

Bacterial Cellulose: A Novel Antibacterial Material for Biomedical Applications, Wound Healing, and Sustainable Infection Control

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Bacterial cellulose (BC) is an emerging biopolymer synthesized by specific microbial strains, such as *Komagataeibacter xylinus*. It is distinguished by its ultrafine nanofibrillar architecture, exceptional mechanical strength, high water-holding capacity, and inherent biocompatibility. Unlike plant-derived cellulose, BC is chemically pure and free from lignin and hemicellulose, making it especially attractive for biomedical use. Recently, BC has gained prominence as a multifunctional platform for applications in wound care, antimicrobial therapies, tissue engineering, and sustainable infection control. Recent advances in bioengineering and materials science have significantly broadened the functional landscape of BC. Through incorporating antibacterial agents, such as silver nanoparticles, chitosan, essential oils, or antibiotics, BC composites demonstrate potent antimicrobial efficacy while maintaining safety and biocompatibility. These hybrid materials address the critical need for novel, biodegradable alternatives to synthetic polymers in the fight against antibiotic-resistant pathogens. This brief review critically examines the latest progress in BC production technologies, structural functionalization strategies, and clinical applications, with particular emphasis on its antibacterial properties and regenerative potential. The molecular mechanisms underlying its interaction with microbial cells and host tissues are also explored. Furthermore, the review outlines key challenges, such as large-scale manufacturing, regulatory hurdles, and clinical validation, and presents forward-looking perspectives on how BC could revolutionize healthcare by supporting next-generation biomaterials and sustainable therapeutic solutions.

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INTRODUCTION

Cellulose, the most abundant biopolymer found in nature, is conventionally isolated from plant sources through a series of mechanical and chemical processes. In these methods, plant biomass such as wood, cotton, or agricultural residues is subjected to treatments that remove non-cellulosic components—including lignin, hemicellulose, and pectin—ultimately yielding purified cellulose fibers. This isolation process involves steps such as pulping, bleaching, and alkaline hydrolysis, rather than simple extraction, reflecting the complexity of separating cellulose from the intricate plant matrix. However, plant-derived cellulose typically contains accompanying substances, such as lignin and hemicellulose, which necessitate rigorous purification processes for biomedical use (Li *et al.* 2025). The lignin and hemicellulose in plant-derived cellulose affect the mechanical strength and result in variability in properties depending on the source and processing method. For example, cotton-derived cellulose requires chemical pretreatment to remove these waxy substances, and even after processing, its crystallinity and purity are lower than bacterial cellulose. As a result, rigorous purification is necessary to meet biomedical standards. In contrast, bacterial cellulose (BC), produced by specific microbial strains such as *Komagataeibacter xylinus* and *Gluconacetobacter hansenii* is synthesized in a highly pure form, exhibiting a unique nanofibrillar architecture that mimics the structure of the extracellular matrix (ECM) (Pandey *et al.* 2024). This fibrous network offers high crystallinity (up to 90%), remarkable tensile strength, and excellent moisture retention, all of which contribute to its compatibility with living tissues and its effectiveness in promoting cell adhesion and proliferation (Singh *et al.* 2020). However, it is important to note that the mechanical strength of BC significantly decreases when dried, which can restrict its use in applications requiring robust dry-state performance. To address this limitation, BC is frequently combined with other polymers or plasticizers, resulting in composite materials with improved mechanical stability in the dry state (Gorgieva and Trček 2019).

In the context of global health, infection control has become increasingly urgent due to the rise of antimicrobial resistance (AMR), which poses a serious threat to modern medical systems. Addressing this challenge requires the development of new materials that possess either inherent or engineered antimicrobial properties (Salam *et al.* 2023). Among these, BC has gained significant attention as a promising biomaterial not only for its mechanical and physicochemical advantages but also for its potential to be functionalized with antimicrobial agents as an excellent host matrix (Gorgieva and Trček 2019; Pandey *et al.* 2024; Selim *et al.* 2025a). This is due to its unique structural and physicochemical properties with a highly porous, 3D nanofibrillar network, which offers an extensive surface area and abundant hydroxyl functional groups. This architecture of BC facilitates the physical adsorption or chemical conjugation of various antimicrobial substances, allowing it to encapsulate and gradually release bioactive agents, thereby enhancing and sustaining antimicrobial activity (Chen *et al.* 2022).

The biocompatibility, biodegradability, and structural integrity of BC in hydrated environments make it especially suitable for biomedical applications, including wound dressings, tissue scaffolds, and vascular grafts (Czaja *et al.* 2007; Portela *et al.* 2019; Pandey *et al.* 2024; Selim *et al.* 2025b). More recently, efforts have focused on enhancing the antibacterial functionality of BC, either by exploiting its intrinsic properties or by integrating antimicrobial compounds such as silver nanoparticles, chitosan, or plant-derived extracts. These composite materials have shown promising results in combating a

broad range of pathogens and are being explored as sustainable alternatives in infection control strategies (Rahman *et al.* 2020; Wang *et al.* 2021).

This review offers a comprehensive analysis of BC as a bioactive antibacterial material, discussing its synthesis, antibacterial mechanisms, and expanding applications in wound healing, drug delivery, and sustainable medical solutions. Particular emphasis is placed on the integration of BC into next-generation biomedical technologies to support infection prevention and address the escalating AMR crisis.

BIOSYNTHESIS OF BACTERIAL CELLULOSE

BC is produced *via* aerobic microbial fermentation, primarily by acetic acid bacteria, which secrete cellulose as an extracellular product. However, bacterial cellulose synthesis is not limited to acetic acid bacteria. Other groups, including certain lactic acid bacteria (*e.g.*, *Lactiplantibacillus plantarum*, *Lactobacillus acidophilus*) and various species of *Sarcina* and *Agrobacterium*, have also been reported to generate BC, albeit typically at lower yields. This broader microbial diversity offers unique structural and functional properties for the resulting BC, expanding its potential applications in biomedical and industrial fields (Saleh *et al.* 2022; Umamaheswari *et al.* 2017; Gutierrez-Fernández *et al.* 2024). The biosynthesis process involves the polymerization of glucose into β -1,4-glucan chains, which then crystallize to form a robust nanofibrillar network. Among the most studied BC-producing genera is *Komagataeibacter*, previously classified under *Gluconacetobacter*, which includes strains, such as *Komagataeibacter xylinus*, which are known for their high cellulose yield and stable production performance (Table 1) (Li *et al.* 2019; Brown *et al.* 2021).

Table 1. Key Bacterial Strains Involved in BC Production

Bacterial Strain	Features	Reference
<i>Komagataeibacter xylinus</i>	High-yield, extensively studied; robust producer; well-characterized	Sumini <i>et al.</i> (2025)
<i>Gluconacetobacter hansenii</i>	Produces thick, gelatinous pellicles; high crystallinity	de Paiva <i>et al.</i> (2023)
<i>Acetobacter pasteurianus</i>	Industrial scalability; rapid growth; adaptable to different substrates	Nie <i>et al.</i> (2022)
<i>Komagataeibacter rhaeticus</i>	High cellulose productivity; tolerant to varying pH	Quiñones-Cerna <i>et al.</i> (2024)
<i>Komagataeibacter medellinensis</i>	Efficient at low pH; promising for industrial fermentation	Gorgieva <i>et al.</i> (2023)
<i>Gluconacetobacter entanii</i>	Tolerant to high ethanol concentrations; suitable for biofilm reactors	Rahman <i>et al.</i> (2021)
<i>Bacillus velezensis</i>	Engineered strain; high-yield in synthetic media	Bektas <i>et al.</i> (2025)

While BC production is most commonly associated with acetic acid bacteria such as *Komagataeibacter xylinus* and *Gluconacetobacter hansenii*, recent studies have demonstrated that certain lactic acid bacteria (LAB) also possess the capability to synthesize BC. For example, *Lactiplantibacillus plantarum* isolated from rotten fruit was

shown to produce up to 4.51 g/L of BC under optimized culture conditions, with the resulting membranes exhibiting antimicrobial activity against several pathogenic bacteria (Saleh *et al.* 2022). Similarly, *Lactobacillus acidophilus* has been reported to generate BC yields of approximately 1.84 g/L when cultured with glucose as the primary carbon source (Umamaheswari *et al.* 2017). Additionally, probiotic LAB strains such as *L. plantarum* and *L. fermentum* have been successfully immobilized within BC matrices, supporting the potential for developing functional probiotic-BC constructs for biomedical or food applications (Gutierrez-Fernández *et al.* 2024). These findings broaden the diversity of BC-producing microorganisms and highlight opportunities for novel applications where probiotic compatibility or specific membrane functionalities are desirable.

The efficiency and quality of BC production are influenced by several physicochemical and nutritional factors. These include the type and concentration of carbon and nitrogen sources, pH, temperature, and dissolved oxygen levels. For instance, glucose, fructose, glycerol, and mannitol are frequently used as carbon sources, while yeast extract, peptone, or ammonium sulfate provide essential nitrogen (Gorgieva and Trček 2019). Maintaining the pH within an optimal range (typically 4.0 to 7.0) and supplying sufficient oxygen is also critical, as BC synthesis is an oxygen-dependent process (Gullo *et al.* 2018).

Fermentation can be carried out under static or agitated conditions. In static cultures, BC forms as a thick gelatinous pellicle at the air-liquid interface, which is ideal for applications requiring high structural integrity. However, static fermentation is typically limited by lower productivity, longer cultivation times, and uneven oxygen diffusion, which can lead to variability in BC quality. In contrast, agitated cultures often produce irregular-shaped BC aggregates or spheres, which may be more suitable for certain composite or drug delivery applications (Portela *et al.* 2019). Nevertheless, agitated fermentation can result in lower degrees of polymerization and crystallinity, as well as increased risk of contamination and reduced mechanical properties due to shear forces. It has been shown that supplementation with 1% vegetable oil can boost BC production by over 500% while preserving or enhancing its mechanical and swelling properties (Żywicka *et al.* 2018).

Recent advances in metabolic engineering and synthetic biology have enabled the creation of genetically modified *Komagataeibacter* strains with dramatically improved BC yield, controlled microstructure, and the ability to incorporate functional polymers or pigments. Methods such as overexpressing the *bcsABCD* operon, introducing glycolytic enzymes from *E. coli*, and deleting the PQQ-dependent glucose dehydrogenase gene have led to 2- to 4-fold increases in BC production, along with reduced gluconic acid byproduct and improved crystallinity. Additionally, synthetic biology platforms—such as the *Komagataeibacter* Tool Kit (KTK)—now permit programmable expression of inducible promoters for biosynthesis of hyaluronic acid, melanin, and curli fibers directly within the BC pellicle (Singh *et al.* 2020; Goosens *et al.* 2021). Using microfluidic-based directed evolution, researchers have also screened tens of thousands of mutants to isolate strains with enhanced cellulose output and novel regulatory gene mutations, enabling BC materials tailored to distinct biotechnological or therapeutic uses (Zhong 2020). The metabolic steps involved in the biosynthesis of bacterial cellulose from various monosaccharides are illustrated in Fig. 1.

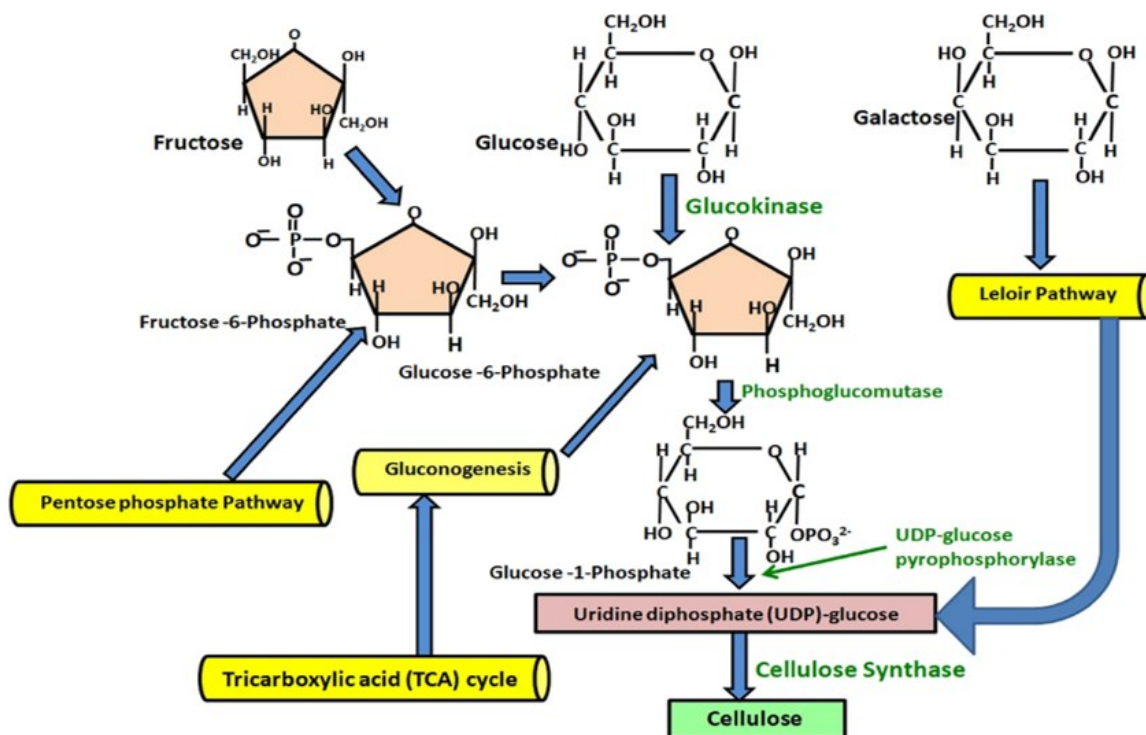


Fig. 1. Schematic representation of the bacterial cellulose biosynthesis pathway. The figure illustrates the metabolic conversion of simple sugars, such as glucose, fructose, and galactose, into cellulose. Key enzymatic steps—including phosphorylation by glucokinase, conversion by phosphoglucomutase, and formation of uridine diphosphate (UDP)-glucose—are highlighted, along with their respective intermediates. Branching metabolic routes, such as the pentose phosphate pathway, tricarboxylic acid (TCA) cycle, gluconeogenesis, and the Leloir pathway for galactose utilization, are shown in yellow. The pathway culminates in the synthesis of cellulose by cellulose synthase. Arrows indicate the direction of metabolic flow and key regulatory points are labeled for clarity. The figure has been reproduced with the permission from Pandey *et al.* (2024). Copyright 2024 by the Authors. Published by Springer under a Creative Commons Attribution 4.0 International License.

PHYSICOCHEMICAL PROPERTIES OF BACTERIAL CELLULOSE

BC is characterized by its ultrafine, nanoscale fibrous architecture, with scanning electron microscopy analyses revealing individual fibril diameters typically ranging from 20 to 100 nm (Martirani-VonAbercron *et al.* 2023). This intricate network results from the self-assembly of β -1,4-glucan chains during microbial fermentation, forming a highly porous, three-dimensional structure. Unlike plant-derived cellulose, BC is synthesized in a form almost completely free from lignin, hemicellulose, and pectin, as confirmed by compositional and spectroscopic analysis (Pogorelova *et al.* 2020). Such chemical purity contributes to its superior physical properties—Chunyan Zhong (Zhong 2020) has reported crystallinity indices of up to 90%, alongside exceptional water-holding capacity and mechanical strength. Collectively, these features make BC an ideal material for biomedical and advanced engineering applications. One of the most notable physical characteristics of BC is its high mechanical strength, with tensile strength values ranging between 70 and 250 MPa and Young's modulus of 7 to 14 GPa, particularly when measured in the hydrated or wet state, which is highly relevant for biomedical applications such as tissue scaffolds

and wound dressings (Gorgieva *et al.* 2023; Girard *et al.* 2024a; Lee *et al.* 2012). Remarkably, these values are significantly higher than those typically reported for conventional plant-based cellulose, even under similar conditions, highlighting BC's exceptional performance in physiological environments where moisture retention is critical. Figure 2 details intracellular metabolic conversions of sugars, such as fructose and glucose, into key intermediates (fructose-1-phosphate, fructose-6-phosphate, glucose-6-phosphate, glucose-1-phosphate), leading to the formation of UDP-glucose.

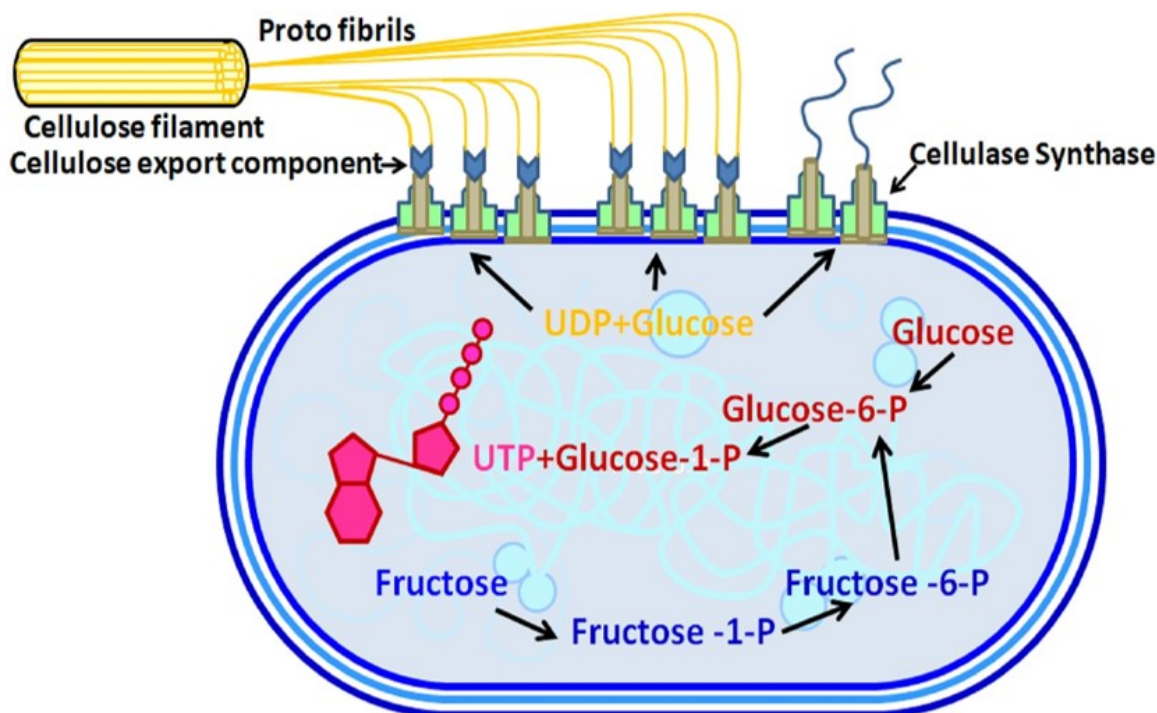


Fig. 2. Illustration of the cellular and enzymatic processes involved in bacterial cellulose production by *Acetobacter xylinum*. The figure illustrates intracellular metabolic conversions of sugars, such as fructose and glucose, into key intermediates (fructose-1-phosphate, fructose-6-phosphate, glucose-6-phosphate, glucose-1-phosphate), leading to the formation of UDP-glucose. UDP-glucose is then polymerized by cellulose synthase complexes in the cell membrane to generate protofibrils, which are exported outside the cell as cellulose filaments. The roles of cellulase synthase and cellulose export components are highlighted, demonstrating the coordinated process of cellulose biosynthesis and secretion. Arrows indicate the metabolic flow from substrate uptake to extracellular cellulose production. The figure has been reproduced with the permission from Pandey *et al.* (2024). Copyright 2024 by the Authors. Published by Springer under under a Creative Commons Attribution 4.0 International License.

Bacterial cellulose is renowned for its impressive mechanical properties, particularly in the hydrated state, where it exhibits high tensile strength (ranging from 70 to 300 MPa) and remarkable flexibility, making it well-suited for biomedical applications such as wound dressings and tissue scaffolds (Portela *et al.* 2019; Gorgieva *et al.* 2023). These favorable properties arise from its unique nanofibrillar network, high crystallinity, and exceptional water retention, which together provide the structural integrity and elasticity required for performance in moist environments. However, it is essential to note that these mechanical advantages are primarily observed when bacterial cellulose remains hydrated. In the dry state, bacterial cellulose loses much of its flexibility and becomes brittle and easily crushable, limiting its utility in applications where robust dry-state

performance is necessary (Gorgieva and Trček 2019; Pogorelova *et al.* 2020). Therefore, for uses that demand dry strength, bacterial cellulose is often modified or blended with other polymers to overcome this inherent limitation.

BC retains an impressive up to 99% of its dry weight in water due to its nanofibrillar, porous network—typically in hydrated membranes. This exceptional water-holding capacity helps maintain a moist wound environment, which accelerates re-epithelialization, supports angiogenesis, and minimizes scarring (Czaja *et al.* 2007). Moreover, BC exhibits high oxygen permeability in the hydrated (wet) state, facilitating gas exchange at the wound interface, promoting tissue regeneration, and reducing hypoxic stress (Rackov *et al.* 2025).

Importantly, BC is characterized by excellent biocompatibility, low cytotoxicity, and minimal immunogenic responses when applied *in vivo*. Studies have demonstrated its safety in contact with human skin and tissue, with no signs of irritation or rejection, supporting its use in implantable devices, dermal substitutes, and drug delivery systems (Helenius *et al.* 2006; Chen *et al.* 2022). BC's physicochemical stability, biodegradability, and ability to form flexible films or hydrogels make it an attractive platform for further functionalization with bioactive compounds, nanoparticles, or crosslinking agents for targeted biomedical applications (Chen *et al.* 2022). A detailed quantitative comparison of the key properties of bacterial cellulose and plant-derived cellulose is presented in Table 2.

Table 2. Quantitative Comparison Between Bacterial Cellulose and Plant-Derived Cellulose

Property/Feature	Bacterial Cellulose (BC)	Plant-Derived Cellulose
Source	Microbial fermentation	Wood, cotton, hemp, <i>etc.</i>
Purity (% cellulose)	>99%	40–60% (raw); requires purification
Fiber Diameter (nm/ μ m)	20 to 100 nm	5 to 50 μ m
Crystallinity Index (%)	80 to 90%	60 to 70%
Water Holding Capacity	Up to 100 to 200 times dry weight	60 to 70 times dry weight
Tensile Strength (MPa)	200 to 300 MPa	20 to 80 MPa
Young's Modulus (GPa)	7 to 14 GPa	2 to 6 GPa
Biocompatibility	Excellent (low cytotoxicity)	Good, but may require purification
Porosity (%)	60 to 90%	30 to 70% (varies by processing)
Production Rate	1 to 5 g/L/day (lab scale)	Not applicable (harvested from plants)
Environmental Impact	Low (fermentation, minimal waste)	Moderate–high (deforestation, chemicals)
Functionalization	Easy (can be <i>in situ</i> or <i>ex situ</i>)	More challenging; chemical modification
Typical Applications	Wound dressings, tissue scaffolds, drug delivery	Paper, textiles, composites, some biomedical

FUNCTIONALIZATION OF BACTERIAL CELLULOSE FOR ANTIBACTERIAL APPLICATIONS

Despite its impressive structural and biological traits, native BC does not possess antimicrobial capabilities. To address this, diverse functionalization techniques have been employed—transforming BC into infection-resistant biomaterials through integration with antimicrobial agents including silver nanoparticles, chitosan, essential oils, and antibiotics (Wang *et al.* 2021; Chen *et al.* 2022). The uniform dispersion of AgNPs within BC scaffolds has demonstrated high antibacterial efficiency, particularly against common pathogens such as *Escherichia coli* and *Staphylococcus aureus*. Girard *et al.* (2024b) demonstrated that unmodified BC is highly biocompatible, as shown by in vitro tests using Swiss 3T3 fibroblasts and INS-1 cells, where cell viability on or under BC membranes was comparable to controls (e.g., 3T3 viability under BC: 1.54 ± 0.23 vs. control: 1.00 ± 0.04). *In vivo*, subcutaneous implantation of BC in rats revealed that endotoxin-contaminated BC triggered inflammation, but depyrogenated BC induced only mild, transient inflammation after one week and minimal tissue response after two weeks, similar to medical-grade silicone (Girard *et al.* 2024b). Histological analysis confirmed no encapsulation or fibrosis and healthy integration with host tissue. These findings indicate that, although native BC lacks antimicrobial activity, it is non-cytotoxic and does not elicit chronic inflammation when properly purified.

The co-loading of multiple antimicrobial agents, such as silver nanoparticles and chitosan, onto bacterial cellulose (BC) has been shown to produce synergistic antibacterial effects, often surpassing the efficacy observed with single-agent composites. This synergy arises because each agent targets bacteria through distinct molecular mechanisms: silver nanoparticles primarily disrupt cell membranes, generate reactive oxygen species, and interfere with essential enzymes, while chitosan interacts with bacterial surfaces to increase membrane permeability and inhibit vital genetic functions. When combined within the nanofibrillar BC network, these agents can act in a complementary manner, leading to more rapid bacterial killing, enhanced inhibition of biofilm formation, and prolonged antimicrobial action. The BC matrix itself facilitates the uniform dispersion and close proximity of these active agents, further amplifying their collective impact and reducing the likelihood of bacterial resistance compared to the use of a single antimicrobial compound. The comparative antibacterial efficacy and duration of activity of various functionalized BC composites are summarized in Table 3.

Another promising agent is chitosan, a naturally derived polysaccharide known for its broad-spectrum antibacterial and antifungal activity. When integrated with BC, chitosan enhances the material's resistance to bacterial colonization and biofilm formation, especially against Gram-positive and Gram-negative bacteria, including *Staphylococcus epidermidis* and *Pseudomonas aeruginosa* (Rahman *et al.* 2020). In addition, essential oils—such as tea tree, clove, or oregano oils—have been successfully embedded into BC membranes. These natural extracts contain bioactive compounds like terpenes and phenolics that disrupt bacterial membranes and metabolic processes. The combination of BC and essential oils has shown broad-spectrum antimicrobial efficacy, making it suitable for wound dressings and packaging applications (Alves *et al.* 2023). Some essential oils incorporated into BC composites, such as tea tree and clove oil, are known skin sensitizers and may cause allergic reactions in sensitive individuals, including contact dermatitis. The risk depends on the specific oil, its concentration, and individual susceptibility. While BC

matrices may help control the release and reduce irritation, careful selection and testing of essential oils are needed before clinical use, especially for long-term skin contact.

Table 3. Antibacterial Composites of BC and Their Efficacy

Composite Material	Target Organisms	Observed Efficacy	Duration of Antibacterial Activity	Reference
BC + AgNPs	<i>E. coli</i> , <i>S. aureus</i>	> 90% reduction	Inhibition rate: 95% (3d), 93% (7d), 87% (14d)	Wang <i>et al.</i> (2021)
BC + Chitosan	<i>S. epidermidis</i> , <i>P. aeruginosa</i>	Biofilm inhibition	Biofilm inhibition: 80% (3d), 76% (7d), 69% (14d)	Rahman <i>et al.</i> (2020)
BC + Tea tree oil	Mixed flora	Inhibits both Gram-positive and Gram-negative bacteria (broad-spectrum activity)	Sustained inhibition (>70%) up to 7 days, moderate after 14 days	Alves <i>et al.</i> (2023)
BC + Tetracycline	<i>Streptococcus pyogenes</i>	Targeted antibiotic delivery	High efficacy (>90%) maintained for 7 days, gradual decline after 14 days	Klemm <i>et al.</i> (2011)

Antibiotic loading is a well-established strategy for imparting antimicrobial functionality to otherwise non-antimicrobial BC. By incorporating antibiotics into BC matrices, controlled release can be achieved at the site of infection, minimizing systemic toxicity and enhancing localized therapeutic effects. For example, BC loaded with tetracycline has been shown to effectively inhibit the growth of *Streptococcus pyogenes* in infected wound models (Klemm *et al.* 2011; Pal *et al.* 2017; Shaaban *et al.* 2023). Such modifications endow BC with strong antimicrobial activity while preserving or even improving its inherent biocompatibility, making it suitable for use in advanced wound dressings, implantable medical devices, and drug delivery systems. As illustrated in Fig. 3, the functionalization of BC with agents including AgNPs, chitosan, essential oils, and antibiotics enables a multipronged antibacterial mechanism, including membrane disruption, ROS-mediated oxidative stress, and targeted drug release.

Molecular Mechanisms Underlying the Antibacterial Activity of Functionalized BC

The antibacterial activity of functionalized BC composites is driven by a combination of the nanofibrillar structure and the incorporated bioactive agents, with the specific mechanism varying by agent. Silver nanoparticles (AgNPs) act by releasing Ag⁺ ions that disrupt proteins and cell membranes, increase membrane permeability, and generate reactive oxygen species (ROS), leading to oxidative damage and bacterial cell death (Morones *et al.* 20005; Dakal *et al.* 2016; Pal *et al.* 2017). Chitosan-functionalized BC employs electrostatic interactions to destabilize bacterial cell walls, increase membrane permeability, and inhibit gene expression, resulting in impaired growth and survival. Essential oils work through their hydrophobic components, which disrupt membrane integrity, affect metabolic processes, and interfere with quorum sensing and biofilm formation, thereby reducing bacterial virulence. Antibiotic-loaded BC scaffolds deliver drugs directly to infection sites, inhibiting critical bacterial enzymes and ensuring sustained exposure to minimize regrowth and resistance. Additionally, the porous BC network

enhances the uniform distribution and controlled release of antibacterial agents, and can physically trap bacteria, further boosting antimicrobial efficacy. Together, these mechanisms result in strong and broad-spectrum antibacterial properties in functionalized BC materials, making them highly effective for biomedical and infection control applications (Pal *et al.* 2017).

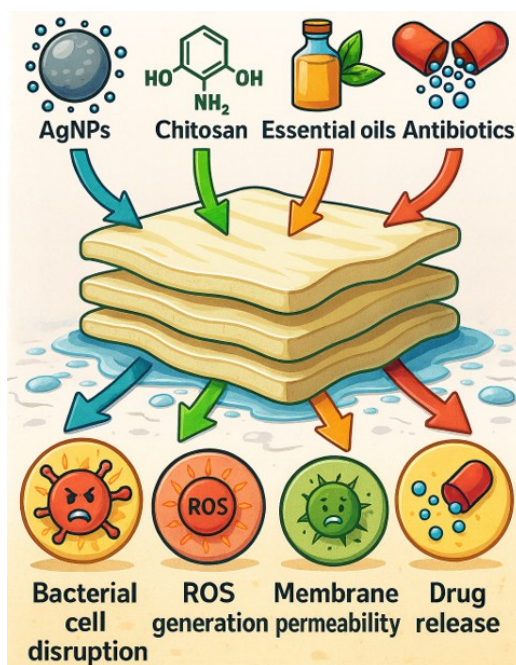


Fig. 3. Functionalization Strategies for Antibacterial BC Composites.

BIOMEDICAL APPLICATIONS OF BACTERIAL CELLULOSE

Wound Healing

BC is recognized as a promising material for wound healing applications because of its outstanding physicochemical properties and excellent biocompatibility. Its nanofibrous structure enables it to retain up to 99% of its weight in water, providing a moist wound environment that is essential for optimal healing. This high moisture content promotes faster re-epithelialization, minimizes scab formation, reduces tissue dehydration, and helps lower patient discomfort. Maintaining a moist wound environment with BC-based dressings accelerates cell proliferation and tissue regeneration, while also reducing trauma associated with wound desiccation. Owing to its high hydration capacity and skin-compatible nature, BC creates an ideal microenvironment for accelerated tissue regeneration. Its ability to retain moisture supports cell proliferation while minimizing scarring and discomfort—making it a superior candidate for treating burns, ulcers, and chronic wounds (Czaja *et al.* 2007; Portela *et al.* 2019).

Moreover, BC demonstrates excellent adherence to the wound bed without adhering to newly formed tissue, making dressing painless and reducing the likelihood of re-injury during changes (Fig. 4). These characteristics make BC especially useful for burn wounds, chronic ulcers, and other sensitive dermal injuries where minimal disturbance to regenerating tissue is paramount (Portela *et al.* 2019). For wound care, Shao *et al.* (2012)

reported on tetracycline hydrochloride-loaded BC membranes, which released approximately 80% of the antibiotic over 48 hours and showed clear inhibition zones against *Streptococcus pyogenes* and *S. aureus* in vitro bath (Shao *et al.* 2012). In another study, Xu *et al.* (2020) developed a vancomycin-loaded BC membrane used as a dural substitute in rabbits; their *in vivo* model demonstrated sustained antibiotic release over 7 days, with histology confirming reduced inflammatory markers and no adverse tissue reactions (Xu *et al.* 2020). For implantable applications, Scherner *et al.* (2014) showed that BC-based small-diameter vascular grafts (4 to 5 mm) implanted in sheep maintained 50% patency at 12 weeks, with histological evidence of endothelial and smooth muscle cell infiltration and minimal inflammation (Scherner *et al.* 2014). Additionally, Correia *et al.* (2024) demonstrated that BC hydrogels loaded with vancomycin effectively inhibited MRSA and MRSE growth and biofilm formation, with vancomycin minimum inhibitory concentrations (MIC) reduced by a factor of 10 when delivered from the BC matrix (Correia *et al.* 2024).

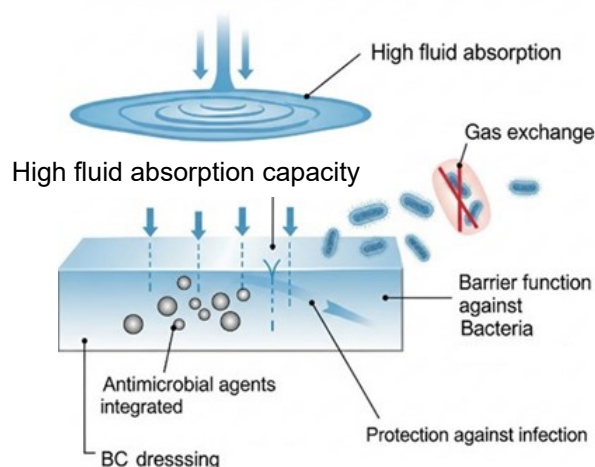


Fig. 4. Multi-functional aspects of the dressing, including antimicrobial agents, fluid absorption, gas exchange, and the prevention of bacterial growth

The incorporation of antimicrobial agents into BC matrices is indeed a form of functionalization, whereby the native BC structure is physically or chemically modified to impart new, desired properties—in this case, antimicrobial activity. Each additive operates *via* distinct mechanisms: silver nanoparticles (AgNPs) disrupt bacterial cell membranes and generate reactive oxygen species, leading to cell death; zinc oxide (ZnO) and cerium dioxide (CeO₂) nanoparticles exert antibacterial effects through oxidative stress and the release of metal ions, which interfere with microbial metabolism; essential oils contain bioactive compounds that disrupt membrane integrity and inhibit bacterial enzyme systems; chitosan, a cationic polysaccharide, binds to negatively charged bacterial surfaces, altering membrane permeability and preventing biofilm formation; and antibiotics function by specifically targeting microbial cell wall synthesis or protein production. This functionalization strategy allows the BC-based composite dressing to not only physically protect and maintain a moist wound environment but also to actively prevent infection through sustained, localized antimicrobial action (Meng *et al.* 2023; Dogaru *et al.* 2025).

Such antimicrobial BC dressings contribute in the following ways: Firstly, they provide infection prevention by inhibiting bacterial growth directly at the wound interface. The presence of antimicrobial agents disrupts bacterial cell membranes and biofilm formation, reducing the risk of secondary infections (Wang *et al.* 2021). Secondly, BC's porous nanofibrillar network enables it to absorb and retain large quantities of wound exudate. This exudate management helps maintain a clean wound environment while protecting the surrounding skin from maceration and inflammation (Portela *et al.* 2019). Thirdly, its soft, gel-like consistency not only provides a cushioning effect but also maintains a humid microenvironment that protects nerve endings and promotes pain reduction for patients. This makes BC dressings especially effective in improving patient comfort during long-term wound care (Helenius *et al.* 2006). Lastly, BC is an excellent drug delivery platform, capable of incorporating various therapeutic agents for localized, sustained release. Through delivering antibiotics, anti-inflammatory drugs, or growth factors directly to the wound bed, BC enhances healing outcomes and minimizes the need for systemic drug administration, reducing overall side effects and dosage frequency (Lin *et al.* 2020).

Drug Delivery Systems

BC has garnered significant interest as a highly effective drug delivery platform, primarily due to its unique nanofibrillar matrix, which provides an ideal structural framework for both loading and controlled release of therapeutic agents. This naturally derived polymer possesses an exceptional combination of attributes, including a remarkably high surface area, impressive water retention capabilities, and a valuable degree of structural tunability (Meng *et al.* 2023). BC's unique nano-structured three-dimensional network provides a very high specific surface area, excellent water retention (allowing it to absorb wound exudate and maintain a moist environment), and substantial structural tunability—meaning it can be readily engineered with polymers, inorganic agents, antibiotics, peptides, and antiseptics to meet specific clinical needs. For instance, the porous and hydrophilic network enables BC to uniformly embed antimicrobial agents and therapeutic molecules, supporting sustained release and superior healing. Its tensile strength, non-toxicity, and biocompatibility exceed those of many other biopolymers. Additionally, BC's surface hydroxyl groups and nanofibrillar structure enable both physical and chemical modifications, providing flexibility for the design of advanced wound dressings and composite materials. These characteristics collectively enable BC to effectively encapsulate a wide and diverse range of bioactive compounds, spanning from relatively small-molecule drugs to much larger and complex biomolecules such as peptides and proteins. Furthermore, the versatility of BC can be enhanced through various chemical and physical modifications; these alterations can be precisely employed to adjust critical properties, such as porosity, surface chemistry, or even its degradation rate, within a biological environment.

Ye *et al.* (2024) demonstrate that BC-based drug delivery membranes can be meticulously engineered to achieve different drug release profiles—including rapid burst, delayed, or sustained release—by modulating the chemical structure of the loaded drug and the mode of incorporation. In their experiments, BC membranes loaded with cefoperazone (BC-CEF) showed a high drug loading capacity (46.4 mg/g) and provided sustained release over 48 hours, maintaining antimicrobial activity throughout. In contrast, membranes loaded with cefoperazone sodium (BC-CEF/Na) exhibited a rapid burst release with 70% of the drug released within the first 60 minutes and only 20% released over the subsequent

period. This difference was attributed to variations in molecular interactions: BC-CEF's carboxyl groups formed stable bonds with BC, resulting in prolonged release, while BC-CEF/Na was more loosely incorporated, leading to faster diffusion. Both membrane types retained their nanofibrous architecture and exhibited excellent biocompatibility in cytotoxicity assays. These results highlight how BC's structure and surface chemistry enable precise control over drug release kinetics, making it possible to tailor delivery systems for specific therapeutic requirements (Ye *et al.* 2024).

Among the most extensively studied and promising applications of BC-based drug delivery systems are several critical areas in medicine. These include the localized delivery of antibiotics directly to infected wound sites, a method that offers significant advantages by minimizing systemic side effects typically associated with oral or intravenous administration while simultaneously improving treatment efficiency through targeted action (Carvalho *et al.* 2019).

BC is also being developed for the administration of anti-inflammatory drugs, particularly for chronic wounds and ulcers, where it can effectively modulate the local immune response, promoting better healing outcomes. Furthermore, its capacity to facilitate the release of crucial growth factors, such as VEGF (Vascular Endothelial Growth Factor) or EGF (Epidermal Growth Factor), makes it invaluable in regenerative therapies, where these factors stimulate essential processes such as tissue regeneration and angiogenesis (the formation of new blood vessels). Lastly, BC shows considerable potential in anticancer drug delivery, particularly for topical treatments or *in situ* (on-site) applications; in these scenarios, BC can function as a stable reservoir for cytotoxic agents, delivering them directly to localized tumors.

As noted by Gorgieva and Trček in 2019, these diverse and innovative applications not only substantially enhance therapeutic efficacy but also contribute to a crucial reduction in dosing frequency and, consequently, an improvement in patient compliance, which is especially important in long-term or sensitive treatment scenarios (Gorgieva and Trček, 2019).

BC-based wound dressings, artificial skin, blood vessel grafts, and drug delivery systems take advantage of BC's high crystallinity (84 to 89%), high water-holding capacity (over 100× its weight), flexibility, and biocompatibility. Notably, drug delivery systems using BC and its composites—including those with octenidine, methotrexate, and silymarin-zein nanoparticles—enable controlled, sustained release profiles. For example, octenidine-loaded BC/poloxamer hybrid systems achieved long-term, controlled antimicrobial release, while methotrexate-loaded BC/CMC composites demonstrated extended topical delivery for psoriasis, and silymarin-zein/BC nanocomposites slowed drug oxidation and sustained therapeutic action. Such modifications reduce the frequency of administration required and lead to more consistent therapeutic levels, directly supporting better patient adherence—particularly important in long-term or sensitive therapies.

The inherent ability of bacterial cellulose to conform readily to biological tissues and its remarkable capacity to interact positively with a broad spectrum of therapeutic compounds solidifies its position as an exceptionally versatile and promising tool for the development of next-generation drug delivery technologies (Carvalho *et al.* 2019). A comparative overview of various BC-based drug delivery systems—including their production methods, types of applied substances, release profiles, therapeutic outcomes, advantages, and limitations—is summarized in Table 4.

Table 4. Comparative Overview of BC-Based Drug Delivery Systems: Production, Substances Applied, Release Kinetics, Healing Outcomes, and Limitations

System/Type	Method of Production / Modification	Types of Drugs/ Substances Applied	Release Profile (Time of Action)	Healing/Therapeutic Outcome	Advantages	Limitations / Drawbacks
BC Antibiotic-loaded Membrane	Immersion loading or in situ incorporation of antibiotics	Tetracycline, Vancomycin, Cefoperazone	Sustained: 48h (tetracycline: 80% in 48h); Vancomycin: up to 7 days	Inhibits wound pathogens, accelerates wound healing, reduced inflammation	Localized, controlled delivery; minimizes systemic side effects; adaptable to various drugs	Initial burst release risk (some drugs); limited duration for severe infections; possible resistance
BC-Polymer Hybrid System	BC blended with hydrophilic polymers (e.g., CMC, poloxamer)	Methotrexate (for psoriasis), Octenidine, Silymarin-zein nanoparticles	Controlled and sustained (days–weeks)	Extended topical therapy (psoriasis), long-term antimicrobial action	Improved mechanical properties; tailored release; supports complex wound scenarios	Potential polymer/drug incompatibility; complex manufacturing; regulatory hurdles
BC-Growth Factor Loaded Hydrogel	Growth factors immobilized within BC hydrogel network	VEGF, EGF, Probiotics	Short to moderate (hours–days)	Enhanced tissue regeneration, angiogenesis; supports chronic wound healing	Promotes rapid healing, angiogenesis; biocompatible, minimally immunogenic	Short half-life of some factors; risk of uncontrolled cell growth; cost
BC-Anticancer Drug Carrier	BC membrane as reservoir for cytotoxic/anticancer drugs	Doxorubicin, Mitomycin C, Silymarin	Controlled (site-specific, hours–days)	Targeted tumor therapy; localized effect reduces systemic toxicity	Reduces side effects; suitable for topical/in situ cancer therapy	Limited to accessible tumors; drug diffusion barriers
BC-Essential Oil/Antiseptic Composite	Adsorption or physical entrapment of oils/antiseptics	Tea tree, Clove oil, Octenidine	Moderate (days–weeks, depending on oil/polymer)	Broad-spectrum antimicrobial action; supports wound disinfection	Natural origin; broad antimicrobial range; simple production	Potential allergenicity/sensitization; variable oil release
BC-Probiotic Delivery Matrix	Immobilization of live probiotics in BC network	Probiotic strains (L. plantarum, L. fermentum)	Sustained (hours–days; gradual release)	Combats drug-resistant infections, promotes gut/wound microbiota balance	Supports live cell delivery; unique approach for infection control	Probiotic viability; limited shelf-life; not for all indications

Tissue Engineering

BC has been extensively explored and recognized as a highly promising scaffold material for tissue engineering applications, largely because of its unique combination of properties. Its inherent biocompatibility ensures it is well-tolerated by biological systems, while its remarkable mechanical strength provides the necessary structural integrity for tissue constructs. Critically, BC's structural resemblance to the native extracellular matrix (ECM), the natural support network surrounding cells in tissues, makes it an ideal environment for promoting cellular functions. Specifically, it effectively supports cell adhesion, encourages cell proliferation (growth), and facilitates cell differentiation (specialization), all of which are fundamental processes for successful tissue regeneration. This versatility makes BC suitable for regenerating a diverse array of tissues, including complex structures, such as skin, cartilage, and even bone, as highlighted by Singh *et al.* (2020).

A significant advantage of BC scaffolds lies in their capacity for functionalization with antibacterial agents, which allows them to serve a dual purpose. Through incorporating these agents, BC scaffolds can simultaneously promote the vital process of tissue regeneration while also actively preventing post-operative infections, a persistent and major challenge in many implant-based therapies. Recent studies have compellingly demonstrated the broad potential of BC in various specific tissue engineering contexts. These include its use as a dermal substitute for treating severe full-thickness skin injuries, its application as chondrogenic scaffolds designed to facilitate cartilage repair, and its role as osteogenic supports in bone regeneration, particularly when combined with synergistic materials like hydroxyapatite or bioactive peptides, as evidenced by the work of Portela *et al.* (2019) and Gorgieva and Trček (2019).

Implants and Medical Devices

The integration of bacterial cellulose into implants and medical devices has opened new possibilities for infection prevention and long-term biocompatibility. Devices, such as catheters, vascular grafts, orthopedic implants, and prosthetic joints, are often compromised by bacterial adhesion and biofilm formation, which can lead to severe complications and implant failure (Klemm *et al.* 2011). BC can be employed as a coating material or structural component in these devices due to its excellent biocompatibility, flexibility, and ability to conform to complex surfaces. When combined with antimicrobial agents, like silver, copper, or antibiotic compounds, BC coatings create a protective antibacterial layer that actively resists microbial colonization while supporting tissue integration (Wang *et al.* 2021).

Studies have shown that BC-coated implants reduce the incidence of device-associated infections, enhance tissue integration, and extend the functional lifespan of implants. Its application in biosensors, wound closure systems, and artificial blood vessels is also gaining attention due to its non-toxic, biodegradable, and customizable nature (Helenius *et al.* 2006; Lin *et al.* 2020). Future innovations in this area may include smart BC-based coatings that respond to infection signals or inflammation by releasing antimicrobial agents on demand, paving the way for next-generation bioactive medical implants.

While BC offers exceptional purity, biocompatibility, and structural properties, several drawbacks must be considered. BC exhibits significant loss of mechanical strength when dried, limiting its use in applications requiring robust dry-state performance. Native BC also lacks inherent antimicrobial activity, necessitating further functionalization, which

adds complexity and regulatory hurdles. Challenges such as low industrial-scale yields, high production costs, and variability between batches remain barriers to commercialization. Additionally, incomplete purification can lead to endotoxin contamination, and the incorporation of certain additives, like essential oils or metal nanoparticles, may cause sensitization or allergic reactions in some individuals. Addressing these limitations is essential for the broader biomedical adoption of BC-based materials.

SUSTAINABLE INFECTION CONTROL

The growing demand for sustainable biomedical materials has directed attention toward BC as an environmentally responsible and clinically effective solution for infection control. BC offers numerous advantages aligned with the principles of green chemistry and sustainable healthcare, positioning it as a preferred material for combating infections in both clinical and community settings.

One of the primary advantages of BC is its renewability. It is synthesized through microbial fermentation using inexpensive, renewable carbon sources such as glucose, fructose, and even agricultural or food industry waste. This low-energy biosynthetic process generates minimal byproducts, distinguishing BC from petroleum-derived synthetic polymers that have greater environmental footprints (Gorgieva and Trček 2019).

Figure 5 provides a cyclical approach to sustainable infection control using bacterial cellulose. The cycle begins with the eco-friendly production of bacterial cellulose, emphasizing the use of agricultural byproducts as renewable feedstock. This raw cellulose then undergoes a functionalization process, where it is enhanced with antimicrobial agents, such as essential oils and silver nanoparticles, to impart infection-fighting properties. This stage transforms the basic cellulose into an active material ready for medical use.

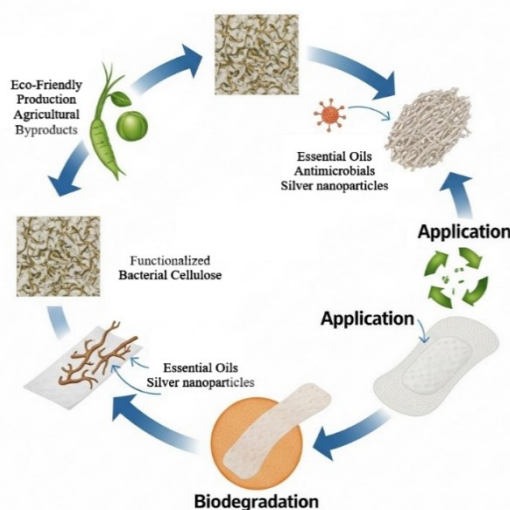


Fig. 5. Cellulose sustainable infection control cycle

The second part of the cycle focuses on the application and end-of-life of the functionalized bacterial cellulose. It is shown to be used as a medical application, for example, in wound dressings, where it helps manage and prevent infections. Crucially, the diagram highlights the material's biodegradability, showing the used product breaking

down and returning to the environment. This completes the sustainable loop, underscoring bacterial cellulose as an environmentally responsible alternative to conventional, non-degradable medical materials for infection control.

Table 5. Advantages and Disadvantages of BC for Biomedical Applications

Feature	Advantages	Disadvantages
Purity	Free from lignin and hemicellulose, high chemical purity (>99%), minimal need for further purification	—
Biocompatibility	Excellent compatibility, low cytotoxicity, minimal immunogenicity, suitable for implants and dressings	—
Mechanical Properties (Wet)	High tensile strength (70–300 MPa), good flexibility and integrity in hydrated state	Mechanical strength decreases sharply when dried; brittle in dry state; requires modification for dry applications
Water-Holding Capacity	Absorbs up to 100–200× dry weight, maintains moist wound environment, supports tissue regeneration	—
Structural Versatility	Nanofibrillar, 3D network supports cell adhesion, growth, and drug loading	Production of uniform, high-quality material can be inconsistent at large scale
Functionalization Potential	Easily modified with antimicrobial agents, drugs, polymers; customizable for diverse applications	Native BC lacks inherent antimicrobial activity; functionalization adds complexity and regulatory challenges
Production Process	Can use renewable substrates; environmentally friendly, low waste, biodegradable	Industrial yields are low, high cost of fermentation media, scale-up is challenging
Drug Delivery	Supports sustained and controlled release, localizes therapy, reduces systemic side effects	Possible burst release, limited duration for some drugs, potential incompatibility with some compounds
Antibacterial Application	Can be combined with AgNPs, chitosan, essential oils, antibiotics for potent antibacterial effects	Risk of allergenicity or sensitization (essential oils, some agents); resistance development possible
Environmental Impact	Biodegradable, reduces medical waste, supports green healthcare initiatives	—
Clinical Translation	Demonstrated in wound dressings, implants, drug delivery, tissue scaffolds	Batch-to-batch variability, need for stringent endotoxin removal, regulatory approval needed
Cost & Economic Viability	Potential use of waste streams as substrate	Overall production costs still higher than plant cellulose or synthetic polymers

BC is also fully biodegradable, meaning that it decomposes naturally in the environment without releasing toxic residues. This characteristic reduces the accumulation of medical waste and aligns well with the objectives of circular bioeconomy models. Medical products made from BC, such as wound dressings or disposable antimicrobial sheets, can thus serve as eco-friendly alternatives to non-degradable plastics. In addition to its environmental merits, BC supports sustainable infection control strategies by offering a

platform for localized and targeted antimicrobial delivery. Through incorporating silver nanoparticles, essential oils, or antibiotics directly into the BC matrix, medical devices or wound dressings can deliver site-specific antibacterial action, reducing the need for systemic antibiotics. This approach helps to lower the risk of antibiotic resistance—a major global health concern (Wang *et al.* 2021).

Furthermore, BC's non-toxic, non-immunogenic nature ensures that it can be safely applied to the skin, and mucosal surfaces, or implanted without provoking adverse reactions. Its use in reusable personal protective equipment (PPE), antimicrobial packaging, and filter membranes (*e.g.*, for air or water purification) is being actively explored, making it a versatile material for public health applications beyond traditional clinical use (Lin *et al.* 2020). Looking ahead, integrating BC into smart infection control systems—such as responsive dressings that release antimicrobials upon detecting bacterial enzymes or changes in pH—could further improve its utility and reduce the reliance on broad-spectrum antibiotics. As regulatory frameworks and industrial-scale production methods advance, BC is poised to become a cornerstone in sustainable, high-performance biomaterials for infection prevention. A comparative summary of the major advantages and disadvantages of bacterial cellulose for biomedical applications is provided in Table 5.

A summary of major commercially translated bacterial cellulose-based products, their applications, regulatory status, and key challenges is provided in Table 6.

Table 6. Commercial Translation of Bacterial Cellulose: Companies, Products, Applications, and Challenges

Company/ Initiative	Product Name/Type	Primary Application	Notable Features	Challenges / Limitations	References
JeNaCell (Evonik, Germany)	epicite@hydr o, epicite@bala nce	Advanced wound dressings	Maintains moist environment, adaptable to chronic and acute wounds	High production costs, limited dry strength	https://www.jenacell.com/en
Axcelon Biopoly- mers (Canada)	Axcelon BC Scaffold	Tissue engineering, wound healing	Customizable for cell growth, regenerative applications	Regulatory approval pending, scalability	https://axcelonbp.com/
Amferia (Sweden)	Antimicrobial BC wound dressing	Infection control, wound care	Incorporates anti-microbial peptides	Clinical validation and regulatory pathway ongoing	https://www.amferia.com/

CONCLUSION AND FUTURE PERSPECTIVES

Bacterial cellulose is emerging as a highly sustainable and multifunctional biomaterial, offering a rare combination of mechanical resilience, physiological compatibility, and exceptional functional versatility. Its unique nanofibrillar structure, high water-holding capacity, and chemical purity distinguish it from plant-derived cellulose, making it particularly attractive for advanced biomedical applications such as wound healing, drug delivery, tissue engineering, and infection control. One of the most compelling advantages of bacterial cellulose lies in its adaptability to functionalization: by incorporating antimicrobial agents—including metal nanoparticles, natural extracts, and antibiotics—bacterial cellulose-based materials can directly address urgent healthcare challenges, notably the rapid emergence of antimicrobial resistance. The resulting

composite materials provide effective platforms for advanced wound dressings, controlled drug delivery, and anti-infective coatings for implantable medical devices.

Beyond its technical merits, bacterial cellulose aligns closely with the principles of sustainable development. Its microbial fermentation process can utilize renewable carbon sources and generate minimal waste, thereby supporting environmentally responsible manufacturing and reducing the ecological footprint of biomedical materials. However, the path from laboratory-scale innovation to widespread clinical adoption is not without significant challenges. The production of bacterial cellulose on an industrial scale is hindered by relatively low yields, high costs of fermentation media, batch-to-batch variability, and the need for stringent purification to eliminate endotoxin contamination. Moreover, the mechanical strength of bacterial cellulose diminishes substantially when dried, requiring additional processing—such as blending with polymers or incorporating plasticizers—to achieve adequate dry-state performance. The absence of intrinsic antimicrobial activity in native bacterial cellulose further necessitates additional functionalization steps, which may introduce regulatory and safety complexities, especially regarding the long-term effects of incorporated agents.

Looking forward, the outstanding properties of bacterial cellulose raise the expectation of numerous future applications, not only in wound care and drug delivery but also in tissue engineering scaffolds, artificial blood vessels, biosensors, and sustainable personal protective equipment. Realizing these opportunities will require continued interdisciplinary collaboration among material scientists, microbiologists, clinicians, and regulatory authorities. Key priorities include optimizing the fermentation process for higher yield and lower cost, developing scalable and reproducible manufacturing methods, ensuring consistent product quality, and thoroughly evaluating clinical safety and efficacy. Furthermore, a balanced assessment of bacterial cellulose-based technologies must account for both their potential and their limitations—including processability, economic viability, and safety considerations—to support the responsible and effective integration of this promising biomaterial into mainstream healthcare.

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Data Availability

All datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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