Bacterial Cellulose: A Multifunctional Platform for Biomedical Applications

Ricardo Barbosa de Sousa[1,*], Guilherme Pinesso[1], Rennzo Rodrigues Diedrichs[1], Carla Cristina da Silva[1] and Luana Priscilla Rodrigues Macêdo[1]

[1]*Research and Development Center for Advanced Materials, Federal Institute of Tocantins, Araguaina Campus, Brazil*

Abstract: Bacterial cellulose (BC), a biopolymer synthesized by various bacterial species, has emerged as a promising material for biomedical applications due to its unique properties, including high purity, biocompatibility, mechanical strength, and structural similarity to the extracellular matrix. This review explores the advancements in BC research over the last decade, focusing on its applications in tissue engineering, wound healing, and drug delivery systems. While BC offers numerous benefits, challenges such as large-scale production, structural modification, however regulatory approval hinder its broader clinical use. Recent studies have introduced innovative solutions, such as using agro-industrial waste to lower production costs and combining BC with other materials to enhance its bioactivity. As research progresses, BC has the potential to revolutionize the field of biomedicine, offering sustainable, versatile, and effective solutions for a wide range of medical applications.

Keywords: Antibacterial properties, Bacterial cellulose, Biocompatibility, Drug delivery systems, Tissue engineering, Wound healing.

1. INTRODUCTION

Cellulose is the most abundant biopolymer in nature, and generally is obtained from plant sources, consisting of lignin, hemicelluloses and pectin beside cellulose. On the other hand, currently industries and public health sectors are demanding for new biodegradable and eco-friendly materials [1-3].

Bacterial cellulose (BC) also named microbial cellulose is an alternative material biosynthesized extracellularly mainly by Gram-negative bacteria, such as *Gluconacetobacter, Rhizobium, Agrobacterium, Aerobacter, Achromobacter, Azotobacter, Salmonella, Escherichia,* and *Sarcina* bacterial genera [4]. *Gluconacetobacter,* namely as *Komagataeibacter*, is the most prominent and efficient BC producer, industrially explored [5]. Compared to plant cellulose, BC has various advantages, starting from the purification process, that is sustainable, generating less wastes [1].

Moreover, BC exhibits excellent and superior mechanical and structural properties than plant cellulose, such as high flexibility, high water uptake capacity (up to 400 times its dry weight), hydrophilicity, elevated purity and crystallinity, ultrafine fiber network, high porosity, high tensile strength, and ability to be shaped into different structures [6-8]. This whole set of satisfactory properties are due to BC formation that involves 3D-ultra thin entangled cellulose nanofibers randomly distributed forming a gelatinous film [5, 8]. In addition, despite plant-based cellulose fibers being renewable, abundant, cheap and biodegradable, it is associated with lignin and hemicellulose, non-biodegradable molecules [9].

All those characteristics, associated with biocompatibility and biodegradability, makes BC a promisor candidate for biomedical applications, such as: artificial skin, vascular grafts, scaffolds for tissue engineering, medical pads, artificial blood vessel repair, drug delivery, wound healing, and dental implants [7, 9].

This article discusses the advances of the last decade in bacterial cellulose research as a versatile and multifunctional platform for biomedical applications.

2. BIOMEDICAL APPLICATIONS OF BACTERIAL CELLULOSE

Since the beginning of humanity, society has found a way to use cellulose in medicinal products or procedures, such as teas or dressings based on some leaves. Currently, we still use cellulose to support the field of human health, however, with the difference that the cellulose used in medicine comes largely from bacteria. Bacterial cellulose has numerous advantages, such as helping to combat deforestation to obtain traditional cellulose [10]. In addition, BC has easy handling during the strain production process, thus adding improved functional characteristics to its by-products.

*Address correspondence to this author at the Federal Institute of Education, Science, and Technology of Tocantins, Campus Araguaina, 56, Amazonas Avenue, 77826-170, Araguaina, TO, Brazil;
Tel: +55 (63) 3411-0328; E-mail: ricardo.sousa@ifto.edu.br

E-ISSN: 2410-4701/24

The potential that BC has in advancing biomedical sciences is undeniable, from nursing and diagnosis to highly complex theranostic and regenerative tissue engineering products. Bacterial cellulose, since its effectiveness in tissue remodeling, has been used as a strong pillar of tissue engineering and biomedicine, its functions range from wound dressing, production and improvement of drugs, artificial reconstruction of blood vessel tunics, engineering of bone tissue, among countless other functions. Furthermore, BC is easy to manipulate from the strain production process, thus adding improved functional characteristics to its byproducts [11].

Mechanical and physicochemical properties such as porosity, malleability, bendability, hemocompatibility are attributes rigorously analyzed to obtain a good final product, in this case, the production of artificial blood vessels. This production of artificial vessels is done by protecting the tunica adventitia, especially in smaller vessels, such as the thorax or legs. Porosity analysis is one of the most important points in tissue construction, as the systematics and migration of endothelial cells are essential when we take synthetic biological products into consideration. Figure **1** shows some biomedical applications of bacterial cellulose.

3. BACTERIAL CELLULOSE AS A SCAFFOLD FOR TISSUE ENGINEERING

Certainly, one of the most prominent biomedical applications of BC is the development of scaffolds for tissue engineering. Tissue engineering (TE), according to Langer and Vacanti (1993) [12] and Pollok and Vacanti (1996) [13], is a promisor field of regenerative medicine which applies the principles of biology and engineering, in order to first understand structure/function relationships in tissues, and then, to provide functional biomaterials to restore, maintain, or improve damaged tissues.

The foundations of TE are based on the cell cultivation on scaffolds, three-dimensional structures manufactured from synthetic or natural polymers. TE scaffolds allow cell attachment, growth and proliferation, enabling effective tissue regeneration. Besides, biocompatibility, biodegradability and interconnected pores resulting in suitable mechanical properties are some requirements to a good TE scaffold [14].

In this context, BC membranes have been extensively exploited due to its similarity to natural extracellular matrices (ECMs), with an ultrafine and ordered 3D-network of cellulose nanofibers, like collagen nanostructures [15].

Although these are satisfying properties, some obstacles have critically limited BC application as a scaffold, mainly the lack of large pores and poor cell affinity [16]. BC has a microstructure with pore sizes less than 200 nm, which contributes to inhibit cell proliferation, differentiation and adhesion. To overcome these barriers, researchers have implemented modifications to BC chemical structure which besides providing large pores, enhancing cell biocompatibility, is an usual strategy to improve cellulose biodegradation. Another limitant characteristic of natural BC is the low bioactivity. Researchers have circumvented that by loading bioactive materials such

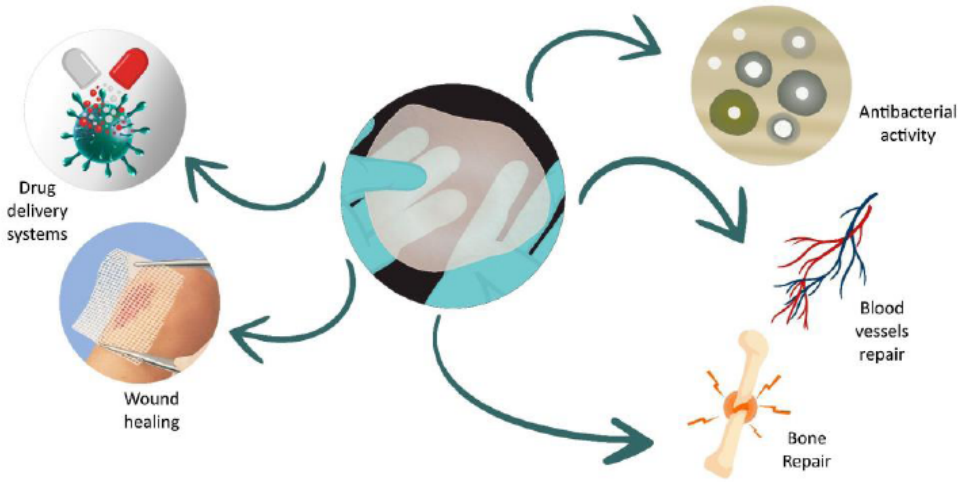

Figure 1: Some biomedical applications of bacterial cellulose.

as collagen, bone morphogenetic protein-2, gelatin, sodium alginate, as some examples [17]. Table **1** summarizes some of the main recent findings about modified BC and BC composites applied to tissue engineering.

Table 1: Recent Publications and their Main Findings about Modified Bacterial Cellulose and Bacterial Cellulose-Based Composites as Tissue Engineering Scaffolds Since 2018 to July 2023. The Research was Performed Web of Science™

Material	Main Findings	Reference
BC modified with incorporated gelatin microspheres	By incorporating gelatin microspheres into BC culture medium, the researchers have obtained interconnected macropores, good swelling degree and mechanical properties. Cell migration to affinitive BC macropores was enhanced besides better spreading and proliferation.	[16]
BC rinsed with poly(ethylene glycol) (PEG-400)	PEG-400 administration to BC enhanced its biocompatibility and the results indicated that the water uptake and porosity properties of the scaffolds are adequate for the viability of the NIH-3T3 murine fibroblast cell line. Cell culture studies also showed that NIH-3T3 murine fibroblast cells presented good attachement and proliferation on scaffolds.	[18]
Polyvinyl Alcohol (PVA)/Hexagonal Boron Nitride (hBN)/Bacterial Cellulose (BC) composite	Bone tissue scaffolds were prepared through 3D-printing technology. The scaffolds presented a good cell adhesion. Bacterial cellulose doped 3D printed scaffolds showed well-defined porous structures with potential as a suitable tissue scaffold for bone repair.	[19]
Bacterial cellulose/quince seed mucilage composite	Quince seed mucilage into BC structure promoted a more compact fibrillary network with a closed pore structure. The composite scaffold revealed excellent fibroblast cell proliferation and attachment. This novel scaffold provides great potential in wound dressing for clinical application.	[20]
Polycaprolactone (PCL), gelatin (GEL), bacterial cellulose (BC), and different hydroxyapatite (HA) concentrations	Large porous scaffolds (~300 μm) were fabricated through 3D-printing with ideal pore size for use in bone tissue engineering. The incorporation of bacterial cellulose and hydroxyapatite into PCL/GEL scaffold increased cell proliferation and attachment. PCL/GEL/BC/HA composite scaffolds provide a potential for bone tissue engineering applications.	[21]
Keratin/Bacterial Cellulose composite scaffold	Bacterial cellulose/keratin composite hydrogel was prepared and evaluated for its physical–chemical and morphological properties. *In vitro* assays demonstrated that the materials were non-toxic on cells. *In vitro* tests performed by burned wounds on rabbits' dorsal region revealed the regenerative potential of the scaffolds.	[22]
Bacterial Cellulose with Chondroitin Sulfate/Gelatin	Chondroitin sulfate (CS) modified with gelatin (Gel) coating was applied to porous BC to improve its biocompatibility. The incorporation of CS/Gel coatings increased mechanical properties, as tensile strength and Young's modulus and promoted cell proliferation, adhesion, differentiation, and ingrowth into scaffolds. The PBC-CS/Gel scaffolds are expected to be used in tissue engineering.	[23]
Bacterial cellulose-chitosan-alginate-gelatin hydrogel scaffold	The composite scaffolds exhibited good three-dimensional (3D) architecture with suitable pore sizes (326.6 μm) for tissue engineering. Besides, the scaffolds presented good compressive strength, stability and excellent biocompatibility, revealing its potential use as scaffolds for application in cartilage tissue engineering.	[24]
Bacterial cellulose scaffolds with different oxidation degrees using sodium periodate	The scaffolds were prepared to evaluate their potential use in peripheral nerve repair. It was demonstrated that the biodegradability of the oxidized bacterial cellulose (OBC) improved significantly. OBC scaffolds with lower oxidation degrees demonstrated high porosity with interconnected pores, suitable mechanical property, and biodegradability for peripheral nerve repair.	[25]
Bacterial cellulose crosslinked with oxidized sucrose	Defibrillated bacterial cellulose (BC) sponges were functionalized with oxidized sucrose (OS). The scaffolds presented a good thermal stability, comparable to that of pristine cellulose and much improved mechanical properties and high porosity, suitable for soft tissue engineering.	[26]

4. ANTIBACTERIAL PROPERTIES OF BACTERIAL CELLULOSE AND ITS ROLE IN WOUND HEALING

BC itself does not possess significant intrinsic antibacterial properties. However, its structure allows the incorporation of various antibacterial agents, such as silver or gold nanoparticles, antibiotics, and natural antimicrobial compounds like chitosan and essential oils. These agents can be embedded into the BC matrix or coated onto its surface, enhancing its antibacterial efficacy [27].

Windarsih *et al.* (2022) [28] synthesized gold-modified bacterial cellulose nanoparticles (Au-BCNP) from waste of coconut water. According to their results, the Au-BCNP composites provided good antibacterial activity against *Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, and Salmonella typhi* indicating the potential applications of Au-BC for biomedical applications. On the other hand, Jalili and Emtiazi (2018) [29] produced transparent antibacterial wound dressings based on silver nanoparticles reduced in the presence of sodium tripolyphosphate and *in situ* impregnation into the bacterial cellulose membranes as a template. Transparency is an important characteristic in agreement with the authors once it is possible to examine the wound without removing the dressing. Besides, the dressings presented long lifetime and strong antibacterial activity against *E. coli* (100%) and *S. aureus* (99.99%).

Similarly, by using silver nanoparticles (AgNPs), Gupta and coworkers (2020) [30] described the green synthesis of AgNPs using curcumin as a natural reducing agent, that is known by its wound-healing properties. Curcumin was microencapsulated into hydroxypropyl-β-cyclodextrin and this complex with AgNPs was loaded into bacterial cellulose hydrogel. The composite hydrogel exhibited high cytocompatibility and revealed promisor properties for applications as wound dressings, once it presented antimicrobial activity against some common wound-infecting pathogenic microbes: *Staphylococcus aureus,Pseudomonas aeruginosa*, and *Candida auris.*

Conversely, there are some studies that focus on natural antimicrobial agents such as essential oils. Nagmetova *et al*. (2020) [31] describes the use of BC as a food packaging impregnated with oregano oil against *Cronobacter* strains. The results revealed that this composite presents a strong and moderate antibacterial activity. In relation to biomedical applications of BC-essential oils composites, Mamouri *et al*. (2023) [32] reported the preparation of a BC/polyvinyl alcohol (PVA, 5 % *w*/*v*)/Barhang seed gum (BSG, 0.5 % w/v) composite loaded with summer savory (*Satureja hortensis* L.) essential oil (SSEO) for application as wound dressings. According to the authors, SSEO-loaded composite film had a robust antibacterial activity against gram-negative bacteria and *in vivo* model revealed a promising potential for wound healing, improved collagen deposition and reduced inflammatory response.

Regarding the use of antibiotics impregnated into BC matrix, there are many reports such as the research conducted by Shao and coworkers (2016) [33] that describes tetracycline hydrochloride-loaded bacterial cellulose membranes, a system where BC matrix is able to control the release of the antibiotic. The composites named as TCH-BC displayed excellent antibacterial activity solely associated with the loaded TCH drug. This result reveals that BC by itself does not present antibacterial activity, however is an excellent template to impregnate and release compounds that have antimicrobial activity. In the next topic we will discuss with more details some recent research where bacterial cellulose works as a drug delivery system.

5. BACTERIAL CELLULOSE AS A DRUG DELIVERY SYSTEM

The human body is truly complex with tissues subject to disorders and diseases. In this context, several drugs are developed and administered into the human body to interact with unhealthy tissues, causing therapeutic effects [34]. This administration involves varied delivery systems. According to Mensah *et al*. (2021) [35], the choice of material of drug delivery is crucial to determine the most suitable route of administration and to assure therapeutic success.

Traditional methods of administering medication include taking it orally or through injections, where the drug molecules are either delivered directly to the target area or circulated throughout the body. Nonetheless, there are some limitations associated with these methods, such as: accurate dosing, time duration, targeted delivery, and tunable release rate [34]. To overcome these limitations, nanoparticles, liposomes, microemulsions, and other advanced drug delivery systems (DDS) have been created to enhance bioavailability [35, 36]. In recent decades, bacterial cellulose (BC) have gained significant attention as an optimal candidate for DDS because of their exceptional biocompatibility, biodegradability, and non-toxicity. Additionally, the abundant hydroxyl (OH) groups on the

surface of BC offer plentiful binding sites for physical, chemical, and mechanical modifications [37].

Luo *et al*. (2017) [38] developed graphene-based nanocarriers embedded into BC matrix to produce a graphene oxide/bacterial cellulose nanocomposite drug carrier. Ibuprofen (IBU) is frequently chosen as a drug model for sustained/controlled release studies, based on some features such as short biological half-life (2 h), good pharmacological activity and suitable molecule size of about 1.0–0.6 nm. According to the authors, IBU was successfully incorporated into BC/GO nanocomposites via in situ biosynthesis. The bacterial cellulose/graphene oxide (BC/GO) composites show a higher IBU loading capacity compared to pure BC. The IBU release depends on the pH of the medium and fits the Korsmeyer-Peppas model. The IBU@BC/GO system demonstrates a more sustained release than IBU@BC, indicating the crucial role of GO in controlled release. The release mechanism is non-Fickian for IBU@BC/GO and zero-order for IBU@BC. These results suggest that BC/GO nanocomposites have great potential as a new drug delivery system.

Jianbin Ye *et al*. (2024) [39] synthesized antibacterial membranes based on bacterial cellulose (BC), including BC-cefoperazone (BC-CEF) and BC-cefoperazone sodium (BC-CEF/Na). Thus, the results demonstrated that both types of drugs were successfully absorbed, and the membranes exhibited identical morphology and FT-IR peaks. Regarding the comparison between both drugs, it was found that BC-CEF had lower XRD crystallinity, which was probably caused by the combination of carboxyl and hydroxyl. However, there were no drug peaks seen in the membranes, indicating no change in BC ribbon crystallization. In this sense, it was observed that the release of the drugs was significantly different. The drug loading rate of CEF (46.4 mg/g) was significantly higher than CEF/Na (30.3 mg/g). Cumulative drug release profiles showed that only BC-CEF continued to release drugs for a long period of up to 48 h and exhibited good antimicrobial activity against *S. aureus* and *E. coli* up to 48 h. It is important to highlight that the authors discussed that the idea that BC membranes can naturally incorporate the carboxyl groups of antibiotics is also innovative and can be useful in the development of drug delivery systems.

Lígia Costa *et al*. (2024) [40] portrayed a simple and direct approach for the development of a bacterial nanocellulose drug delivery system (BNC-DDS), providing for the local administration of immunomodulatory drugs in order to prevent foreign body reaction (FBR). Therefore, in this work the aim was to make the most of the self-adhesion properties of BNC after drying, to trap commercial crystalline drugs (dexamethasone-DEX and GW2580) in a sandwich system. The stability of the bilayer BNC-DDS was demonstrated by the high interfacial energy of the bilayer films, 150 ± 11 and 88 ± 7 J/m^2 respectively for 2 mm and 10 mm thick films, corresponding to an increase of 7.5 and 4.4 times compared to commercial fabric adhesives. Regarding *in vitro* release experiments, the adjustment capacity of the BNC-DDS bilayer was observed by showing prolonged drug release when thicker BNC membranes were used (from 16 to 47 days and from 35 to 132 days, for the bilayer- BNC trapping DEX and GW2580, an inhibitor of the tyrosine kinase activity of CSF1R, respectively). In summary, it can be seen that the work developed had potential, using a simple approach for the development of BNC drug depots for localized and sustained release of therapeutic agents within adjustable time frames. Therefore, the authors reported that this work overcomes current tedious or ineffective strategies for developing BNC-DDS, which often fail to achieve sustained release over long periods.

6. CHALLENGES AND FUTURE PERSPECTIVES IN UTILIZING BACTERIAL CELLULOSE FOR BIOMEDICAL APPLICATIONS

Bacterial cellulose (BC) has garnered increasing interest in biomedicine due to its unique properties, including high purity, biocompatibility, water retention capacity, and nanofibrillar structure that mimics the extracellular matrix of human tissues [41, 42]. These characteristics make BC a promising material for various biomedical applications, such as tissue engineering, controlled drug delivery, and the development of medical devices [43]. However, the transition of this material from the laboratory to clinical use on a large scale faces significant challenges that must be overcome.

One of the major challenges in utilizing BC is the large-scale production needed to meet the demands of the biomedical sector. Although bioreactor cultivation techniques have been developed, the scalability of these processes remains limited. Factors such as optimizing culture conditions, rigorous control of parameters like pH, temperature, and aeration, and the high costs of culture media represent considerable obstacles [44, 45]. Recent studies have explored the use of alternative substrates and agro-industrial waste

for BC production, such as glucose derived from sugarcane bagasse, which could reduce costs and make the process more sustainable [46].

The structural modification of BC to enhance its properties, such as bioactivity and biodegradability, is another significant challenge. Native BC has excellent mechanical strength and stability, but its bioactivity can be limited. Research has focused on the chemical functionalization of BC, incorporating functional groups or combining it with other materials, such as chitosan or collagen, to improve cell interaction and promote tissue regeneration [47, 48]. Recently, Abeer and coworkers (2014) [49] reviewed advances in BC modification for biomedical applications, highlighting the importance of combining it with natural and synthetic polymers to create hybrid materials with adjustable properties.

Another critical point is the reproducibility and standardization of BC production processes. Variability in the material's properties, due to differences in bacterial strains and culture conditions, can affect the quality and functionality of the final products [50]. Abol-Fotouh and coworkers (2020) [51] discussed the importance of controlling these parameters to ensure material consistency, especially in biomedical applications where variability can compromise the efficacy and safety of devices.

Regulation and clinical approval of BC for human use is another complex challenge. The regulatory approval process involves extensive testing for biocompatibility, toxicity, and efficacy, as well as compliance with international standards set by bodies such as the FDA and Anvisa [51, 52]. In a detailed study, Gama and coworkers (2016) [53] explored the requirements for certifying BC-based biomaterials, emphasizing the need for rigorous preclinical studies and the establishment of standardized protocols to ensure patient safety.

Despite these challenges, the future prospects for BC in biomedical applications are promising. In tissue engineering, BC has proven effective in regenerating tissues such as skin, cartilage, and blood vessels due to its nanofibrillar structure that mimics the extracellular matrix [54, 55]. Recent advances in 3D bioprinting have enabled the creation of personalized scaffolds, which can be used to promote tissue regeneration in patients, integrating stem cells to optimize the healing process [56].

The development of nanocomposites is another area of growing interest. Combining BC with nanoparticles, such as silver or metal oxides, has resulted in materials with antimicrobial and conductive properties, expanding their applications in medical devices such as smart wound dressings and biosensors [57, 58]. A study conducted by Lin and coworkers (2013) [59] demonstrated that the incorporation of silver nanoparticles into BC resulted in a dressing with excellent antimicrobial activity, showing potential for use in chronic wounds.

In the field of advanced therapies and regenerative medicine, BC can be used as a platform for controlled drug release, a support for the growth of specific cells, or even as a vehicle for gene therapies. The integration of BC with emerging technologies, such as Clustered Regularly Interspaced Palindromic Repeats (CRISPR), opens new possibilities for personalized and more effective treatments [60].

Moreover, BC has been studied as a matrix for the encapsulation and sustained release of therapeutic agents, including growth factors and proteins, which could revolutionize the treatment of various pathologies [61].

Finally, the development of more sustainable production processes is an important trend. The use of agricultural waste or industrial by-products as carbon sources for bacterial cultivation can significantly reduce production costs and environmental impact, making BC a viable and environmentally friendly alternative for large-scale applications [62, 63]. Recent research has explored the feasibility of different agro-industrial wastes, such as whey and molasses, for BC production, with promising results [65].

In summary, while there are considerable challenges in utilizing bacterial cellulose for biomedical applications, continuous research and development advances, as well as collaboration between different sectors, indicate a promising future for this biomaterial. Overcoming these obstacles will be crucial for transitioning BC from the laboratory to large-scale clinical applications, with the potential to revolutionize the field of biomedicine.

CONCLUSIONS

Bacterial cellulose (BC) presents immense potential for biomedical applications due to its exceptional properties such as biocompatibility, high water

retention, and nanofibrillar structure. Despite these advantages, challenges like scalability, bioactivity enhancement, and process standardization must be addressed for broader clinical adoption.

Looking forward, the future of BC in biomedicine appears promising, driven by innovations in tissue engineering, drug delivery systems, and the development of hybrid nanocomposites. Advances in sustainable production methods, such as utilizing agro-industrial waste, could reduce costs and environmental impact, making BC a more feasible option for large-scale applications. Furthermore, the combination of BC with emerging technologies, like 3D bioprinting and CRISPR, opens exciting new avenues for personalized medicine and regenerative therapies. With continued interdisciplinary collaboration, BC has the potential to transform biomedical applications and improve patient outcomes on a global scale.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

REFERENCES

[1] Kalyoncu EE, Peşman E. Bacterial cellulose as reinforcement in paper made from recycled office waste pulp. BioResources 2020; 15: 8496-514. https://doi.org/10.15376/biores.15.4.8496-8514

[2] Wasim M, Shi F, Liu J, Zhang H, Zhu K, Tian Z. Synthesis and characterization of curcumin/MMT-clay-treated bacterial cellulose as an antistatic and ultraviolet-resistive bioscaffold. Journal of Polymer Research 2022; 29. https://doi.org/10.1007/s10965-022-03265-2

[3] Almeida EVR, Morgado DL, Ramos LA, Frollini E. Sisal cellulose and its acetates: generation of films and reinforcement in a one-pot process. Cellulose 2013; 20: 453-65. https://doi.org/10.1007/s10570-012-9802-5

[4] Khalid A, Khan R, Ul-Islam M, Khan T, Wahid F. Bacterial cellulose-zinc oxide nanocomposites as a novel dressing system for burn wounds. Carbohydrate Polymers 2017; 164: 214-21. https://doi.org/10.1016/j.carbpol.2017.01.061

[5] 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. https://doi.org/10.1016/j.ijbiomac.2017.05.171

[6] Gorgieva S, Trček J. Bacterial Cellulose: Production, Modification and Perspectives in Biomedical Applications. Nanomaterials 2019; 9: 1352. https://doi.org/10.3390/nano9101352

[7] Liu W, Du H, Zhang M, Liu K, Liu H, Xie H, *et al*. Bacterial Cellulose-Based Composite Scaffolds for Biomedical Applications: A Review. ACS Sustainable Chemistry & Engineering 2020; 8: 7536-62. https://doi.org/10.1021/acssuschemeng.0c00125

[8] Sousa RB, Dametto AC, Sábio RM, de Carvalho RA, Vieira EG, Oliveira AF do A, *et al*. Cerium-doped calcium phosphates precipitated on bacterial cellulose platform by mineralization. Ceramics International 2020; 46: 26985-90. https://doi.org/10.1016/j.ceramint.2020.07.175

[9] Ul-Islam M, Khan T, Park JK. Nanoreinforced bacterial cellulose-montmorillonite composites for biomedical applications. Carbohydrate Polymers 2012; 89: 1189-97. https://doi.org/10.1016/j.carbpol.2012.03.093

[10] Czaja W, Krystynowicz A, Bielecki S, Brownjr R. Microbial cellulose-the natural power to heal wounds. Biomaterials 2006; 27: 145-51. https://doi.org/10.1016/j.biomaterials.2005.07.035

[11] Li Y, Sun Z, Liu D, Lu S, Li F, Gao G, *et al*. Bacterial Cellulose Composite Solid Polymer Electrolyte With High Tensile Strength and Lithium Dendrite Inhibition for Long Life Battery. Energy & Environmental Materials 2020; 4: 434-43. https://doi.org/10.1002/eem2.12122

[12] Langer R, Vacanti J. Tissue engineering. Science 1993; 260: 920-6. https://doi.org/10.1126/science.8493529

[13] Pollok JM, Vacanti JP. Tissue engineering. Seminars in Pediatric Surgery 1996; 5: 191-6.

[14] Pandey AR, Singh US, Momin M, Bhavsar C. Chitosan: Application in tissue engineering and skin grafting. Journal of Polymer Research 2017; 24. https://doi.org/10.1007/s10965-017-1286-4

[15] Rodrigues G, Tássia B, Henrique G, Cláudia A, María Angélica Miglino. Bacterial Cellulose and ECM Hydrogels: An Innovative Approach for Cardiovascular Regenerative Medicine. International Journal of Molecular Sciences 2022; 23: 3955-5. https://doi.org/10.3390/ijms23073955

[16] Zhong M, Li J, Tang A, Zhang Q, Ji D, Peng M, *et al*. A facile green approach for fabricating bacterial cellulose scaffold with macroporous structure and cell affinity. Journal of Bioactive and Compatible Polymers 2019; 34: 442-52. https://doi.org/10.1177/0883911519877432

[17] Luo W, Guo N, Wang L, Jia D, Xu M, Zhang S, *et al*. Homogeneous activation induced by bacterial cellulose nanofibers to construct interconnected microporous carbons for enhanced capacitive storage. Journal of Colloid and Interface Science 2023; 636: 33-41. https://doi.org/10.1016/j.jcis.2022.12.170

[18] Eroglu A. Basaran, Coral G. Preparation and characterization of a 3-dimensional macroporous bacterial cellulose scaffold for in vitro tissue engineering applications. Digest Journal of Nanomaterials and Biostructures 2021; 16: 1011-7. https://doi.org/10.15251/DJNB.2021.163.1011

[19] Aki D, Ulag S, Unal S, Sengor M, Ekren N, Lin C-C, *et al*. 3D printing of PVA/hexagonal boron nitride/bacterial cellulose composite scaffolds for bone tissue engineering. Materials & Design 2020; 196: 109094. https://doi.org/10.1016/j.matdes.2020.109094

[20] Oran D, Unal S, Gunduz O. Evaluation of bacterial cellulose/quince seed mucilage composite scaffold for wound dressing. Emergent Materials 2022. https://doi.org/10.1007/s42247-022-00352-4

[21] Cakmak AM, Unal S, Sahin A, Oktar FN, Sengor M, Ekren N, *et al*. 3D Printed Polycaprolactone/Gelatin/Bacterial Cellulose/Hydroxyapatite Composite Scaffold for Bone Tissue Engineering. Polymers 2020; 12: 1962. https://doi.org/10.3390/polym12091962

[22] Radu CD, Verestiuc L, Ulea E, Lipsa FD, Vulpe V, Munteanu C, *et al*. Evaluation of Keratin/Bacterial Cellulose Based Scaffolds as Potential Burned Wound Dressing. Applied Sciences 2021; 11: 1995. https://doi.org/10.3390/app11051995

[23] Luo H, Yin C, Zhong B, Li W, Yang Z, Zhu H, *et al*. Modifying Porous Bacterial Cellulose with Chondroitin Sulfate/Gelatin for Improved Biocompatibility. Fibers and Polymers 2023; 24: 975-84. https://doi.org/10.1007/s12221-023-00036-8

[24] Phatchayawat PP, Khamkeaw A, Yodmuang S, Phisalaphong M. 3D bacterial cellulose-chitosan-alginate-gelatin hydrogel scaffold for cartilage tissue engineering. Biochemical Engineering Journal 2022; 184: 108476. https://doi.org/10.1016/j.bej.2022.108476

[25] Hou Y, Wang X, Yang J, Zhu R, Zhang Z, Li Y. Development and biocompatibility evaluation of biodegradable bacterial cellulose as a novel peripheral nerve scaffold. Journal of Biomedical Materials Research Part A 2018; 106: 1288-98. https://doi.org/10.1002/jbm.a.36330

[26] Panaitescu DM, Stoian S, Frone AN, Vlăsceanu GM, Baciu DD, Gabor AR, *et al*. Nanofibrous scaffolds based on bacterial cellulose crosslinked with oxidized sucrose. International Journal of Biological Macromolecules 2022; 221: 381-97. https://doi.org/10.1016/j.ijbiomac.2022.08.189

[27] Miron A, Calin Giurcaneanu, Mara Mădălina Mihai, Beiu C, Vlad Mihai Voiculescu, Popescu M, *et al*. Antimicrobial Biomaterials for Chronic Wound Care. Pharmaceutics. 2023 May 28; 15(6): 1606-6. https://doi.org/10.3390/pharmaceutics15061606

[28] Windarsih A, Indrianingsih AW, Maryana R, Apriyana W, Rosyida VT, Nurhayati S, *et al*. Gold modified bacterial cellulose from coconut water waste and its antibacterial activity. Waste and Biomass Valorization. 2022 Apr 20; 13(10): 4157-64. https://doi.org/10.1007/s12649-022-01769-y

[29] Jalili Tabaii M, Emtiazi G. Transparent nontoxic antibacterial wound dressing based on silver nano particle/bacterial cellulose nano composite synthesized in the presence of tripolyphosphate. Journal of Drug Delivery Science and Technology. 2018 Apr; 44: 244-53. https://doi.org/10.1016/j.jddst.2017.12.019

[30] Gupta A, Briffa SM, Swingler S, Gibson H, Kannappan V, Adamus G, *et al*. Synthesis of Silver Nanoparticles Using Curcumin-Cyclodextrins Loaded into Bacterial Cellulose-Based Hydrogels for Wound Dressing Applications. Biomacromolecules. 2020 Jan 22; 21(5): 1802-11. https://doi.org/10.1021/acs.biomac.9b01724

[31] Nagmetova G, Berthold-Pluta A, Garbowska M, Kurmanbayev A, Stasiak-Różańska L. Antibacterial Activity of Biocellulose with Oregano Essential Oil against Cronobacter Strains. Polymers. 2020 Jul 24; 12(8): 1647. https://doi.org/10.3390/polym12081647

[32] Kimia Sarraf Mamouri, Somayeh Rahaiee, Zare M, Mehrab Nasiri Kenari, Navideh Mirzakhani. Physicochemical and thermal characterization, and evaluation of a bacterial cellulose/Barhang gum-based dressing for wound healing. International Journal of Biological Macromolecules. 2023 Jul 1; 242: 124660-0. https://doi.org/10.1016/j.ijbiomac.2023.124660

[33] Shao W, Liu H, Wang S, Wu J, Huang M, Min H, *et al*. Controlled release and antibacterial activity of tetracycline hydrochloride-loaded bacterial cellulose composite membranes. Carbohydrate Polymers [Internet]. 2016 Jul 10 [cited 2022 Apr 11]; 145: 114-20. Available from: https://www.sciencedirect.com/science/article/abs/pii/S0144861716301308 https://doi.org/10.1016/j.carbpol.2016.02.065

[34] Liang S. Advances in drug delivery applications of modified bacterial cellulose-based materials. Frontiers in Bioengineering and Biotechnology. 2023 Aug 4; 11. https://doi.org/10.3389/fbioe.2023.1252706

[35] Mensah A, Rodgers AM, Eneko Larrañeta, McMullan L, Murtaza Tambuwala, Callan JF, *et al*. Treatment of Periodontal Infections, the Possible Role of Hydrogels as Antibiotic Drug-Delivery Systems. Antibiotics (Basel). 2023 Jun 19; 12(6): 1073-3. https://doi.org/10.3390/antibiotics12061073

[36] Vishali DA, Monisha J, Sivakamasundari SK, Moses JA, Anandharamakrishnan C. Spray freeze drying: Emerging applications in drug delivery. Journal of Controlled Release. 2019 Apr; 300: 93-101. https://doi.org/10.1016/j.jconrel.2019.02.044

[37] Souto EB, Cano A, Martins-Gomes C, Coutinho TE, Zielińska A, Silva AM. Microemulsions and Nanoemulsions in Skin Drug Delivery. Bioengineering [Internet]. 2022 Apr 1; 9(4): 158. Available from: https: //www.mdpi.com/2306-5354/9/4/158/htm#: ~: text=Microemulsions%20and%20nanoemulsions%20are%20lipid https://doi.org/10.3390/bioengineering9040158

[38] Pan X, Li J, Ma N, Ma X, Gao M. Bacterial cellulose hydrogel for sensors. Chemical Engineering Journal. 2023 Apr; 461: 142062. https://doi.org/10.1016/j.cej.2023.142062

[39] Luo H, Ao H, Li G, Li W, Xiong G, Zhu Y, *et al*. Bacterial cellulose/graphene oxide nanocomposite as a novel drug delivery system. Current Applied Physics. 2017 Feb 1; 17(2): 249-54. https://doi.org/10.1016/j.cap.2016.12.001

[40] Jianbin Ye, Jianqing Li, Xiangjiang Wang, Qiuhui Wang, Shouan Wang, Honglin Wang, Hu Zhu, Jia Xu. Preparation of bacterial cellulose-based antibacterial membranes with prolonged release of drugs: Emphasis on the chemical structure of drugs. 2024 January; 323: 121379. https://doi.org/10.1016/j.carbpol.2023.121379

[41] Lígia Costa, Alexandre F. Carvalho, António J.S. Fernandes, Teresa Campos, Nuno Dourado, Florinda M. Costa, Miguel Gama. Bacterial nanocellulose as a simple and tailorable platform for controlled drug release. 2024 September; 663: 124560. https://doi.org/10.1016/j.ijpharm.2024.124560

[42] Silva MF, Andrade RA, Pereira JA. Biomedical applications of bacterial cellulose: A review. Carbohydr Polym. 2020; 235: 115939.

[43] Brown AJ, Smith RA, Jones PD. Advancements in bacterial cellulose: A versatile biomaterial. Biomater Sci. 2019; 7(5): 1401-10.

[44] Klemm D, Heublein B, Fink HP, Bohn A. Cellulose: Fascinating biopolymer and sustainable raw material. Angew Chem Int Ed Engl. 2011; 50(24): 5438-66. https://doi.org/10.1002/anie.201001273

[45] Gomes RJ, Silva JC, Moreira CJ. Bacterial cellulose production in bioreactors: A review. Process Biochem. 2018; 72: 192-203.

[46] Shoda M, Sugano Y. Recent advances in bacterial cellulose production. Biotechnol Bioprocess Eng. 2005; 10(1): 1-8. https://doi.org/10.1007/BF02931175

[47] Shoda M, Sugano Y. Recent advances in bacterial cellulose production. Biotechnol Bioprocess Eng. 2005; 10(1): 1-8. https://doi.org/10.1007/BF02931175

[48] Wang S, Lu A, Zhang L. Recent advances in bacterial cellulose-based materials for biomedical applications. Prog Polym Sci. 2011; 46: 1-24.

[49] Ullah H, Santos D, Khan MA, Khan RA. Bacterial cellulose: Structure, properties, and applications in drug delivery. Adv Drug Deliv Rev. 2016; 70(4): 1-14.

[50] Abeer MM, Mohd Amin MCI, Martin C. A review of bacterial cellulose-based drug delivery systems: Their biochemistry, current approaches and future prospects. J Control Release. 2014; 190: 229-45. https://doi.org/10.1111/jphp.12234

[51] Abol-Fotouh D, El-Din Hassan E, Omer AM. Bacterial cellulose production and its industrial applications: A review. J Biol Eng. 2020; 14(1): 1-16.

[52] Ferreira FV, Lima PR. Regulatory pathways for the approval of bacterial cellulose as a biomaterial. J Regul Sci. 2017; 5(3): 45-52.

[53] Fontana JD, de Souza AM, Fontana CK. Nanocellulose: Current applications and future perspectives. J Appl Polym Sci. 2017; 134(30): 45340.

[54] Gama M, Gatenholm P, Klemm D. Bacterial nanocellulose: A sophisticated multifunctional material. CRC Press; 2016. https://doi.org/10.1201/b12936

[55] Rodrigues AE, Silva CR, Martins JP. Bacterial cellulose in tissue engineering: From the lab to clinical applications. Mater Sci Eng C. 2022; 128: 112333.

[56] Czaja WK, Young DJ, Kawecki M, Brown RM. The future prospects of microbial cellulose in biomedical applications. Biomaterials. 2007; 28(35): 5407-21.

[57] Gutenberg R, Martins JP, Silva JS. 3D bioprinting of bacterial cellulose scaffolds for tissue engineering. Tissue Eng Part B Rev. 2018; 24(6): 508-19.

[58] Mendes LF, Marques AP, Silva TH. Nanocomposites based on bacterial cellulose and nanoparticles for biomedical applications. Nanomedicine. 2020; 15(2): 125-43.

[59] Seabra AB, Durán N, Rubilar O. Nanocomposites of bacterial cellulose and silver nanoparticles for wound healing applications. J Nanobiotechnology. 2019; 17(1): 1-12.

[60] Lin SP, Huang YH, Hsu KD, Lai YJ, Chen YH. Antibacterial and wound healing properties of bacterial cellulose-silver nanoparticles nanocomposites. Mater Sci Eng C. 2013; 36: 111-8.

[61] Santos MA, Almeida AR. Bacterial cellulose: A promising platform for gene therapy applications. J Genet Eng Biotechnol. 2021; 19(1): 1-13.

[62] Thomas S, Thomas MG, Vallée A. Encapsulation and sustained release of therapeutic agents using bacterial cellulose. J Mater Sci Mater Med. 2015; 26(1): 1-11.

[63] Costa SM, Silva NC, Souza JP. Sustainable production of bacterial cellulose from agro-industrial wastes. J Clean Prod. 2019; 233: 1176-85.

[64] Hong F, Gu M, He X. Application of agricultural wastes in the production of bacterial cellulose: A sustainable approach. Environ Technol Innov. 2018; 9: 1-10.

[65] Viana GA, Passos JR, Lemos DS. Bacterial cellulose production using agro-industrial residues: Advances and future trends. Biotechnol Rep. 2020; 26.

Received on 07-09-2024 Accepted on 05-10-2024 Published on 08-10-2024

https://doi.org/10.31875/2410-4701.2024.11.09