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Potential of Bacterial Cellulose for Various Medical Applications

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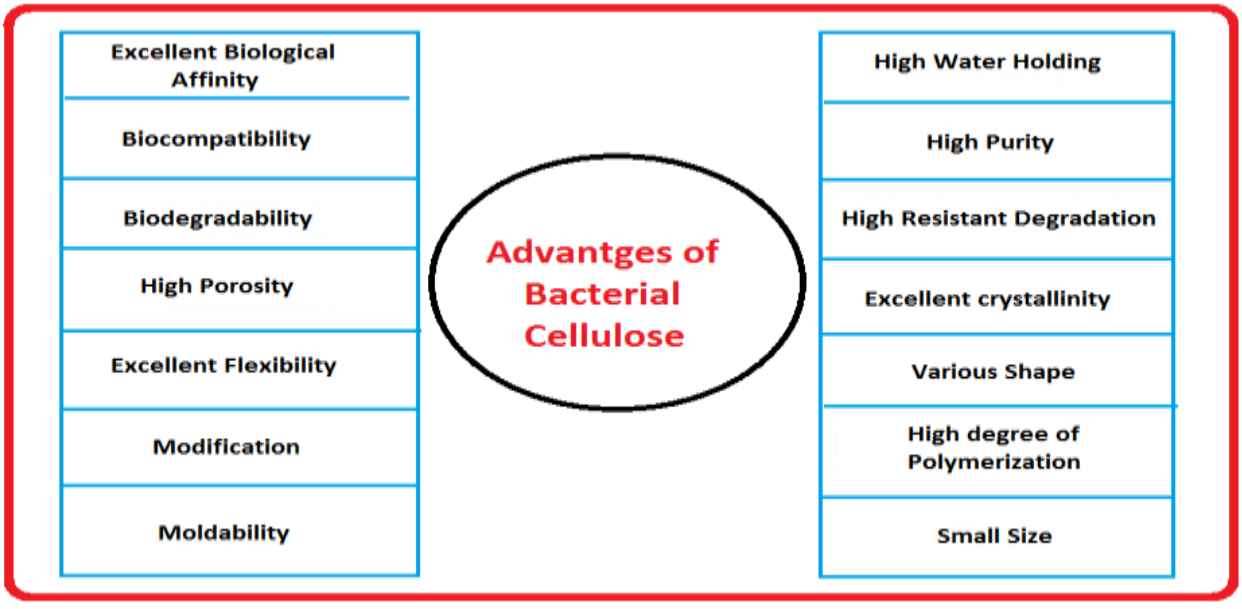
Abstract
Bacterial cellulose (BC) is a highly pure and crystalline biopolymer produced by various aerobic bacteria, exhibiting unique properties compared to plant cellulose, such as transparency, porosity, high water-holding capacity, and flexibility. BC, alone or in combination with other components (e.g., biopolymers and nanoparticles), has a wide range of applications, including medical products, electronic devices, and food ingredients. Biomedical applications of BC have attracted significant attention due to the growing demand for advanced wound care, tissue regeneration, disease diagnostics, and drug delivery systems. Bacterial cellulose offers substantial potential for developing innovative materials in healthcare, and this review presents comprehensive information on BC production by *Acetobacter xylinum* and its medical applications. The latest advances in the use of BC in medicine, both in pure and composite forms, are thoroughly discussed.

Keywords: Bacterial cellulose, *Acetobacter xylinum*, *Tissue engineering, Drug delivery, Skin care, wound dressing and factor affecting*

Graphical abstract:



1. Introduction

Cellulose is the most abundant natural biopolymer in the world, synthesized by plants, algae, tunicates, and certain bacteria, and it plays a vital role in numerous industries such as textiles, packaging, paper, food, and biomedicine owing to its renewable, biodegradable, and versatile properties [1,2]. Four main pathways of cellulose production are recognized: seed fibers such as cotton contain up to 90% cellulose, bast fibers such as jute and flax contain about 60%, regenerated natural polymers contain approximately 50%, while bacterial cellulose (BC) contains nearly 100% cellulose in a highly pure form [3]. Plant-derived cellulose requires extensive processing to remove lignin and hemicellulose, which increases cost and energy consumption, whereas BC is synthesized directly as pure cellulose without such impurities, making it a sustainable alternative [4]. The discovery of BC was first reported by Brown in 1886, who described the production of unbranched pellicles with a structure chemically equivalent to plant cellulose [5]. Since then, bacterial cellulose has been studied extensively, with *Acetobacter xylinum* (reclassified as *Komagataeibacter xylinus*) recognized as the most efficient cellulose-producing bacterium due to its high yield, stable biosynthesis, and ability to produce cellulose with remarkable physical and mechanical properties including high crystallinity, water-holding capacity, tensile strength, flexibility, biocompatibility, and biodegradability [6]. The biosynthesis of BC occurs through microbial metabolism, in which carbon sources such as glucose, sucrose, fructose, glycerol, ethanol, and various agro-industrial residues are converted into uridine diphosphoglucose (UDP-glucose), which is then polymerized into β-(1→4)-D-glucan chains [7]. These glucan chains undergo crystallization and assemble into elementary nanofibrils with diameters of 3–8 nm, which further aggregate into microfibrils 50–80 nm wide, forming a three-dimensional porous network stabilized by intra- and intermolecular hydrogen bonding [8]. This unique nanostructure gives BC superior mechanical strength, high surface area, and the ability to hold up to 90–99% water, distinguishing it from plant cellulose, which typically contains impurities and lower crystallinity [9]. To reduce production cost and increase yield, researchers have investigated the use of low-cost substrates such as molasses, fruit juices, starch hydrolysates, and agricultural by-products like corn steep liquor, rice husk hydrolysate, and sugarcane bagasse [10].

The fabrication of BC can be achieved by several techniques, including static culture, agitated culture, and advanced bioreactor systems. In static culture, BC forms pellicles at the air–liquid interface, yielding highly crystalline membranes with dense fibrillar networks, which are particularly suitable for biomedical applications [11]. In agitated or shaking culture, BC is produced in the form of irregular particles, fibers, or spheres, with reduced crystallinity but scalability advantages [12]. More recently, bioreactor-based fermentation methods such as stirred-tank reactors, airlift reactors, rotating disk bioreactors, and trickling bed systems have been developed to overcome oxygen transfer limitations and to enable controlled, large-scale production [13]. Each method influences the morphology, crystallinity, and mechanical properties of BC, allowing tailoring of its structure for specific applications. Despite these advances, the commercial production of BC still faces challenges of high cost, relatively low productivity, and scale-up limitations, which continue to be addressed by optimizing fermentation strategies and genetic engineering of strains [14].

Although BC inherently exhibits superior physical and biological properties compared to plant cellulose, it lacks certain functional characteristics such as antibacterial activity, optical transparency, and adequate load-bearing capacity, which limit its direct use in advanced applications. To overcome these drawbacks, various modification strategies have been employed, including physical, chemical, and biological approaches. One common strategy is blending BC with natural polymers such as collagen, alginate, chitosan, hyaluronic acid, and fibrin glue, which enhances its biocompatibility, cell adhesion, and biological performance [15]. Similarly, incorporation of synthetic polymers such as polylactic acid (PLA), polyvinyl alcohol (PVA), polyglycolic acid (PGA), polyhydroxyethyl methacrylate (pHEMA), and poly-N-isopropylacrylamide (pNIPAA) has been used to improve mechanical properties, adjust degradation rates, and expand biomedical applications [16]. Functionalization with nanoparticles represents another important modification method, where the introduction of silver nanoparticles, zinc oxide nanoparticles, and hydroxyapatite provides antibacterial, antimicrobial, osteoconductive, or conductive properties, making BC suitable for wound dressings, bone regeneration scaffolds, and bioelectronic devices [17]. In situ modification during

fermentation, by adding reinforcing agents or altering culture conditions, is also an emerging approach to directly control the density and network structure of BC fibrils [18].

These advancements have greatly expanded the range of BC applications. In the biomedical field, BC is utilized in wound dressings, artificial skin, blood vessel grafts, cartilage scaffolds, and drug delivery systems, benefiting from its biocompatibility, porosity, and ability to mimic extracellular matrices [19]. For example, BC wound dressings not only maintain a moist environment conducive to healing but also can be functionalized with antibacterial nanoparticles for infection control [20]. In tissue engineering, BC scaffolds have been engineered to replicate collagen fibril networks, showing promise in vascular grafts and bone regeneration [21]. In food technology, BC is applied in the production of nata de coco, functional dietary fibers, and as a stabilizer or gelling agent in beverages and desserts [22]. In electronics, BC is being investigated as a substrate for flexible displays, acoustic diaphragms, biosensors, and conductive composites due to its flexibility and nanofibrillar structure [23]. Looking toward the future, ongoing research focuses on enhancing BC production by using genetically engineered strains with improved metabolic pathways, exploiting lignocellulosic biomass and industrial waste streams as low-cost substrates, and designing multifunctional BC-based nanocomposites for next-generation applications in healthcare, sustainable packaging, and flexible electronics [24,25]. Collectively, these studies demonstrate that bacterial cellulose is not only an environmentally friendly and renewable biomaterial but also a versatile platform with immense potential to address current and future challenges in biomedicine, food, textiles, and advanced materials science.

2. Biogenesis of Bacterial Cellulose

Biosynthesis of bacterial cellulose (BC) is a complex and highly regulated aerobic process involving multiple enzymes and regulatory proteins. It is closely linked with cellular catabolism but does not interfere with other anabolic pathways such as protein synthesis in bacterial cells. Interestingly, BC can also be synthesized under anaerobic conditions in a cell-free system through cellulose-producing enzymes and cofactors. The pathway of uridine diphosphate-glucose (UDP-glucose) formation is well studied, although the subsequent glucose polymerization into cellulose is not yet completely understood [1, 25].

2.1. Biochemical Pathway of BC Synthesis

Despite cellulose being a relatively simple linear β-(1→4)-linked glucan, the biochemistry of its synthesis is not fully elucidated due to difficulties in establishing in vivo assays and purifying key enzymes such as cellulose synthase. These limitations are gradually being addressed using combined genetic and biochemical techniques with *Acetobacter xylinum* (syn. *Komagataeibacter xylinus*), providing clearer insights into the process [2]. Besides glucose, other carbon substrates including hexoses, hexonates, pyruvate, glycerol, and dihydroxyacetone may serve as precursors for BC biosynthesis [2,25].

The biosynthesis proceeds in two main stages. The first stage involves the synthesis of UDP-glucose (UDP-Glc) from carbon substrates through metabolic routes such as the Krebs cycle, gluconeogenesis, or the pentose phosphate pathway. This involves phosphorylation, catalysis, isomerization of intermediates, and conversion to UDP-Glc by the enzyme UDP-glucose pyrophosphorylase [3–4,24]. The second stage is polymerization, in which UDP-Glc units are assembled into long unbranched β-(1→4)-glucan chains by cellulose synthase. While the involvement of a lipid intermediate in this step has been hypothesized [3,5], structural enzymology and in vitro studies also suggest that polymerization may occur directly through enzymatic transfer of glucosyl moieties from nucleotide sugars to the growing polysaccharide chain [6]. Typically, *A. xylinum* converts carbon substrates to cellulose with nearly 50% efficiency [5]. As illustrated in Figure 1, the pathway begins with the formation of UDP-Glc, followed by polymerization into β-(1→4)-glucan chains, which then aggregate into ribbon-like fibrils consisting of hundreds or thousands of chains. These microfibrils are extruded extracellularly through a membrane protein complex, cellulose synthase, which organizes them into the characteristic three-dimensional nanofibrous structure of BC [7,25].

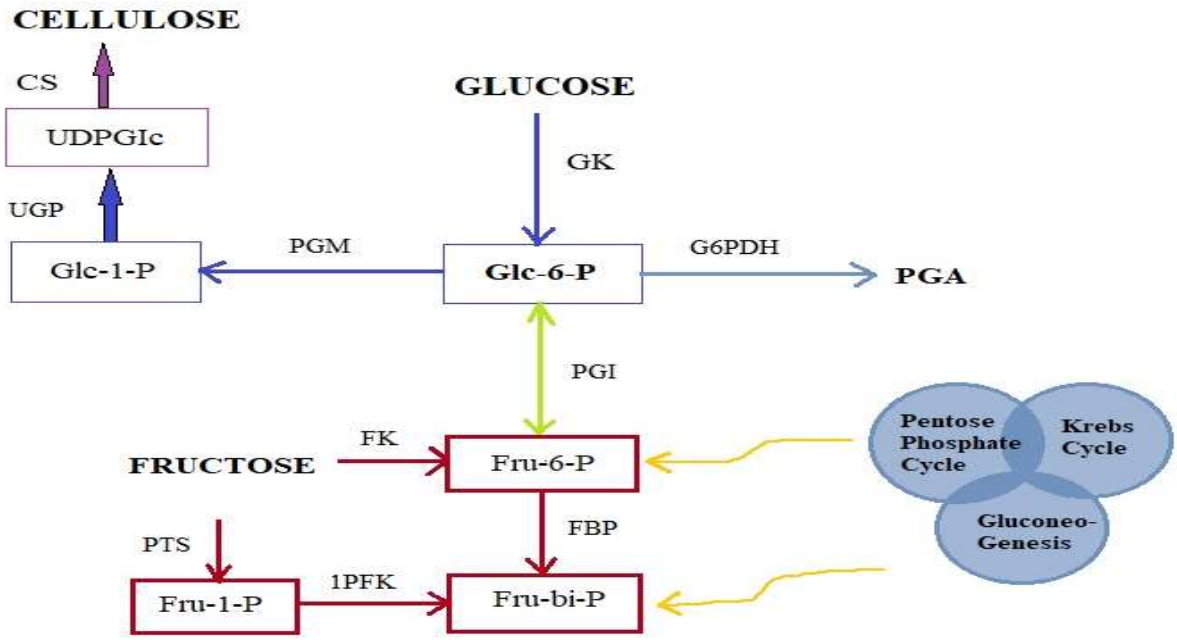


Fig.1- Biochemical Pathway for Cellulose Synthesis.

3. Revival of Bacterial Culture

The first critical step in laboratory synthesis of bacterial cellulose is the revival and maintenance of bacterial cultures. Figure 2 illustrates the process of bacterial revival, BC production, and preservation of bacterial stock for sustained laboratory production. Typically, lyophilized or glycerol-preserved cultures of *K. xylinus* or related species are revived on agar plates supplemented with HS medium. After revival, colonies are transferred to liquid seed cultures where they proliferate and form cellulose at the air–liquid interface. This inoculum is later used for production in larger flasks or bioreactors [8].

Maintaining bacterial stock cultures is essential for ensuring reproducibility and consistency in cellulose production. Stocks are usually stored at –80 °C in cryoprotective agents such as glycerol or dimethyl sulfoxide (DMSO). Periodic revival ensures that the bacterial strains retain their cellulose-producing capability. Variations in storage time, genetic drift, or contamination can significantly reduce yield or alter the morphology of BC pellicles. Therefore, strict aseptic techniques and routine verification of cellulose productivity are indispensable for laboratory practice. Revival also plays a role in standardizing inoculum preparation, which affects the lag phase and overall productivity of bacterial cultures. In BC research, inoculum density, pre-culture time, and revival conditions directly influence the thickness, uniformity, and yield of cellulose pellicles [9]. Laboratory protocols therefore emphasize optimizing revival and stock maintenance as the foundation for scalable and reproducible BC production.

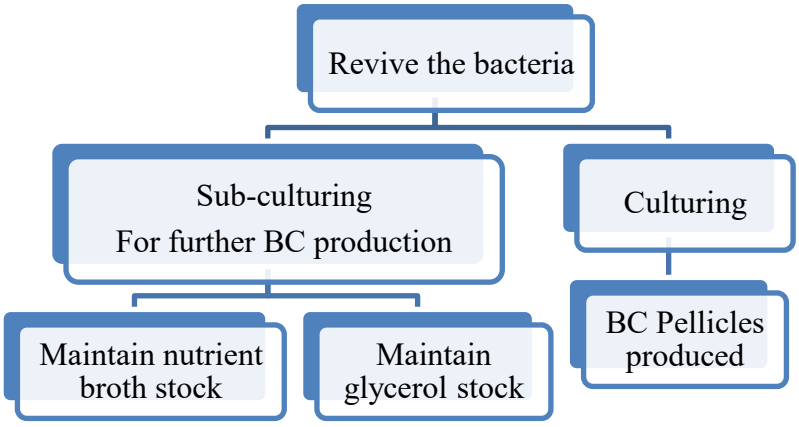


Fig. 2: flow diagram of revival of bacteria for BC production

4. Bacterial Cellulose Production

The biosynthesis of bacterial cellulose is a complex biochemical process that integrates carbon metabolism with cellulose polymerization and crystallization. Figure 3 presents a simplified flow diagram of BC synthesis by *Acetobacter xylinum*. The pathway begins with the uptake of glucose, which is phosphorylated by glucokinase to form glucose-6-phosphate. This intermediate undergoes conversion by phosphoglucomutase into glucose-1-phosphate, which is further catalyzed by UDP-glucose pyrophosphorylase to generate uridine diphosphate glucose (UDP-Glc). Finally, cellulose synthase catalyzes the polymerization of UDP-Glc into linear β-(1→4)-glucan chains, which assemble into microfibrils and subsequently crystallize into a 3D nanofibrillar network [24–25]. During biosynthesis, polymerization and crystallization occur simultaneously, resulting in the characteristic ribbon-like cellulose fibrils that aggregate into microfibrils with widths of 50–80 nm and thicknesses of 3–8 nm [9]. Unlike plant cellulose, which requires extensive purification to remove lignin and hemicellulose, bacterial cellulose is inherently pure, highly crystalline, and produced in a gel-like pulp form. Its nanoscale fibrillar architecture contributes to its unique properties, including high tensile strength, porosity, and water absorption capacity. The efficiency of cellulose synthesis depends on the availability of carbon substrates and cofactors. In addition to glucose, bacteria can utilize other carbon sources such as fructose, sucrose, mannitol, pyruvate, and glycerol for cellulose biosynthesis [10–12]. The conversion efficiency of *K. xylinus* has been reported to be around 50%, with variations based on substrate type, oxygen availability, and nutrient balance [5]. Importantly, the polymerization mechanism is hypothesized to proceed either directly via enzymatic transfer of glucosyl units or through a lipid-linked intermediate [6]. Structural enzymology studies continue to explore the exact mechanism of chain elongation and crystallization. The crystalline microfibrils secreted by the bacterial cells are extruded into the extracellular matrix through terminal complexes embedded in the bacterial cell membrane, where they assemble into the characteristic nanostructured cellulose ribbons. This highly organized biosynthetic machinery distinguishes bacterial cellulose from other microbial polysaccharides and underpins its advanced performance in engineered applications. Similarly, previous studies efforts is showing different route of BC synthesis as shown in Table.1

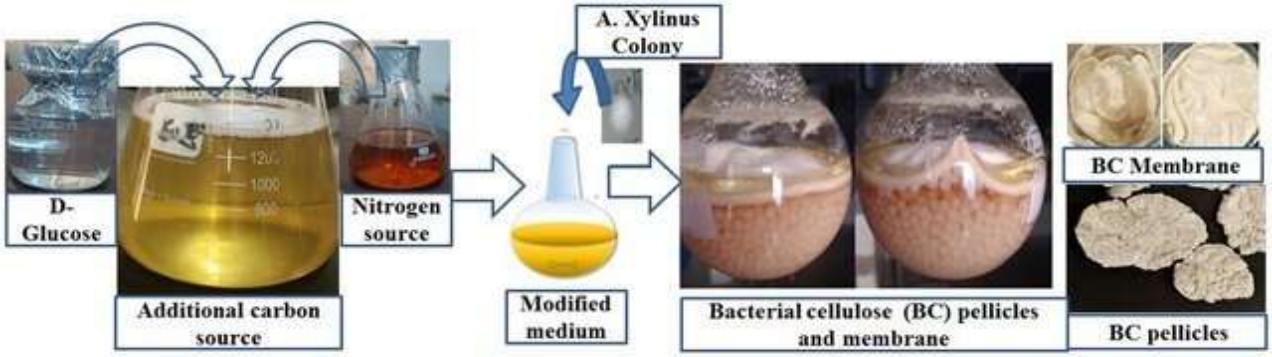


Figure 3: Flow diagram of BC sphere and pellicle synthesis in Hestrin- Schramm medium under four days dynamic incubation and three days static incubation by Acetobacter xylinum.

5. Fabrication of Bacterial Cellulose

Bacterial cellulose (BC) was first reported in 1954 with a yield of 2.2 g/L in Hestrin–Schramm medium, although its cost was significantly higher than plant cellulose [8]. Production depends on strain type, nutrient composition, and culture conditions, with abundant carbon and limited nitrogen favoring cellulose over biomass. The biosynthetic pathway involves enzymatic conversion of glucose into uridine diphosphate glucose (UDP-Glc), which is polymerized by cellulose synthase into linear β-(1→4)-glucan chains that crystallize into nanofibrils [24–25]. These nanofibrils, typically 3–8 nm in thickness, form highly crystalline, lignin-free, and hemicellulose-free networks with superior purity, water-holding capacity, and mechanical strength compared to plant cellulose [9,18].

BC can be fabricated using different culture techniques: static culture, which produces thick pellicles at the air–liquid interface; agitated/shaking culture, which generates irregular or spherical particles but reduces crystallinity; and bioreactor-based systems (stirred-tank, airlift, rotating disk, or trickling bed), which enable scale-up and controlled morphology as shown in Fig.4. Modified fermentation strategies, such as fed-batch and continuous processes, further improve yield and reproducibility. Optimized conditions with mixed carbon sources and agro-industrial wastes have increased yields from a few grams per liter to over 60 g/L [26–40].

6. Enhancing functional properties:

Bacterial cellulose (BC) is a highly pure form of cellulose produced by various Acetobacter and Komagataeibacter species. Unlike plant-derived cellulose, BC is free from lignin, hemicellulose, and pectin, making it a versatile biomaterial. However, its intrinsic properties such as high hydrophilicity, limited mechanical strength in dry state, and lack of functional groups restrict its broader applications. Therefore, modification strategies are essential to enhance and tailor BC's physicochemical, mechanical, and functional characteristics. Modifications can be broadly divided into in situ and ex situ approaches. In situ modification involves altering the fermentation medium or cultivation conditions by adding additives such as ethanol, organic acids, polymers, or nanoparticles to impart desirable properties during biosynthesis. This method allows direct incorporation of functional molecules into the BC network. Ex situ modification is carried out after BC production and includes physical, chemical, and enzymatic treatments as shown in Fig.4. Physical modification involves blending, coating, or crosslinking with natural and synthetic polymers to improve flexibility, hydrophobicity, or barrier properties. Chemical modification includes acetylation, carboxymethylation, phosphorylation, or graft copolymerization, enabling new functionalities such as antimicrobial activity, enhanced adsorption, or improved compatibility with polymers. Enzymatic approaches are used to selectively cleave or rearrange cellulose chains to adjust porosity and mechanical strength. Each modification method offers distinct advantages and disadvantages. In situ modification is simple, scalable, and cost-effective, but it is limited by bacterial tolerance to additives. Ex situ modification allows greater control over functionality but often requires chemicals and additional processing steps, increasing cost and environmental concerns. By combining these approaches, BC can be engineered into advanced materials with applications in biomedical fields (wound dressings, scaffolds), food packaging, environmental remediation, electronics, and composites.

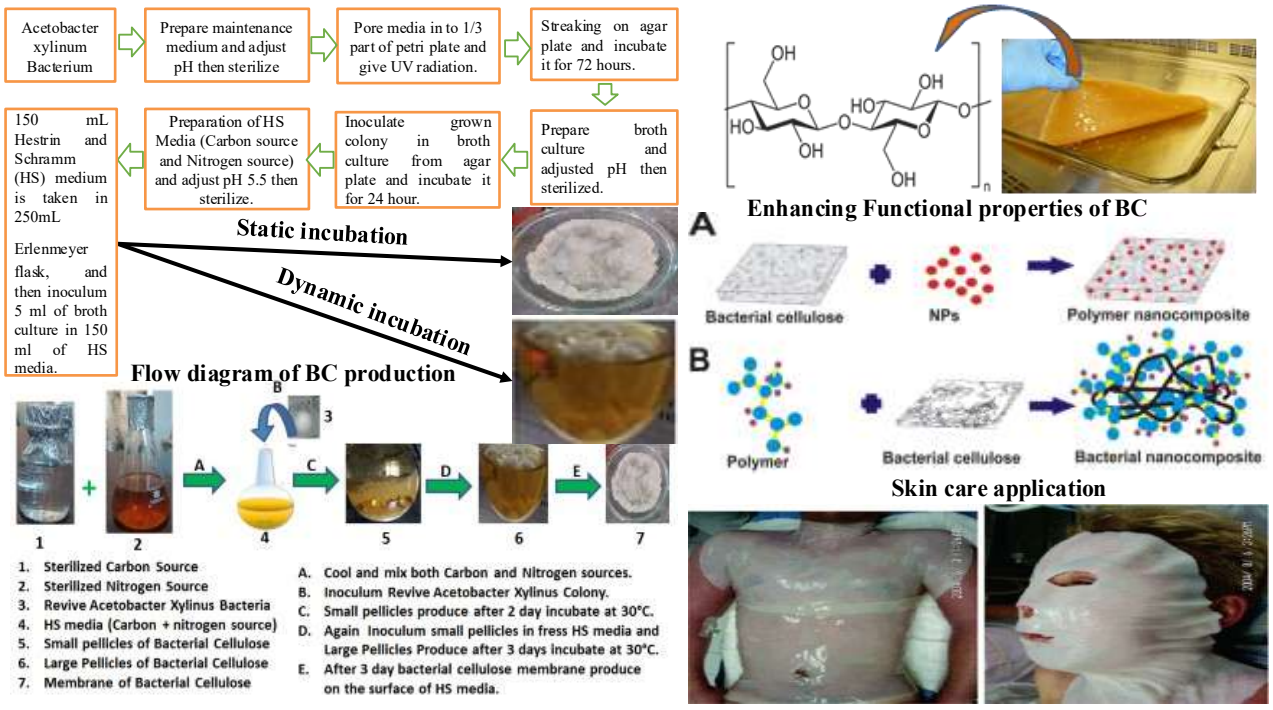


Fig.4 Flow diagram of BC production and its modifications for biomedical applications

Table 1: Existing recipes/condition for production of Bacterial Cellulose by Acetobacter species

Sr. No.	Bacterial strain	Carbon/Nitrogen source & medium composition	Temperature (°C)	Incubation time	pH	Yield (g/L)	Ref.
1	*A. xylinum*	HS medium: 20 g/L glucose, 5 g/L yeast extract, 5 g/L peptone, 2.7 g/L KH_2PO_4, 1.15 g/L citric acid	30	7 days	5–6	2.64	26–28
2	*G. xylinus*	HS medium + 80 g/L sucrose + 3 g/L tea	30	7 days, 60 rpm	5	3.34	29
3	*A. xylinum*	HS medium + 10 mL/L ethanol	28	7 days, 150 rpm	5.5	4.77	30–31
4	*A. xylinum*	HS medium	30	7 days	6–6.8	6–7	32–33
5	*G. xylinus*	Modified medium: 20 g/L glycerol, 9 g/L yeast extract, 9 g/L peptone, 4 g/L Na_2HPO_4, 1.15 g/L citric acid	30	7 days	5	6.93	34
6	*G. xylinus*	HS medium + 20 mL/L corn steep liquor	28	14 days, 100 rpm	5	10	35–36
7	*A. xylinum*	Basal medium: 24.8 g/L fructose, 76.5 g/L sucrose, 1 g/L KH_2PO_4, 0.2 g/L $MgSO_4 \cdot 7H_2O$, 0.1 g/L NaCl, 3 g/L yeast extract	29.3	16 days	4.49	12.67	37
8	*A. sp. A9*	Modified HS medium: 40 g/L glucose, 1 g/L yeast extract, 7 g/L polypeptone, 8 g/L Na_2HPO_4 + 14 mL/L ethanol	25–30	7 days, 200 rpm	6.5	15.2	38
9	*A. xylinum*	Static medium: 70 g/L fructose, 35 g/L glucose, 7.5 g/L acetic acid	30	4–5 days	5.5	28.4	39
10	*G. xylinus*	HS medium using industrial waste as carbon source	30	4 days	6	60	40

7. Factors Affecting the Yield of Bacterial Cellulose

The production of bacterial cellulose (BC) by *Acetobacter* and *Komagataeibacter* species is influenced by several physicochemical and nutritional factors. The most critical parameters include carbon source, nitrogen source, pH of the medium, incubation temperature, and cultivation time. Researchers have consistently emphasized that optimization of these factors is essential for obtaining higher yields and tailoring the structural properties of BC.

7.1 Carbon Source

Carbon serves as the primary substrate for bacterial metabolism and cellulose biosynthesis. *Acetobacter* species can utilize a wide range of carbon sources, including glucose, fructose, sucrose, mannitol, trehalose, arabitol, and lactic acid. Glucose, sucrose, and mannitol have been reported to consistently yield high cellulose production, with typical values around 10 g/L in 14 days under optimized conditions [28, 43]. Advanced studies on *G. hansenii* ATCC 53582 demonstrated significantly enhanced yields up to ~40 g/L when sucrose was used as the carbon source, compared to ~10 g/L reported for glucose-based media [44]. Sugar concentration plays a decisive role. At moderate concentrations (5 wt% or ~50 g/L glucose), the maximum yield is observed, whereas higher sugar levels (up to 15 wt%) inhibit production due to osmotic stress and altered metabolism [48]. Similarly, mixed sugars such as fructose-sucrose and fructose-lactose combinations produced higher yields (5.25–7.38 g/L) compared to glucose alone [47]. Ethanol addition to the medium has also been shown to stimulate BC production, with improved yields of 15.2 g/L at 1.4% ethanol supplementation [45–46]. Overall, the choice and concentration of the carbon source strongly influence not only the yield but also the crystallinity and morphology of BC.

7.2. Nitrogen Source

Nitrogen is essential for microbial growth and enzymatic activity during cellulose biosynthesis. Common nitrogen sources include yeast extract, peptone, corn steep liquor (CSL), ammonium sulfate, casein hydrolysate, glutamate, and glycine. Yeast extract (0.5–2% w/v) has been reported to be the most effective, followed by polypeptone and CSL [51]. Protein-rich nitrogen sources such as casein hydrolysate and glutamate have been shown to enhance cellulose yields compared to inorganic nitrogen salts like ammonium sulfate [50]. Optimization studies revealed that soybean meal and ammonium salts yielded relatively lower BC, while media supplemented with peptone or casein hydrolysate produced significantly higher quantities. Thus, both the type and concentration of nitrogen play a pivotal role in cellulose synthesis, with organic proteinaceous sources proving superior.

7.3. pH of the Medium

The pH of the culture medium critically regulates bacterial metabolism and cellulose production. The optimal pH for BC production lies in the acidic range of 4.5–5.5, although some studies reported maximum yields at pH 3.5 after 8 days of incubation [52–54]. Imbalances in pH occur due to secondary metabolites, such as acetic acid, produced during fermentation, which can inhibit cellulose synthesis. Controlled pH adjustment, particularly with glucose-fructose-acetic acid combinations, significantly enhances yield by stabilizing the culture environment [55]. Studies have also shown that pH variation affects the degree of polymerization and microfibril arrangement in BC, thereby influencing its physical properties.

7.4. Incubation Temperature

Temperature is another key factor influencing bacterial viability and enzymatic activity during BC biosynthesis. Optimum production is typically observed at 28–30 °C [51, 56]. At temperatures below 28 °C, growth and cellulose synthesis slow down, while temperatures above 31 °C cause stress or death of *Acetobacter* cells, despite enzymes continuing to function [57]. Comparative studies revealed that BC synthesized at 30 °C had a lower degree of polymerization (~10,000) but a higher water-binding capacity (164%) than that produced at 25 °C and 35 °C [58]. This demonstrates that small variations in cultivation temperature directly affect yield, polymer chain length, and functional properties of BC.

8. Observation and Characterization Techniques

To evaluate BC production and quality, multiple analytical techniques are employed. Structural and crystallinity changes are assessed using X-ray diffraction (XRD)**,** morphology by field emission scanning electron microscopy (FESEM), and thermal stability by thermogravimetric analysis (TGA). Chemical composition and bonding are analyzed by Fourier-transform infrared spectroscopy (FTIR), while fermentation efficiency is studied by sugar and inhibitor analysis. Mechanical properties are further examined using dynamic mechanical analysis (DMA) [59–62]. These techniques not only confirm yield improvements but also provide insights into tailoring BC for biomedical, packaging, and environmental applications.

9. Bacterial Cellulose and Its Potential in Medical Applications

Bacterial cellulose is a unique material with remarkable characteristics such as high water-binding capacity, high tensile strength, good mechanical toughness, bio-affinity, biocompatibility, biological adaptability, absence of allergic reactions, and biodegradability. Because of these properties, it has significant potential for applications in wound dressings, drug delivery, artificial skin, vascular prostheses, and tissue engineering scaffolds. This section discusses the major biomedical applications of bacterial cellulose.

9.1 Skin Therapy

Bacterial cellulose is used in skin therapy due to its high mechanical strength in the wet state, substantial permeability to liquids and gases, and low skin irritation as shown in Fig.5. These features indicate that the gelatinous membrane of bacterial cellulose can serve as an artificial skin for temporary wound covering [63]. Chitosan, similar to BC, is also widely recognized in biomedical applications due to its ability to absorb exudates, as well as its antifungal, antimicrobial, antiviral, and wound-healing properties [64]. The never-dried microbial cellulose membrane is a nonpyrogenic, fully biocompatible biomaterial with excellent mechanical strength [65–66].

Commercial products such as Biofill® and Gengiflex® are derived from bacterial cellulose and have wide applications in surgery and dental implants. In cases of second- and third-degree burns, ulcers, and other injuries, Biofill® has been used successfully as a temporary substitute for human skin [67]. Other products such as Bioprocess®, XCell®, and Biofill® are already available commercially for topical wound-healing applications. Studies have shown that BC is superior to conventional wound dressings in terms of exudate retention, pain reduction, accelerated reepithelialization and healing times, lower infection rates, ease of wound inspection due to its semitransparency, and reduced scarring. Moreover, BC conforms remarkably well to nearly any body contour and functions as an ideal moisturizing dressing, as it maintains proper water balance by either absorbing or releasing fluid according to wound conditions [68]. The only limitation reported for bacterial cellulose is its restricted elasticity in areas requiring high mobility. Gengiflex® has also been developed for the regeneration of periodontal tissues. Further applications of Biofill® and Gengiflex® have been reported in veterinary medicine, where bacterial cellulose (Cellumed) was successfully used to treat large surface wounds in horses and dogs [69].

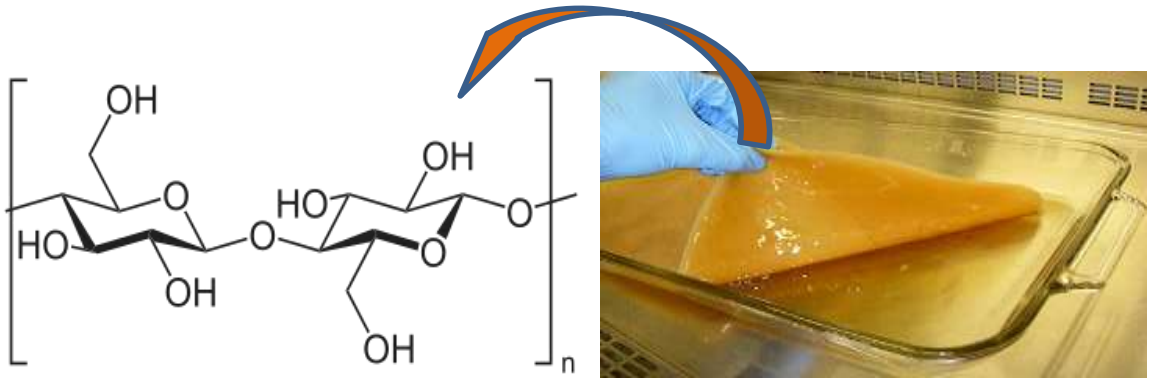


Figure 5: A never-dried microbial cellulose membrane showing excellent conformability to body contours, maintaining a moist environment, and significantly reducing pain [70–72].

9.2 Artificial Blood Vessels

In normal physiology, blood circulates through vessels throughout the body. When vessels are blocked or severely damaged under pathological conditions, artificial blood vessels may be required. Several attempts have been made to develop artificial blood vessels using synthetic materials such as polyester; however, these materials frequently cause thrombosis [73]. Grafts made of Dacron (polyester) and expanded polytetrafluoroethylene (ePTFE) are also prone to thrombosis, making them unsuitable for small blood vessels with diameters less than 6 mm [74]. Due to the absence of reliable synthetic bypass grafts, vessels are often harvested from the thorax or legs of patients. Artificial bypass implants prepared from polytetrafluoroethylene, polyethylene, polyethylene terephthalate, and polyurethane have shown limited success in cardiovascular surgery [75].

Bacterial cellulose presents a promising alternative material that meets the necessary requirements for use as artificial blood vessels, both for small and large vascular grafts. Its excellent mechanical strength, with burst

pressures reaching up to 880 mmHg, and lower risk of clot formation compared to synthetic materials make it particularly attractive for bypass operations [76]. BC interacts favorably with blood and demonstrates properties similar to natural vessels. Real blood vessels are lined with an internal coating of endothelial cells that prevent clot formation. Experimental bacterial cellulose-based vascular grafts, such as BASYC tubes, have been developed with dimensions including an inner diameter of 1 mm, a length of about 5 mm, and a wall thickness of 0.7 mm. These parameters are sufficient for microsurgical applications as shown in Fig.6. The high mechanical strength of BASYC tubes confirms that bacterial cellulose is a suitable candidate for vascular graft development and microsurgery [77–79].

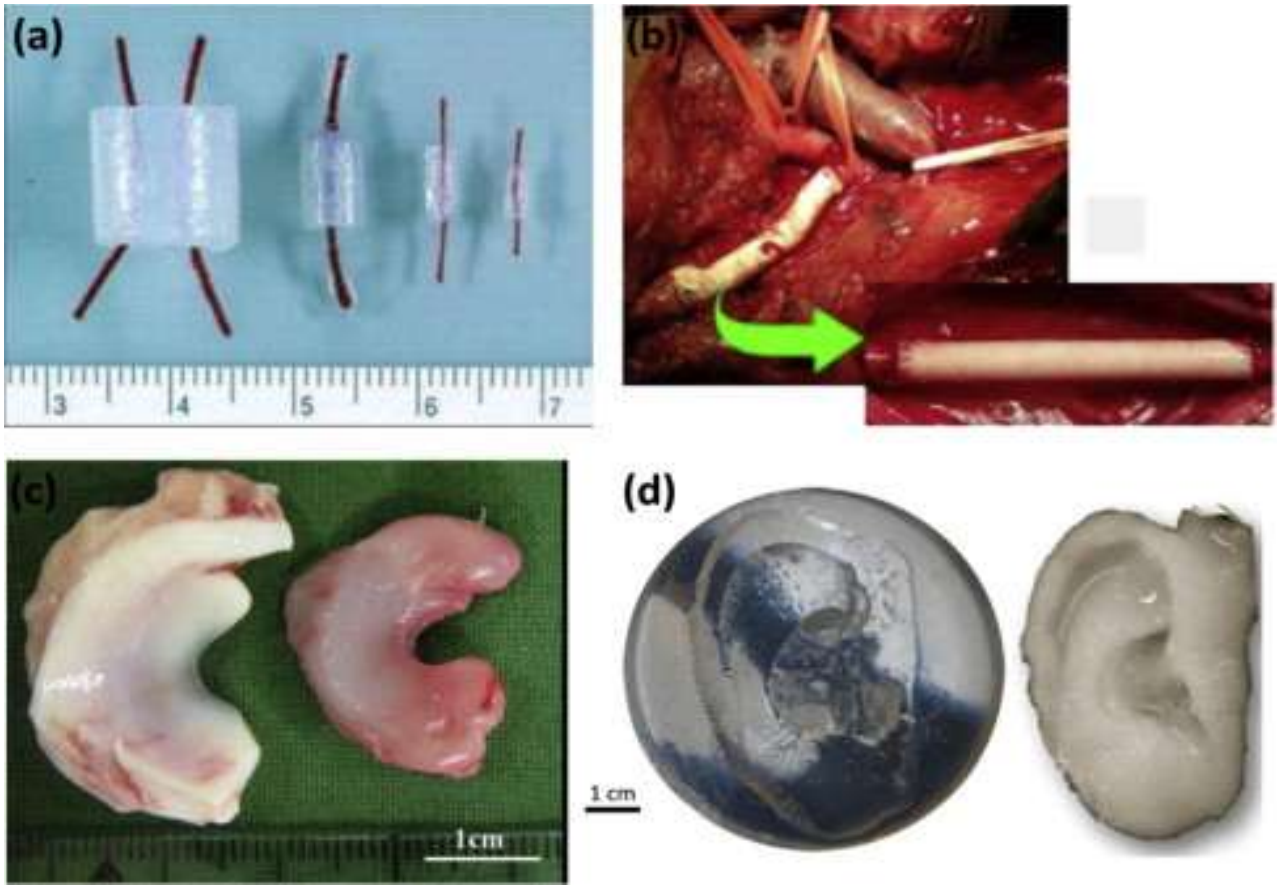


Figure 6.
(a) Bacterial cellulose tubes of different dimensions. BASYC, Bacterial Synthesized Cellulose. (Ruler units are in centimeters) [80].
(b) Vascular prostheses made of CNF–polyurethane placed between the brachiocephalic trunk and the right common carotid artery in a male patient [81].
(c) Comparison between pig meniscus (left) and BC hydrogel (right) [82].
(d) Negative silicone mold used to guide bacteria during bacterial culture to reproduce the large-scale features of the outer ear (left), and 3D BC implant prototype (1% effective cellulose content) produced in the shape of the whole outer ear according to the 3T MRI scanning technique (right) [83].

The material must withstand both mechanical strains during microsurgical preparation and anatomizing as well as blood pressure in the living body. Previous studies show that bacterial cellulose has unique properties not observed in synthetic polymers. For this reason, BC is often compared with organic polymers such as polypropylene, polyethylene terephthalate, and cellophane. When processed into a film or sheet, BC exhibits remarkable mechanical strength with low density. Results confirm that bacterial cellulose is highly crystalline, strongly oriented, and possesses an ultra-fine structured sheet [84–85].

A mismatch between the mechanical properties of synthetic grafts and surrounding native tissue has been reported as a major factor in the failure of currently used cardiovascular graft replacements. Therefore, developing biomaterials with mechanical properties closely matching those of the tissue they are replacing remains a critical objective in biomedical device design [86]. Microsurgical techniques, which allow repair of nerves and blood vessels within very small diameters under optical equipment, further increase the demand for advanced biomaterials. The synthetic implant materials used in surgery of larger vessels, including polytetrafluoroethylene, polyethylene terephthalate, polyethylene, and polyurethane, have not been sufficient for microsurgical applications, as they often result in thrombosis.

The wall of BASYC tubes consists of bacterial cellulose loaded with more than 90% water within a nanofiber network. This structure allows transport of water, monovalent ions, and small molecules, while restricting biopolymers and corpuscular blood constituents. Stored water stabilizes the cellulose network and contributes to tissue compatibility and hemocompatibility of BASYC [87–88].

Polyvinyl alcohol (PVA) and bacterial nanocellulose (BNC) have also been developed into biocompatible hydrogels for artificial blood vessel applications. Several studies indicate that some properties of BNC, such as compliance, do not meet all the requirements of native blood vessels. To address this, a novel thermal processing method under applied strain with the addition of a small amount of BC nanofibers produced anisotropic PVA–BC nanocomposites. Two types of pristine BNC tubes with different inner structures were produced in separate bioreactors. PVA tubes and PVA–BNC tubular composites were then fabricated using a thermally induced phase separation method.

Morphology, water permeability, cytotoxicity, and mechanical properties, including axial stretch strength, suture retention, burst pressure, and compliance, were evaluated. Results showed that impregnation of PVA into BNC tubes significantly enhanced their properties, particularly mechanical strength and water permeability. The BNC tube acted as a skeleton base material, substantially influencing composite performance. The PVA–BNC composite tubes demonstrated great promise as candidates for vascular graft biomaterials [89–91].

9.3 Potential scaffold for tissue engineering

Bacterial cellulose, either alone or in combination with other components such as biopolymers and nanoparticles, is considered a promising material that fulfills the fundamental requirements of tissue engineering applications. Scaffolds in cartilage tissue engineering are essential because they provide physical support for cell proliferation, help maintain cell differentiation, and define the shape of newly growing tissue [92]. Musculoskeletal tissues, including bone and cartilage, are widely studied within this field. A variety of biodegradable and bioresorbable materials and scaffold designs have been evaluated both experimentally and clinically.

An ideal scaffold should possess specific characteristics: (i) it must be three-dimensional and highly porous with an interconnected network that supports cell growth and the transport of nutrients and waste; (ii) it must be biocompatible and bioresorbable with controllable degradation and resorption rates to synchronize with cell or tissue growth in vitro and in vivo; (iii) its surface chemistry should promote cell attachment, proliferation, and differentiation; and (iv) it must have mechanical properties that match those of the tissue at the site of implantation [93]. Natural polymers such as collagen, alginate, hyaluronic acid, fibrin glue, and chitosan have been investigated, as well as synthetic polymers including polyglycolic acid (PGA), polylactic acid (PLA), polyvinyl alcohol (PVA), polyhydroxyethyl methacrylate (pHEMA), and polyisopropylacrylamide (pNIPAA) as shown in Fig.7. However, scaffolds that fully replicate the mechanical properties of native tissues are still lacking [94].

Acetobacter xylinus has been studied as a source of novel scaffold material due to its unusual material properties and biodegradability. Bacterial cellulose combined with PVA forms biocompatible nanocomposites that exhibit a wide range of mechanical properties. These composites can be engineered to have mechanical

properties similar to those of cardiovascular tissues such as the aorta and heart valve leaflets. For instance, stress–strain behavior of porcine aorta has been matched by specific PVA–BC nanocomposites in both circumferential and axial directions. Another type of PVA–BC nanocomposite has demonstrated properties comparable to heart valve tissue. Importantly, relaxation behavior, which influences cardiovascular performance, showed that PVA–BC composites relaxed faster and to lower residual stress compared with the tissues they are designed to replace as shown in Fig.7. These characteristics make PVA–BC composites promising candidates for cardiovascular soft tissue replacement [95].

The three-dimensional porous structure of BC allows the formation of hydroxyapatite/BC (HAp/BC) composites with adjustable pore sizes and connectivity. This property, combined with the high mechanical strength of BC, makes it possible to design composites with characteristics ranging from those of soft tissues to hard tissues by adjusting the HAp-to-BC ratio and structural configuration. Consequently, HAp/BC nanocomposites prepared via biomimetic processes are attractive candidates for use as tissue engineering scaffolds and bone replacement implants [96–97].

Bacterial cellulose/hydroxyapatite nanocomposites have also been synthesized for bone healing applications using biomimetic approaches. For example, BC with varying surface morphologies (pellicles and tubes) was modified by adsorption of carboxymethyl cellulose (CMC) to initiate nucleation of calcium-deficient hydroxyapatite (cdHAp). Subsequent growth of cdHAp in simulated body fluid (SBF) over one week produced mineralized composites. Characterization using X-ray photoelectron spectroscopy (XPS), field emission scanning electron microscopy (FESEM), and energy dispersive spectroscopy (EDS) showed that cdHAp content varied among samples. Atomic ratios of calcium and phosphorus ranged from 0.44 to 7.71 at.% Ca and 0.27 to 11.18 at.% P, with Ca/P ratios between 1.22 and 1.92. FESEM images confirmed that cdHAp crystal size increased with nanocellulose fibril density. In vitro analysis of osteoprogenitor cell morphology and differentiation using fluorescence microscopy and alkaline phosphatase expression indicated enhanced cell attachment on cdHAp-modified BC surfaces [98–100].

Transmission electron microscopy (TEM) and RNA expression studies of type II collagen from human chondrocytes demonstrated that unmodified BC supports chondrocyte proliferation. TEM further confirmed chondrocyte ingrowth into the scaffold, highlighting BC's potential as a cartilage tissue engineering scaffold [101].

9.4 Wound dressing

Bacterial cellulose is an excellent material for wound dressings because it eliminates exudates, prevents infections, and reduces localized pain. Several studies have confirmed that the primary function of wound dressings is to minimize bacterial contamination, which is often responsible for delayed healing. A new strategy for wound management involves the development of BC-based wound dressings with antimicrobial properties. For example, RBC–ZnO nanocomposites have been applied in skin cancer treatment due to their enhanced antimicrobial activity against *Escherichia coli* [102].

Infection remains the principal complication of severe wounds. Antiseptic-soaked gauze has traditionally been used as an early treatment, although evidence supporting this practice is limited. Recently, there has been renewed interest in using silver for acute wound treatment, particularly in the form of dressings designed to deliver sustained elemental silver directly to the wound interface [103]. The antimicrobial activity of AgNPs/BC membranes has been tested against *Escherichia coli*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa* following the AATCC test method 100-2004. The results indicate that AgNP/BC nanocomposites can be effectively applied as antimicrobial wound dressings and implant materials [104–105].

The three-dimensional network and large pore sizes of BC provide an excellent template for silver nanoparticle stabilization. AgNPs with sizes ranging from 5 to 14 nm were uniformly distributed within the BC matrix. The silver content of these composites varied from 0.86% to 1.60%, depending on the carbon source used during BC synthesis. BC derived from sucrose, which had the lowest crystallinity, exhibited the

highest silver loading [106]. The hybrid nanostructure prevented nanoparticle leaching, reducing potential toxicity. Despite the slow release of silver ions, AgNP–BC composites maintained significant antibacterial activity, with more than 99% reductions in *Escherichia coli*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*. Moreover, these composites supported epidermal cell adhesion and growth without cytotoxic effects. The results demonstrated that AgNP–BC dressings reduce inflammation and promote faster wound healing [107].

Other strategies include modifying BC and plant cellulose with natural herb extracts such as bitter gourd (*Momordica charantia*) and Tridax daisy (*Tridax procumbens*), as well as with chitosan, to impart antibacterial activity. Treated samples displayed good antibacterial properties against *Staphylococcus aureus* and *Escherichia coli*. Among these, modified bacterial cellulose demonstrated superior antibacterial performance compared to modified plant cellulose [108].

The development of BC-based drug reservoirs, controlled-release platforms, and delivery systems has also attracted significant interest. The flexibility, macromolecular structure, and transparency of BC membranes allow researchers to monitor wound healing while providing localized and sustained release of therapeutic agents. Functionalization of BC's three-dimensional nanofiber network with drugs and polyelectrolytes enables fine-tuning of drug release kinetics. Consequently, BC membranes serve not only as protective wound dressings but also as advanced drug delivery platforms that enhance epithelialization and tissue regeneration [109].

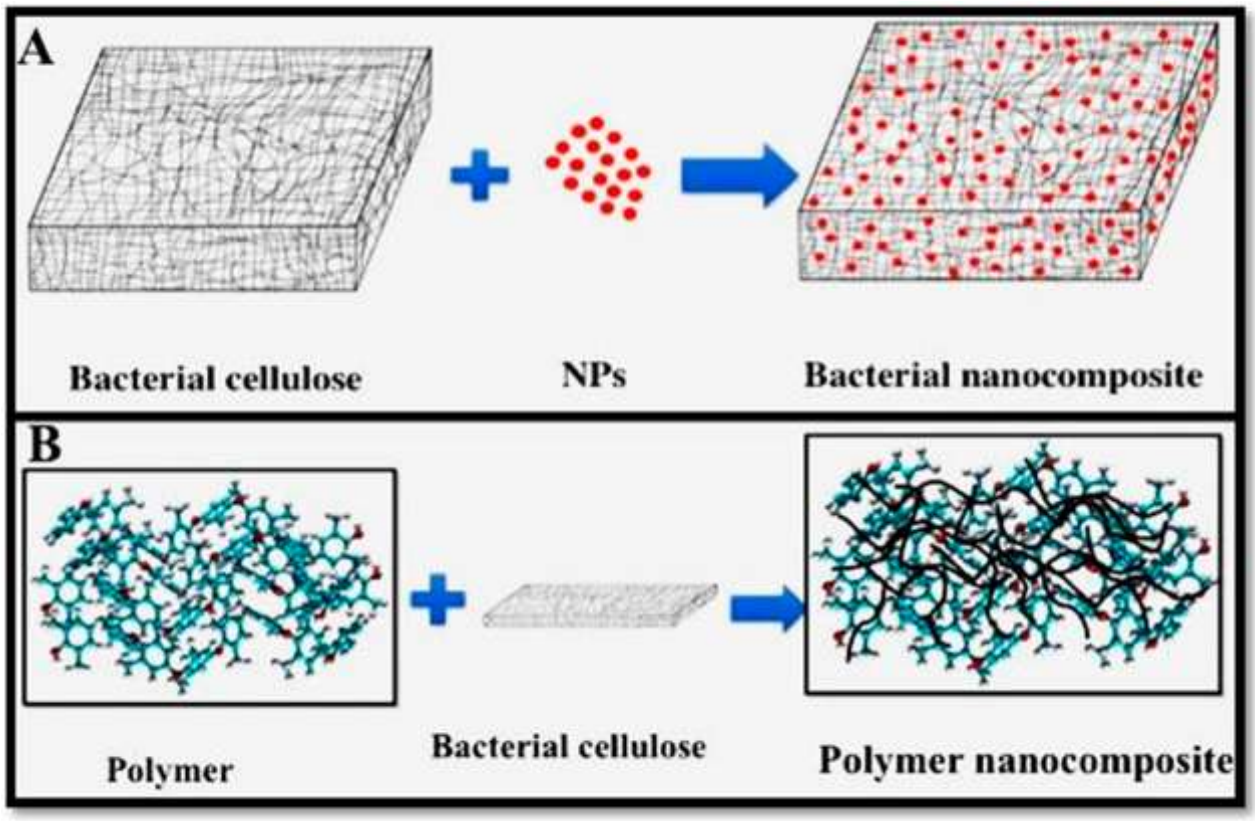


Figure 7. The use of BC as (A) a matrix or (B) reinforcement to prepare nanocomposites [110].

Nanomaterials have attracted worldwide attention in various fields of science due to their remarkable and unique properties. However, despite their advantages, many nanomaterials suffer from toxicity issues and pose potential risks to human health and the environment. Furthermore, most conventional nanoparticle synthesis methods are not environmentally friendly. Thus, with the development of nanotechnology, a key challenge is balancing the beneficial properties of nanosystems with their environmental and health risks [111]. Bacterial cellulose (BC), because of its high purity, high water retention capacity, and biocompatibility, has emerged as a sustainable nanomaterial platform. It is widely applied in wound healing, with several BC-

based wound dressings already commercialized. Cellulose-based hydrogels derived from BC are biodegradable and biocompatible, making them promising for both biomedical and industrial applications where environmental concerns are critical. These hydrogels can be tailored for specific properties such as swelling capacity and responsiveness to external stimuli. In wound management, hydrogels are designed to maintain an optimal moisture balance by hydrating the wound surface and absorbing exudates. They also serve as non-adherent dressings that can be removed without damaging the wound bed. Their transparency further allows direct monitoring of wound healing [112].

9.5. Drug Delivery Applications

Bacterial cellulose is a unique biopolymer that fulfills the essential criteria for drug delivery materials. With rapid advancements in pharmaceutical technology, drug delivery systems require novel materials that provide controlled release, stability, and compatibility. BC is gaining attention as a natural, biodegradable, non-toxic, and biocompatible drug delivery vehicle. Its availability from nata de coco and similar sources makes it cost-effective and scalable [20–21,113]. A number of studies have demonstrated its potential in this field. For instance, the film-coating and drug-release properties of BC films have been investigated in detail. BC films showed favorable physicochemical, morphological, and thermal characteristics. Tablets coated with BC using spray-coating methods demonstrated good drug release behavior. Importantly, BC films were soft, flexible, foldable, and could be produced without plasticizers, yet still matched the performance of commercial coatings such as Aquacoat ECD, which require plasticizers. Differential scanning calorimetry (DSC) results revealed a high glass transition temperature, confirming the thermal stability of BC films [114-115]. These findings suggest that BC can serve as a novel aqueous film-coating material with lower cost and superior film-forming properties compared to conventional coating agents.

Further studies have shown that BC dispersions are suitable for spray coating of drug tablets. The addition of suitable plasticizers or polymers can improve coalescence and film quality, producing strong films with good mechanical properties. This highlights BC's potential for pharmaceutical film coating and sustained-release drug delivery systems [116-117]. Another investigation fabricated a novel hydrogel system from BC using electron beam irradiation. Acrylic acid was successfully grafted onto the cellulose network, as confirmed by FTIR analysis, enabling the prediction of the reaction mechanism. These hydrogels exhibited a macroporous sponge-like structure with tunable pore sizes depending on irradiation dose and acrylic acid concentration. DSC analysis further indicated that the thermal stability of the hydrogels was suitable for drug delivery applications [116–119].

BC has also been used as a nanocomposite support. For example, TiO_2 nanoparticles were arrayed onto BC nanofibers, forming narrow mesopores and creating hybrid nanofibers with enhanced photocatalytic activity. These BC/TiO_2 hybrids were used for methyl orange degradation under UV irradiation and showed higher efficiency compared to commercial TiO_2 (P25) [118-122]. Beyond drug delivery, the intrinsic properties of BC, including high tensile strength, high modulus, excellent wet strength, and its uniform nanofibrous structure, provide additional advantages. It can be sterilized without altering its morphology or properties, further supporting its use in biomedical applications. BC is thus an excellent candidate for both pharmaceutical coatings and sustained drug-release systems [119-124].

10. Conclusions

Bacterial cellulose is a highly attractive biopolymer primarily produced by Acetobacter species. Although it shares the same chemical composition as plant cellulose, its physical and chemical properties differ significantly due to its nanoscale network and higher crystallinity. BC offers several advantages over plant cellulose, including greater purity, superior water-holding capacity, higher mechanical strength, and enhanced biocompatibility. These characteristics make it a versatile material for nanocomposites, wound dressings, hydrogels, drug delivery platforms, and biomedical devices. Looking ahead, research should focus on cost reduction through the use of agro-industrial residues as substrates, the development of greener modification strategies, and large-scale processing techniques that preserve BC's unique nanostructure. Expanding its

applications in pharmaceuticals, environmental remediation, tissue engineering, and advanced composites will further solidify bacterial cellulose as one of the most important sustainable biomaterials of the future.

11. Future prospective:

Bacterial cellulose (BC) is a sustainable biopolymer with unique nanoscale architecture, high purity, excellent mechanical strength, and superior water-holding capacity compared to plant cellulose. Its biocompatibility, biodegradability, and tunable properties make it highly suitable for biomedical applications such as wound dressings, artificial skin, vascular grafts, tissue engineering scaffolds, hydrogels, and drug delivery systems.

Looking ahead, BC research should emphasize large-scale, cost-effective production using agro-industrial residues, environmentally friendly modification methods, and advanced fabrication strategies to engineer multifunctional BC-based materials. Future directions also include integrating BC with nanomaterials, bioactive agents, or smart polymers to develop next-generation composites for regenerative medicine, controlled drug release, and environmental remediation. With continued innovations, BC holds strong potential to emerge as a leading green material in both biomedical and industrial sectors.

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