artificial vessels is that there is no cell modification, thrombus-free patency, no acute signs of inflammatory reaction, and due to its shape retention ability, moldability, and good tear resistance, confirmed this is an excellent material to produce the tubes [9, 18, 32, 50]. To adjust the thickness and size of a BC, we can produce BC tubes based on a planar BC membrane, which is extremely tunable, by changing the time of the bacterial culturing and chamber size [51]. Also, the planar BC membrane can be produced as a multilayered tube to simulate tubular structures in the body [51]. Active proliferation of the cells in the BC tubular structures in vitro for a long time without thrombosis shows the successful performance of that. Each year, many bypass surgeries are performed around the world. So far, vessels are harvested from the legs of patients or the thorax [19]. Some studies have reported, BC as a blood vessel has been effectively applied in animal models for microsurgery [4, 52].

3.4 Neural tissue

The most challenging part of tissue engineering is of nervous tissues [1, 17, 18]. BC is used to adhere to mesenchymal stem cells and leads to increase secretion of nuetrophin kind of nerve growth factor, which stimulates neuronal regeneration [17, 18]. These applications benefit from their unique properties Biocompatibility, low inflammatory response, etc. It was shown in the performed experiments that BC tubes didn`t change their original size and form, and also with the accumulation of neurotrophic factors inside, facilitated the process of nerve regeneration [18]. The data came from in vitro experiment confirmed that BC is well biocompatible with Schwann cells, and without harmful hematological and histological effects [18]. BC was also reported that create a microenvironment that promotes neuronal regeneration, and BC can restore peripheral nerves too. All these studies were in vitro or experiments on small animals, the long-term effect needs to be validated in larger animals [18].

3.5 Adipose tissue

It is necessary to perusal on adipose tissue for studies on adipose biology and metabolic diseases like diabetes and obesity. BNC can be used to build 3D scaffolds for the rebuilding of tissue after trauma, tumor removal, or congenital defects [22]. So with using nanocellulose and hyaluronic acid, alginate, and adipocytes by freeze-drying, 3D porous structure scaffolds were prepared. it`s better to use lower alginate for retained pore integrity. The adipocytes distribute equally in the scaffolds, and high viability and mature phenotype were some of their characteristics against 2D scaffolds [22].

3.6 Dental implant

The incredible potential of BNC to use as a material for dental root canal treatment for intracanal asepsis in animal experiments [18]. BNC demonstrated better compatibility and biological characteristics for dental canal treatment. BC showed a higher liquid absorption capacity and expansion capacity against ordinary method, conventional paper point materials [1]. The absorption rate increased, and also it has more tensile strength and drug release efficiency.[53] Due to

BC`s unique features, like crystallinity, mechanical strength, and adsorption capacity of BC significant that is good material in root canal filling, and dentin mineralization.

3.7 Artificial cornea

Corneal malfunction is one of the reasons people lose their eyesight, therefor artificial cornea should be built for corneal transplants [8, 17]. Similarly, as mentioned before, BNC's unique properties, including nanoporous structure, definite pellucidness, and its tremendous mechanical that leads to maintaining the intraocular pressure, make it the best biomaterial for artificial cornea generation. BC-polyvinyl alcohol hydrogel with having great water holding capacity, light transmittance comparable, incredible mechanical and thermal properties shows that BNC is defiantly a promising material to synthesis optically functional nanocomposites. The scientist also understood that we can use BNC for the construction of contact lenses [22]. UV-blocking, refractive index too close to water, excellent transparency, shows the importance of this material in the future of making contact lenses [8].

3.8 Urinary conduits tissue

Due to the amount of bladder cancer rise, shows the reason why it is necessary to find a functional way to produce urinary tissue as soon as possible [1, 18, 31, 54, 55]. 3D porous BNC scaffold evolved tissue-engineered urinary conduits, which is promising for patients of bladder disease requiring bladder reconstruction. The studies confirmed that this kind of scaffold assists differentiation of urine-derived stem cells in the development of a tissue-engineered urinary channel. Bodin [56] produced BNC scaffolds with human urine-derived stem cells to use as conduits in the urinary diversion. The cells differentiated into multilayers smooth muscle and urothelial cells. In vivo results on a rabbit showed that BNC scaffolds seeded with lingual keratinocytes promote regeneration of urethral tissue without any inflammatory reactions [18, 53].

3.9 Tympanic membrane tissue

Perforation of the tympanic membrane (TM) leads to hearing loss and chronic perforations acute persistent, which need surgery to solve [18]. With the use of tissue engineering, conventional surgery is reduced. Recent studies described that TM perforation with the use of BNC as a wound-healing scaffold is promising to repair due to its properties that have been said over and over again (biocompatibility, transparency, nanostructured surface, and appropriate mechanical, etc.) [18] that cause to enhance proliferation, adhesion, and migration of tympanic membrane cells. BNC incredibly increased the tympanic membrane healing rate and is better than spontaneous healing [18].

3.10 Artificial skin

BNC`s ability to retain moisture, excellent tensile strength, elasticity, and biocompatibility, caused bacterial cellulose use in skin reconstruction [57]. For skin tissue engineering need to reconstruct two main layers of the skin, epidermis, and dermis. Keratinocytes construct the epidermis the outer skin layer, and fibroblasts mainly construct the inner skin layer, the dermis [22, 27, 57]. BNC is similar to natural soft tissues in comparison with other biomaterials. BNC is used as a culture medium for keratinocytes and promotes proliferation, growth, spreading, and migration in keratinocytes and fibroblasts that create clusters. Therefore BNC confirmed that its great substrates for the adhesion, spreading, and growth of keratinocytes and fibroblasts [19, 22]. Proliferation can be increased by adding chitosan and keratin to the culture medium [27]. But with the salient advantages, there are some disadvantages like, non-degradability in the human body that can enforce scar formation [22]. This problem can be solved by degradable cellulose and cellulase enzymes like glucosidase or oxidation [22, 58].

4. Wound healing

To repair the wounded tissue, some cellular and biochemical factors play a key role. The three steps of the wound healing process are homeostasis/inflammation, proliferation, and remodeling [3, 9, 22, 32]. BNC helps accelerate wound healing in all three stages. At first in 1990 bacterial cellulose use for wound healing [41]. Today BNC use to heal infected wounds, acute traumatic injury, and diabetic wounds, second-and third-degree burns, ulcers, abrasions, pressure sores, venous stasis, ischemic, lacerations, and biopsy sites, and other skin injuries [8, 9, 18, 27, 30, 46]. Wound dressings must have certain characteristics for excellent performance, BNC has great properties which make it an excellent choice to produce wound dressing [9, 37]. some of these most important properties are kept moist in the wound bed, high exudate absorption ability, adhesion to the wound bed, less irritation, antibacterial activity, easy handling and exchanging (removal can cause trauma and damage to the wound site in usual wound dressing), permeability for substances, reduced infection, avoid allergic reactions, and reduce wound pain, and also some other features that increase healing rate, reduce scar formation, therefore it leads to reduce treatment time and cost [1, 8, 18, 22, 34, 39, 59-62]. These features are all beneficial for skin repairing. Briefly, the BC prepares the ideal conditions for the wound to heal as quickly as possible without infection. Some drawbacks of traditional wound dressings are they don't retain moisture and also they can`t stimulate wound healing. It has been examined that BC can regenerate greater thickness of epidermis and dermis, regulate angiogenesis and connective tissue formation, express more collagen, so it speeds wound healing [18]. Also, we can improve its properties with physical modification, microbial fermentation, chemical modification, and compound modification to create better wound dressing. Generally, it can be concluded with the current facilities BNC is one of the best materials for wound dressing [9].

5. Other applications

The results of using BNC in several biomedical fields have been very amazing and promising so far. In addition to all the points and applications mentioned, there are more expectations in the field of body simulation and production of artificial organs in the body such as kidneys and so on [18]. Nowadays experiments and studies have been done like BC-based ear-shaped designed by Nimeskern et al. [63] that have provided encouraging results in 3D bioprinting and solving many health problems in the future.

6 Conclusion

As mentioned in this mini-review due to the incredible properties of bacterial nanocellulose that can be produced in virtually any shape (because of its great moldability) and also it has high crystallinity, mechanical properties, high purity, lignin and hemicellulose free, high water-holding capacity, etc. is emerging biopolymer and promising material that has shown excellent potential for a wide range of applications especially in medical science and health care including tissue engineering and wound healing, industry, technology, biotechnology, and, food industry and packaging, cosmetics and sanitary products, paper industry, and many more. Here in this mini-review some of the most important applications of BNC in medical science, such as the production of various composites and tissue engineering, and its potential for use in numerous fields were examined. According to what has been said, BNC has a bright future in medicine and other sciences, and therefore it should be researched and studied more seriously so that it can be the solution to many problems in the future.

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References

1. Naz S, Ali JS, Zia M. *Nanocellulose isolation characterization and applications: a journey from non-remedial to biomedical claims*. Bio-Design and Manufacturing. 2019;2:187-212.
2. de Amorim JDP, de Souza KC, Duarte CR, da Silva Duarte I, Ribeiro FdAS, Silva GS, et al. *Plant and bacterial nanocellulose: Production, properties and applications in medicine, food, cosmetics, electronics and engineering. A review*. Environmental Chemistry Letters. 2020;18:851-69.
3. Pang M, Huang Y, Meng F, Zhuang Y, Liu H, Du M, et al. *Application of bacterial cellulose in skin and bone tissue engineering*. European Polymer Journal. 2020;122:109365.
4. Cacicedo ML, Castro MC, Servetas I, Bosnea L, Boura K, Tsafrakidou P, et al. *Progress in bacterial cellulose matrices for biotechnological applications*. Bioresource technology. 2016;213:172-80.
5. Abootalebi SN, Mousavi SM, Hashemi SA, Shorafa E, Omidifar N, Gholami A. *Antibacterial Effects of Green-Synthesized Silver Nanoparticles Using Ferula asafoetida against Acinetobacter baumannii Isolated from the Hospital Environment and Assessment of Their Cytotoxicity on the Human Cell Lines*. Journal of Nanomaterials. 2021;2021.
6. Wang J, Liu X, Jin T, He H, Liu L. *Preparation of nanocellulose and its potential in reinforced composites: a review*. Journal of Biomaterials Science, Polymer Edition. 2019;30:919-46.
7. Thomas B, Raj MC, Joy J, Moores A, Drisko GL, Sanchez C. *Nanocellulose, a versatile green platform: from biosources to materials and their applications*. Chemical reviews. 2018;118:11575-625.
8. Picheth GF, Pirich CL, Sierakowski MR, Woehl MA, Sakakibara CN, de Souza CF, et al. *Bacterial cellulose in biomedical applications: A review*. International journal of biological macromolecules. 2017;104:97-106.
9. Xue Y, Mou Z, Xiao H. *Nanocellulose as a sustainable biomass material: structure, properties, present status and future prospects in biomedical applications*. Nanoscale. 2017;9:14758-81.
10. Palaninathan V, Raveendran S, Rochani AK, Chauhan N, Sakamoto Y, Ukai T, et al. *Bioactive bacterial cellulose sulfate electrospun nanofibers for tissue engineering applications.* Journal of tissue engineering and regenerative medicine. 2018;12:1634-45.
11. Moohan J, Stewart SA, Espinosa E, Rosal A, Rodríguez A, Larrañeta E, et al. *Cellulose nanofibers and other biopolymers for biomedical applications. A review*. Applied Sciences. 2020;10:65.
12. Goudarzian N, Sadeghi Z, Mousavi SM, Hashemi SA, Banaei N. *Chemical constituent and determination of antimicrobial and antifungal activities of Ulva lactuca species obtained from Iranian Gheshm Island*. Int J Sci Eng Res. 2017;8:1275-9.
13. Takmil F, Esmaeili H, Mousavi SM, Hashemi SA. *Nano-magnetically modified activated carbon prepared by oak shell for treatment of wastewater containing fluoride ion*. Advanced Powder Technology. 2020;31:3236-45.
14. Emami-Meibodi M, Parsaeian M, Amraei R, Banaei M, Anvari F, Tahami S, et al. *An experimental investigation of wastewater treatment using electron beam irradiation*. Radiation Physics and Chemistry. 2016;125:82-7.
15. Tayeb AH, Amini E, Ghasemi S, Tajvidi M. *Cellulose nanomaterials—Binding properties and applications: A review*. Molecules. 2018;23:2684.
16. Abdul Rashid ES, Muhd Julkapli N, Yehye WA. *Nanocellulose reinforced as green agent in polymer matrix composites applications*. Polymers for Advanced Technologies. 2018;29:1531-46.
17. Rajwade J, Paknikar K, Kumbhar J. *Applications of bacterial cellulose and its composites in biomedicine*. Applied microbiology and biotechnology. 2015;99:2491-511.
18. de Oliveira Barud HG, da Silva RR, da Silva Barud H, Tercjak A, Gutierrez J, Lustri WR, et al. *A multipurpose natural and renewable polymer in medical applications: Bacterial cellulose*. Carbohydrate Polymers. 2016;153:406-20.
19. Gorgieva S, Trček J. *Bacterial cellulose: Production, modification and perspectives in biomedical applications*. Nanomaterials. 2019;9:1352.
20. Gualdron NHA. Production of Chitosan Micro and Nanospheres for the Formulation of Antibacterial Food

Packaging Materials: Ecole Polytechnique, Montreal (Canada); 2017.

21. Hu W, Chen S, Yang J, Li Z, Wang H. *Functionalized bacterial cellulose derivatives and nanocomposites*. Carbohydrate polymers. 2014;101:1043-60.

22. Bacakova L, Pajorova J, Bacakova M, Skogberg A, Kallio P, Kolarova K, et al. *Versatile application of nanocellulose: From industry to skin tissue engineering and wound healing*. Nanomaterials. 2019;9:164.

23. Stumpf TR, Yang X, Zhang J, Cao X. *In situ and ex situ modifications of bacterial cellulose for applications in tissue engineering*. Materials Science and Engineering: C. 2018;82:372-83.

24. Choi SM, Shin EJ. *The nanofication and functionalization of bacterial cellulose and its applications*. Nanomaterials. 2020;10:406.

25. Andriani D, Apriyana AY, Karina M. *The optimization of bacterial cellulose production and its applications: a review*. Cellulose. 2020;27:6747-66.

26. Brown AJ. *XLIII.—On an acetic ferment which forms cellulose*. Journal of the Chemical Society, Transactions. 1886;49:432-9.

27. He W, Wu J, Xu J, Mosselhy DA, Zheng Y, Yang S. *Bacterial cellulose: Functional modification and wound healing applications*. Advances in wound care. 2020.

28. Nehra P, Chauhan R. *Eco-friendly nanocellulose and its biomedical applications: current status and future prospect*. Journal of Biomaterials Science, Polymer Edition. 2021;32:112-49.

29. Torres F, Arroyo J, Troncoso O. *Bacterial cellulose nanocomposites: An all-nano type of material*. Materials Science and Engineering: C. 2019;98:1277-93.

30. Sharma C, Bhardwaj NK. *Bacterial nanocellulose: Present status, biomedical applications and future perspectives*. Materials Science and Engineering: C. 2019;104:109963.

31. Hosseini H, Kokabi M, Mousavi SM. *Dynamic mechanical properties of bacterial cellulose nanofibres*. Iranian Polymer Journal. 2018;27:433-43.

32. Moniri M, Boroumand Moghaddam A, Azizi S, Abdul Rahim R, Bin Ariff A, Zuhainis Saad W, et al. *Production and status of bacterial cellulose in biomedical engineering*. Nanomaterials. 2017;7:257.

33. Ruhs PA, Malollari KG, Binelli MR, Crockett R, Balkenende DW, Studart AR, et al. *Conformal bacterial cellulose coatings as lubricious surfaces*. ACS nano. 2020;14:3885-95.

34. Blanco Parte FG, Santoso SP, Chou C-C, Verma V, Wang H-T, Ismadji S, et al. *Current progress on the production, modification, and applications of bacterial cellulose*. Critical reviews in biotechnology. 2020;40:397-414.

35. Hsieh J-T, Wang M-J, Lai J-T, Liu H-S. *A novel static cultivation of bacterial cellulose production by intermittent feeding strategy*. Journal of the Taiwan Institute of Chemical Engineers. 2016;63:46-51.

36. Mousavi SM, Zarei M, Hashemi SA, Ramakrishna S, Chiang W-H, Lai CW, et al. *Gold nanostars-diagnosis, bioimaging and biomedical applications*. Drug metabolism reviews. 2020;52:299-318.

37. Amalraj A, Gopi S, Thomas S, Haponiuk JT, editors. Cellulose nanomaterials in biomedical, food, and nutraceutical applications: a review. Macromolecular Symposia; 2018: Wiley Online Library.

38. Moteshafi H, Mousavi S, Shojaosadati S. *The possible mechanisms involved in nanoparticles biosynthesis*. Journal of Industrial and Engineering Chemistry. 2012;18:2046-50.

39. Torgbo S, Sukyai P. *Biodegradation and thermal stability of bacterial cellulose as biomaterial: The relevance in biomedical applications*. Polymer Degradation and Stability. 2020;179:109232.

40. Moniri M, Moghaddam AB, Azizi S, Rahim RA, Saad WZ, Navaderi M, et al. *Molecular study of wound healing after using biosynthesized BNC/Fe3O4 nanocomposites assisted with a bioinformatics approach*. International journal of nanomedicine. 2018;13:2955.

41. Fontana J, De Souza A, Fontana C, Torriani I, Moreschi J, Gallotti B, et al. *Acetobacter cellulose pellicle as a temporary skin substitute*. Applied biochemistry and biotechnology. 1990;24:253-64.

42. Meftahi A, Nasrolahi D, Babaeipour V, Alibakhshi S, Shahbazi S. *Investigation of nano bacterial cellulose coated by sesamum oil for wound dressing application*. Procedia Materials Science. 2015;11:212-6.

43. Mousavi SM, Low FW, Hashemi SA, Samsudin NA, Shakeri M, Yusoff Y, et al. *Development of hydrophobic reduced graphene oxide as a new efficient approach for photochemotherapy*. RSC Advances. 2020;10:12851-63.

44. Patil TV, Patel DK, Dutta SD, Ganguly K, Santra TS, Lim K-T. *Nanocellulose, a versatile platform: From the delivery of active molecules to tissue engineering applications*. Bioactive Materials. 2021.

45. Sharma C, Bhardwaj NK, Pathak P. *Ternary nano-biocomposite films using synergistic combination of bacterial cellulose with chitosan and gelatin for tissue engineering applications*. Journal of Biomaterials Science, Polymer Edition. 2021;32:166-88.

46. Zhang P, Chen L, Zhang Q, Hong FF. *Using in situ dynamic cultures to rapidly biofabricate fabric-reinforced composites of chitosan/bacterial nanocellulose for antibacterial wound dressings*. Frontiers in microbiology. 2016;7:260.

47. Abdelraof M, Hasanin MS, Farag MM, Ahmed HY. *Green synthesis of bacterial cellulose/bioactive glass nanocomposites: Effect of glass nanoparticles on cellulose yield, biocompatibility and antimicrobial activity*. International journal of biological macromolecules. 2019;138:975-85.

48. Torgbo S, Sukyai P. *Bacterial cellulose-based scaffold materials for bone tissue engineering*. Applied Materials Today. 2018;11:34-49.

49. Jiang P, Ran J, Yan P, Zheng L, Shen X, Tong H. *Rational design of a high-strength bone scaffold platform based on in situ hybridization of bacterial cellulose/nano-hydroxyapatite framework and silk fibroin reinforcing phase*. Journal of Biomaterials science, Polymer edition. 2018;29:107-24.

50. Vellayappan MV, Balaji A, Subramanian AP, John AA, Jaganathan SK, Murugesan S, et al. *Tangible nanocomposites with diverse properties for heart valve*

application. Science and technology of advanced materials. 2015;16:033504.
51. Li Y, Jiang K, Feng J, Liu J, Huang R, Chen Z, et al. *Construction of Small‐Diameter Vascular Graft by Shape‐Memory and Self‐Rolling Bacterial Cellulose Membrane*. Advanced healthcare materials. 2017;6:1601343.
52. Scherner M, Weber C, Reinhard S, Madershahian N, Sterner-Kock A, Guschlbauer M, et al. *Tissue-engineered Blood Vessels of Bacterial Cellulose as Small Arterial Substitutes: In Vivo Results of a 6 Month Trial*. The Thoracic and Cardiovascular Surgeon. 2016;64:OP265.
53. Avval ZM, Malekpour L, Raeisi F, Babapoor A, Mousavi SM, Hashemi SA, et al. *Introduction of magnetic and supermagnetic nanoparticles in new approach of targeting drug delivery and cancer therapy application*. Drug metabolism reviews. 2020;52:157-84.
54. Tech JET. *Investigating the Activity of Antioxidants Activities Content in Apiaceae and to Study Antimicrobial and Insecticidal Activity of Antioxidant by using SPME Fiber Assembly Carboxen/Polydimethylsiloxane (CAR/PDMS)*. Journal of Environmental Treatment Techniques. 2020;8:214-24.
55. Ahmadi S, Fazilati M, Mousavi SM, Nazem H. *Anti-bacterial/fungal and anti-cancer performance of green synthesized Ag nanoparticles using summer savory extract*. Journal of Experimental Nanoscience. 2020;15:363-80.
56. Bodin A, Bharadwaj S, Wu S, Gatenholm P, Atala A, Zhang Y. *Tissue-engineered conduit using urine-derived stem cells seeded bacterial cellulose polymer in urinary reconstruction and diversion*. Biomaterials. 2010;31:8889-901.
57. Shahriari-Khalaji M, Hong S, Hu G, Ji Y, Hong FF. *Bacterial nanocellulose-enhanced alginate double-network hydrogels cross-linked with six metal cations for antibacterial wound dressing*. Polymers. 2020;12:2683.
58. Rahmani J, Miri A, Namjoo I, Zamaninour N, Maljaei MB, Zhou K, et al. *Elevated liver enzymes and cardiovascular mortality: a systematic review and dose–response meta-analysis of more than one million participants*. European journal of gastroenterology & hepatology. 2019;31:555-62.
59. Ahmed J, Gultekinoglu M, Edirisinghe M. *Bacterial cellulose micro-nano fibres for wound healing applications*. Biotechnology advances. 2020;41:107549.
60. Rasoulnia P, Mousavi Sá. *V and Ni recovery from a vanadium-rich power plant residual ash using acid producing fungi: Aspergillus niger and Penicillium simplicissimum*. RSC advances. 2016;6:9139-51.
61. Mousavi SM, Hashemi SA, Zarei M, Bahrani S, Savardashtaki A, Esmaeili H, et al. *Data on cytotoxic and antibacterial activity of synthesized Fe3O4 nanoparticles using Malva sylvestris*. Data in brief. 2020;28:104929.
62. Mousavi SM, Hashemi SA, Ramakrishna S, Esmaeili H, Bahrani S, Koosha M, et al. *Green synthesis of supermagnetic Fe3O4–MgO nanoparticles via Nutmeg essential oil toward superior anti-bacterial and anti-fungal performance*. Journal of Drug Delivery Science and Technology. 2019;54:101352.
63. Nimeskern L, Ávila HM, Sundberg J, Gatenholm P, Müller R, Stok KS. *Mechanical evaluation of bacterial nanocellulose as an implant material for ear cartilage replacement*. Journal of the mechanical behavior of biomedical materials. 2013;22:12-21.