BACTERIAL CELLULOSE-BASED COMPOSITES: RECENT TRENDS IN PRODUCTION METHODS AND APPLICATIONS

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Received April 4, 2024

Bacterial cellulose (BC) has attracted significant attention due to its distinct structural attributes and remarkable physico-mechanical properties, making it highly popular in biomedical applications, such as artificial skin, blood vessels, tissue scaffolds, and wound dressings. However, its widespread application in a variety of fields is often limited by poor mechanical properties and functional characteristics. The development of BC-based composites by incorporating synthetic materials has been widely investigated to address these limitations. This review paper summarizes the fabrication strategies for BC composites *in-situ* and *ex-situ* methods for their development, and highlights their wide range of applications in diverse fields. Various strategies have been designed for the synthesis of BC composite functionalized materials, tailored to the specific nature of their intended application. In the synthesis of BC composites, either *in-situ* addition of reinforcing materials to the synthetic media or *ex-situ* incorporation of these materials into the microfilaments of the BC microfilaments is primarily involved. A wide range of materials have been used as reinforced materials, ranging from organic polymers to inorganic nanoparticles. These composite materials have the potential to be used for tissue regeneration, wound healing, enzyme immobilization, and the development of medical devices. Recent years have seen the development of BC composites incorporating conductive materials, being used in the production of various electrical products, such as biocatalysts, enzymes, e-papers, displays, electrical instruments, and optoelectronic devices. In summary, the synthesis of BC composites and their applications offers a path for producing advanced biomaterials with enhanced properties and diverse functionalities, exploring their potential as environmentally friendly and versatile materials applicable across multiple sectors.

Keywords: bacterial cellulose, sustainable, biomaterial, BC-composites, functionalization

INTRODUCTION

Cellulose attracts attention as the most abundant organic compound found on Earth, mostly found as a structural component in the cell walls of algae and plants.[1,2] Bacterial cellulose (BC) is a fascinating and renewable natural biomaterial produced extracellularly by various microorganisms, including *Acetobacter xylinum* (also known as *Gluconacetobacter xylinum*), *Agrobacterium*, *Salmonella*, *Pseudomonas* and *Rhizobium*.[3] In comparison with plant cellulose, BC is a pure form of cellulose, which does not have lignin, pectin, hemicelluloses, or other biogenic compounds, and shares the same molecular structure as plant cellulose. In addition to its high crystallinity, exceptional water-holding capacity, improved mechanical strength, complex 3-D network structure, and moldability give BC advantages over plant cellulose.[4,5] BC may be synthesized in a variety of forms, such as fibers, membranes, tubes, aerogels, hydrogels, and films, which are suitable for various applications, including biomedicine, electroconductive materials, and cosmetics.[4] Due to its good biocompatibility, excellent biodegradability, high mechanical and physical properties, crystallinity, purity, as well as significant water retention capacity, BC is widely used in the medical field. However, BC does exhibit certain drawbacks when applied in biomedical conditions, particularly lacking the ultrahigh strength required for specialized applications like bone tissue engineering, and missing antimicrobial properties, which are crucial for wound healing.[6,7]

To address these limitations and meet the wide-ranging demands of applications, such as drug delivery systems, tissue engineering

scaffolds, artificial blood vessels, wound healing membranes, optical devices, osteoconductive films, and cosmetic delivery systems, researchers have incorporated a range of reinforcement materials into BC matrixes.[8-10] These include biomolecules, nanomaterials, synthetic polymers, natural polymers, and carbon materials, which improve the properties of BC-based composite materials for specific applications.[11,12] There is still a lack of comprehensive reports on existing BC-based products and their preparation methods for these applications, despite several reviews that summarize the applications of BC-based composites in the biomedical and cosmetic sectors.[12-14] This gap underscores the need for further research and documentation in the field to facilitate the broader understanding and utilization of BC-based materials in various sectors. Given the wide range of applications offered by BC, it is essential to develop basic synthetic approaches to increase the production of BC, in line with environmental considerations and industrial requirements.[15] It is important to understand the approaches that have been applied so far to address the limitations of pure BC before considering practical applications. To advance these materials for specific purposes, it is essential to know the synthesis methods of BC composites and their respective benefits and drawbacks.[16] The literature review revealed that the nature of the reinforced material used and its proposed application have a significant outcome on the development of BC composite materials.[17]

The review summarises the evolution of the subject area of bacterial cellulose and its composites, highlighting the advances in production techniques, synthesis strategies, and applications. Previous evaluations of pure BC limits have focused on a method for the systematic development of composite materials that address limitations and expand applications. This review, which summarises efforts to achieve cost-efficient production and diverse synthesis methods, as well as the pros and cons of current strategies, provides a unique perspective on composite production for BC. These modifications are usually carried out using *in-situ* and *ex-situ* methods. In particular, the review describes the use of BC and its composites in biomedical materials, conducting devices, and cosmetic products, focusing on practical applications. This review will contribute to the progress of this area and inspire further research efforts, as it provides a framework for developing new strategies in BC composite preparations, specifically aimed at certain applications. This review is expected to attract interest from readers, to improve their understanding of BC composite characteristics and potential for advanced applications.

BACTERIAL CELLULOSE AS A RENEWABLE AND COST-EFFECTIVE MATERIAL FOR COMPOSITES

Production of bacterial cellulose

Bacterial cellulose (BC) stands as a promising material in biomedicine, industry, and technology, but challenges in large-scale production and commercial use persist because of high manufacturing costs and low productivity of producer strains.[18] To address these issues, further research is needed to develop highly efficient production methods for bacterial cellulose.[19] Recent studies have highlighted the need to explore the cost-effective sources of nutrients, the diversity of cellulose-producing organisms, and the optimization of the culture conditions to increase the cost-effectiveness of the production of BC.[20] To produce the desired quality and quantity of BC, growth conditions, including temperature, pH, oxygen, and carbon-nitrogen sources, play an essential role. Variations in the macrostructure morphology of BC are caused by the selection of cultivation methods, *viz.* static or agitational fermentation.[21,22]

Static cultivation results in the formation of a filmlike cellulose on the surface of the medium, while the agitated conditions result in a variety of shapes. Dynamic fermentation, which improves dissolved oxygen content, while increasing the risk of cells undergoing mutation during agitation and could limit their ability to produce BC, poses a challenge.[23] On the other hand, cell-free culture, a synthesis method without living cells, shows promising development prospects.[24] The use of expensive nutrient media, which accounts for around 30% of the overall process cost, poses a major challenge for large-scale production of BC.[25] The commonly used chemically defined Hestrin–Shramm (HS) medium comprises media components like glucose, peptone, yeast extract, citric acid, and disodium phosphate, contributing to the overall production expenses.[26,27] Figure 1 presents a comprehensive summary of the production of BC using a variety of agro-industrial wastes.

To reduce costs, research is being carried out on the use of different sugars as carbon sources

both synthetically and *in vitro*. Other carbohydrates, such as fructose, maltose, xylose and glycerol, have the potential to be efficient depending on the type of the producer strain, although glucose and sucrose are widely used. Depending on the carbon source, various strains are capable of synthesizing differing amounts of BC from 0.5-1.2 g/L or up to 15 g/L.[28]

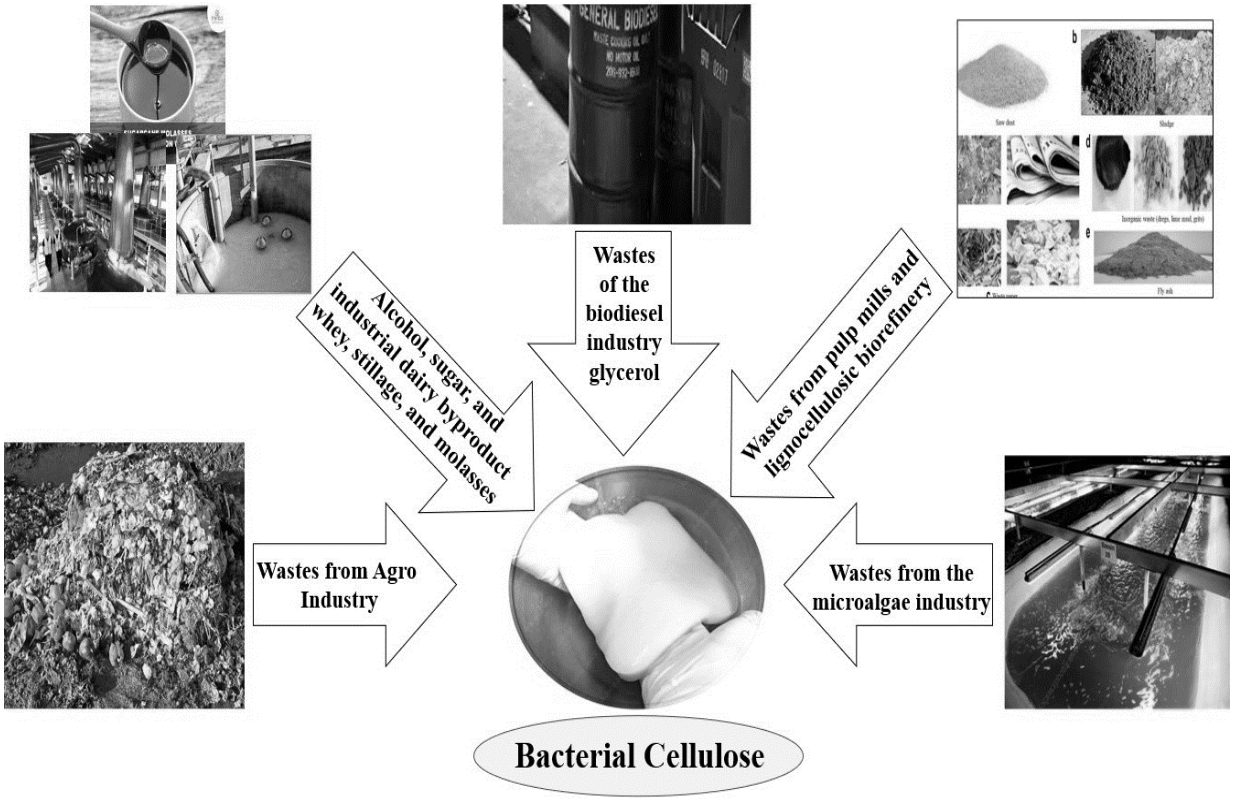

Figure 1: Sustainable production of bacterial cellulose from agro-industrial wastes[18]

As potential substrates for sustainable production of BC, different industrial waste has been categorized in six groups, including brewery and beverage waste, agro-industrial waste, and lignocellulosic biorefineries. Numerous studies have shown the feasibility of using different agricultural wastes, such as sisal juice, cane and pineapple waste, guava, mango purees, or any other sources.[16] Overall, key strategies to overcome the challenges in the production of BC are to explore alternative sources of nutrients and to use industrial waste to improve sustainability and economic viability.[29]

Current research efforts focus on industrial waste streams and by-product streams as a viable and cost-effective substrate for the production of BC, given the significant cost limits of BC production.[30] Industrial wastes were systematically categorized into six groups: (1) brewery and beverages industries wastes; (2) agro-industrial wastes; (3) lignocellulosic biorefineries, pulp mills, and sugar industries wastes; (4) textile mills; (5) micro-algae industry wastes; and (6) biodiesel industry wastes, as shown in Table 1.[28]

In addition, wastes from the biodiesel industry, in conjunction with pulp mill and lignocellulosic waste,[24] acetone-butanol-ethanol (ABE) fermentation wastewater and micro-algae biomass industry waste, have demonstrated potential as growth media for BC production. The comprehensive exploration of industrial waste as a substrate not only addresses the costs associated with BC production, but also contributes to sustainable practices through recycling and innovative use of these wastes.[31]

Table 1
Various industrial by-products utilized for BC production[18]

Industrial wastes	Additional nutrients	Microbial strains	Maximum BC productivity	Refs
Wastes from agro-industry				
Wheat straw hydrolyzed by enzymes	HS medium	*Acetobacter xylinus*	8.30 g/L	[25]
Juice samples of pineapple and watermelon	HS medium	*Acetobacter pasteurianus*	7.70 g/L	[20]
Low-quality apple residues	Citric acid, glycerol, ammonium sulfate, and apple glucose ratios	*Acetobacter xylinum*	8.60 g/L	[32]
Wastes from brewery/beverages industries				
Pomace and peel from citrus enzymolysis intermediate	Peptone, ethanol, and yeast extract	*Komagataeibacter xylinus*	5.70 g/L	[27]
Bagasse made from grapes	CSL and phosphorus diammonium	*Gluconacetobacter xylinus*	8.0 g/L	
Wastes from sugar industries, and lignocellulosic biorefineries				
Sulfate and sulfite fiber sludges from waste materials	Both tryptone and yeast extract	*Gluconacetobacter xylinus*	11.0 g/L	[24]
Molasses	Corn steep liquor	*Acetobacter xylinum*	5.3 g/L	[29]
Sugar cane molasses	Vitamins, minerals, amino acids, and carbs	*Acetobacter xylinum*	223% as compared to 100% in HS medium	[34]
Wastes from the textile and biofuel industries				
Unrefined, raw glycerol	Pineapple with HS medium	*Gluconaceter xylinus*	12.32 g/L	[17]
Hydrolysate from waste dyes of cotton textiles	yeast extract and peptone	*Gluconacetobacter xylinus*	12.80 g/L	[21]
Glycerol derived from the biodiesel industry	Ammonium sulfate, magnesium sulfate, potassium hydrogen, yeast extract, and orthophosphate	*Gluconacetobacter xylinus*	2.87 g/L	[18]

BACTERIAL CELLULOSE IN COMPOSITES

BC is an essential component in the production of composite materials. It is capable of being used as a matrix or as a material for reinforcement.[11] Many BC-based composite materials have been developed, each to improve specific characteristics or offer new possibilities, due to their adaptability.[32] Due to its unique structural characteristics, BC is a flexible material for the synthesis of composite materials, serving as a matrix and a reinforcement material. To improve mechanical properties, conductivity, and magnetic characteristics and facilitate biological activities, different BC composites have been developed.[33] Table 2 provides an overview of different BC-based composites and their potential applications, showing the broad range of possibilities.[21,34] The polymer composite is based on the type of polymer reinforcing agent, using *in-situ* and *ex-situ* synthesis techniques.[35] *In-situ* synthesis, incorporating reinforcing agents during polymer synthesis, faces challenges due to the antibacterial properties that can harm BC manufacturing cells.[34,36] On the other hand, *ex-situ* preparation involves impregnating the polymeric matrix with reinforcement materials and utilizing the porous BC network for material integration. Polyethylene glycol, gelatin, chitosan, silver and gold nanoparticles, and carbon nanotubes are examples of *ex-situ* synthesis BC composite materials.[3,37,111]

Despite its advantages, *ex-situ* approaches have limitations, such as limited permeation of particles into BC fibers and challenges of mixing materials with BC due to their hydrophobic nature. Synthesis of composite materials from BC solutions is the most advanced strategy, which allows for an efficient blending of materials with

various characteristics.[38,51] Although this method offers control over the homogenous dispersion of reinforcing agents and matrix, a major drawback is poor BC dissolution, given its insolubility in water and many organic solvents. Furthermore, material saturation and adherence are facilitated by the hydrophilic nature of BC and its porosity. To overcome limitations, such as the lack of antibacterial, magnetic, and conductive properties in pure BC, researchers have extensively explored composite materials.[39,40] The synthesis of BC composites with various materials aims to achieve enhanced mechanical and magnetic properties, conductivity, biocompatibility, and bactericidal activities, making BC an excellent biopolymer for diverse applications.[8,10]

Table 2
Overview of various BC composites, including their synthesis methods, characteristics, and applications

Type	Synthesis method	Composite	Characteristics	Applications	Refs
Reduced graphene oxide (RGO)	*In-situ* reduction	Carbon-based	Conductivity	Flexible sensors	[79]
Silver nanoparticles	*In-situ* synthesis	Polymer-metal	Antibacterial, biocidal	Wound dressing, membranes	[111]
Graphene oxide (GO)	Sonochemical *in-situ* biosynthesis method	Carbon-based	Exhibits antibacterial properties	Biomedical	[33]
Alginate	Coagulation method	Polymer-polymer	Highly porous structure	Separating membranes	[55]
Silica nanoparticles	Physical blending	Polymer-particle	Improves mechanical properties	Industrial	[96]
Carbon nanotubes (CNT)	*In-situ* addition	Carbon-based	Enhances mechanical, electrical, and thermal conductivity	Electronic devices, biosensors, hydrogen storage	[45,62]
Gold nanoparticles	*In-situ* synthesis	Polymer-metal	Conductive properties	Bio electroanalysis, bio electrocatalysis	[37]
Zinc oxide	Physical blending	Polymer-particle	Enhanced biological, mechanical, thermal, and antibacterial properties	Biomedical applications, bio electroanalysis	[82]
Magnetic nanoparticles	*In-situ* synthesis	Polymer-metal oxide	Improved biocompatibility, enhanced mechanical properties	Blood vessel adhesion	[112]

Synthesis of BC-based composites

The synthesis and fabrication of polymer composite materials use two primary approaches: *in situ* and *ex situ*. In the *in-situ* synthesis process, reinforcement materials are added during the synthesis of polymers, which become part of the polymer structure, while *ex-situ* synthesis involves impregnation of the polymer matrix with reinforcement materials.[3,41]

Functionalized BC can be obtained by incorporating materials of interest during production (*in-situ*) or after production (*ex-situ*) based on the requirements of the application.[4,42] The full potential of BC in tissue engineering remains partially exploited, despite recent advances, due to inherent disadvantages, such as irregular pore configuration and slow degradation, in particular under physiological conditions. For better applicability, it is necessary to modify and

improve the properties of BC to address these limitations. Reinforcing BC with preferred materials to create BC composites offers a solution. Modifications of the intrinsic chemical, physical, and mechanical properties of BC can be performed both *in-situ* and *ex-situ*. After the production process, cleaned BC can be obtained by removing bacteria and ectopic components with alkaline sodium hydroxide modification techniques.[43,44] This purified BC is then modified to produce blends and composites by reinforcing it with other beneficial materials.

Several characterization techniques, including Raman and Fourier transform infrared (FTIR) spectroscopy, scanning electron microscopy (SEM), X-ray diffraction (XRD), crystallography, surface analysis by profilometer spectroscopy, mechanical testing, and water absorption testing, are employed to assess the functionalization or modification of BC scaffolds.[14,45] The common approach to the synthesis of BC composite materials includes, *inter alia*, insoluble and *ex-situ* modifications that provide flexible solutions for different applications. Table 3 shows the comparison of various synthesis methods for BC composites, along with their advantages and disadvantages. In general, the method of synthesis and modification of BC composites for a wide range of applications is selected considering the desired properties.[3,39]

Synthesis of BC composites via in-situ *techniques*

At the beginning of the *in-situ* synthetic process, the BC composite synthesis method involves adding reinforcement materials to bacterial cellulose culture media, as shown in Figure 2(a).[21,43] As the micro-BC fibrils progress over time, they develop a denser web shape that traps different materials incorporated into synthetic media and leads to the formation of a composite material. To create BC composites with a variety of materials, this approach has been used, indicating its flexibility.[31,46] The agitation culture is often preferred in *in-situ* synthesis to overcome the challenges faced in static BC culture. Agitation prevents particles from settling, ensuring a constant entrapment of added materials in the BC fibrils.[47,48] For example, BC-Aloe vera composite films were synthesized by adding aloe vera to BC synthetic media cultured under static conditions, leading to superior physico-mechanical properties. Similarly, multi-walled carbon nanotubes (CNTs) added to synthetic media became entrapped between BC fibrils, demonstrating the versatility of this method.[49] Because of their toxic effects on microorganisms, certain bioactive substances with antibacterial properties cannot be directly added to the media. Additionally, BC composites synthesized through agitation culture may not be suitable for certain biomedical applications, limiting their applicability.[39,43]

In-situ modification is a more sustainable way of creating BC and CPs (calcium phosphates) composite materials, avoiding the disadvantages associated with post-production modifications.[50] Growth conditions may be different and additives or reinforcing agents may be added in real time during fermentation. This process has proven to be successful in producing composite BCs with unique and enhanced properties.[4,50] One notable example involves the *in-situ* production of BC/CPs composites, where sheets of reduced graphene oxide (RGO) were incorporated into the BC membrane during production.[52,79] As a result, a 3D mesh-like network of BC nanofibrils wrapped around RGO resulted in a flexible matrix, with exceptional electrical conductivity and mechanical properties. In the same way, using sodium alginate as an additive, *in-situ* BC nanohydrogel composite has been created, which shows potential for drug delivery systems with improved thermal stability.[53,54]

In-situ modification techniques extend to antibacterial applications, such as the self-polymerization of dopamine (PDA) to embed Tollen's Reagent (Ag) into BC, forming a BC/PDA/Ag nanocomposite with good biocompatibility and antimicrobial activity.[55] Carboxymethylation of pure BC using sodium carboxymethyl cellulose as an additive resulted in improved tensile strength and reduced elasticity, enhancing cell adhesion, proliferation, and biocompatibility for potential *in-vivo* implantation. These examples show the ability and potential of *in-situ* modification to adapt BC properties for different applications.[45,56]

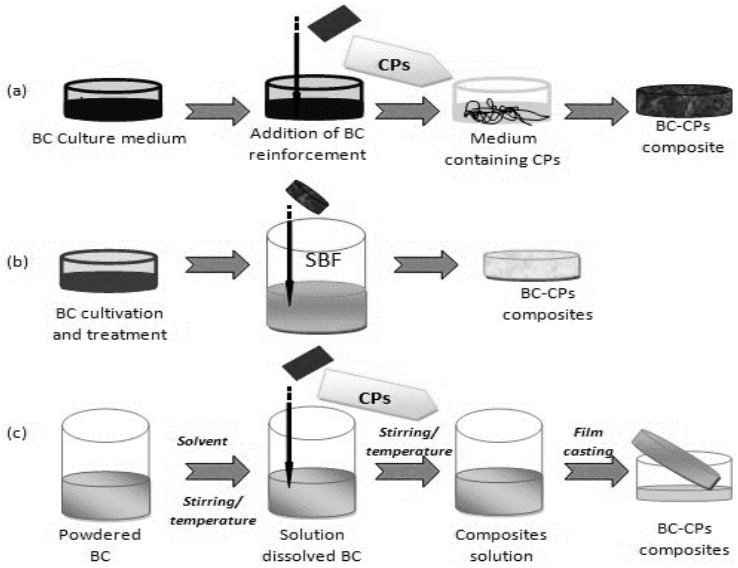

Figure 2: (a) BC composites prepared using *in-situ* synthetic approach – particles captured between BC fibrils as they developed; (b) *Ex-situ* synthetic approach to making BC composites; (c) BC composites produced from dissolved BC solutions using the solvent casting method[4,42,43]

Synthesis of BC composites using* ex-situ *techniques

Due to the inherent insolubility in most organic solvents, bacterial cellulose BC composites pose unique challenges. Before mixing with alginate, a chemical treatment strategy has been implemented to solubilize BC using an aqueous system of lithium hydroxide/urea/thiourea.[45] Previous research has successfully shown the production of a clear BC solution that was mixed with alginate and spun into fibers using a wet-spinning apparatus.[57] This approach will overcome the drawbacks of BC and allow composite materials with improved properties to be developed. An alternative strategy is to incorporate liquids and nanoparticles into a structural matrix of prepared BC to address the problems related to *in-situ* composite synthesis.[3,58] Physical interactions or hydrogen bonds between BC and reinforcement materials may help in this. The presence of hydroxylamine moieties in cellulose chains facilitates hydrogen bonding with reinforcement materials, allowing liquids and small solid particles to easily penetrate the porous BC matrix and absorb it.[59] The strategy is simpler and more useful than *in-situ* synthesis, since the initial structure of BC has not changed.[30,33]

For this strategy, BC sheets are commonly produced in a static method, making them suitable for a variety of biomedical and industrial applications.[3,36] This approach has been used to synthesize BC composite materials with polymers, inorganics, metals, and metal oxides, as shown in Figure 2 (b).[41,43] Depending on the reinforcement material, the characteristics of BC are different.[4] For example, through strong hydrogen bond interactions between chitosan-CH-CH molecules and BC-Fibrils, BC-CH-CH composites have shown improved mechanical properties. Similar strategies to synthesize BC composites with gelatin, simulated body fluid (SBF), and additional materials have been used to enhance their medical applications.[55,56] The incorporation of calcium phosphates (CPs) into BC sheets through a green route, without chemical reagents, improved the antibacterial activity of BC composites. BC-Pd, BC-CNT, and BC-MMT composites were also synthesized through the *ex-situ* composite production strategy, demonstrating versatility.[3,60]

However, the *ex-situ* composite synthesis strategy has limitations related to the size and nature of the reinforcement material. Only submicron to nanosized materials can be impregnated into the BC matrix, and hydrophobic materials may not effectively combine with BC.[61,62] Additionally, the structural arrangement of BC fibrils may not always be uniform, leading to uneven distribution of penetrating materials inside the BC matrix. Addressing these challenges requires the identification of new BC composite synthesis routes to ensure uniform and effective

incorporation of various reinforcement materials.[63,64]

Synthesis of BC composites by the sonochemical method

Utilizing solutions of dissolved bacterial cellulose (BC) offers a promising approach for the formation of a diverse range of BC composites with various materials.[4] This method allows for easy control over the composition of matrix and reinforcement materials, ensuring homogenous distribution and mixing. The schematic representation of BC composite development through this approach is illustrated in Figure 2 (c).[3,65] However, a significant challenge is the limited solubility of BC, as it is insoluble in water, most organic solvents, and non-polar solvents due to its polar nature. The strong inter- and intra-molecular hydrogen bonding and high crystallinity of BC contribute to its low solubility. Several compounds, such as N-methyl morpholine N-oxide (NMMO), calcium phosphates CPs, ionic liquids, $ZnCl_2$ ($3H_2O$), NaOH, and LiOH/urea/thiourea, have been identified as solvents capable of dissolving BC.[60,66]

Dissolved BC presents opportunities for synthesizing various materials, including BC films, microfibers, nanofibers, nanocrystals, and composite materials.[58,67] Regenerated BC films prepared from BC dissolved in NMMO, for instance, exhibited a uniform fibril arrangement with superior mechanical and thermal properties. While this dissolution and regeneration method has been extensively applied for polymeric composites with inorganic materials, its application in BC composites has been limited.[10] The dissolution method has shown promise, and recent efforts, such as synthesizing BC-CPs composites, demonstrated enhanced thermal, mechanical, and antibacterial properties.[28] The approach facilitates the thorough mixing of different materials in the BC solution, providing ease in processing composite films or fibers. The strong interactions between BC and the combining material in composites produced through this method signify its potential significance in future BC composite development strategies.[2,68] Table 3 provides a comparison of each of the three approaches based on benefits and drawbacks.

Table 3
Different synthetic approaches for the production of BC composites, their benefits, and limitations

Synthesis approach	Advantages	Limitations	Refs
In-situ combination of BC composites	• Easy processing • Assortment of strong and fluid support materials • Assortment of BC blend techniques (static, shaking, and agitated)	• Difficulties in composite blending because of the speedy infiltration of suspended particles • Limitation of bacterial cellulose blending with antibacterial agents • Limited uses of BC composites combined through fermentation strategy	[45,48,49]
Ex-situ combination of BC composites	• Combination of composites with BC films • Antimicrobial materials are not an issue • BC essential primary features are maintained	• Only particles with a diameter less than a micron or less than a nanometer can penetrate BC • In BC, there are difficulties with inhomogeneous particle transport • BC composites cannot be made with hydrophobic materials	[50,53]
Combination of BC composites from BC solution	• Controllable composites work • Wide variety of support materials • No limitation with bactericidal, attractive, directing materials	• Limited solvency of BC • Expensive methodology • Destruction of native BC structure	[58,60]

APPLICATIONS OF BC-BASED COMPOSITES

Bacterial cellulose (BC) exhibits a unique set of properties, including chemical nature, biocompatibility, hemocompatibility, biodegradability, porosity, high mechanical strength, crystallinity, transparency, and a 3D fibrous structure, making it an ideal material for diverse biomedical applications.[69,70] The polysaccharide characteristics of BC render it less immunogenic compared to proteins. BC composites, synthesized through various approaches and incorporating different reinforcement materials, have found applications in wound dressings, blood vessels, dental implants, scaffolds for tissue engineering (cornea, heart valve, bone, and cartilage), and drug delivery systems.[71] These composites are tailored to enhance existing properties and introduce additional functionalities for specific biomedical applications, making BC a versatile and multifunctional biomaterial. The diverse range of BC composites designed for various applications is depicted in Figure 3.[3,15]

Biomedical applications of bacterial cellulose composites

Table 2 provides the development of new biomedical materials derived from natural polymers, and bacterial cellulose (BC) has emerged as a promising candidate for a wide range of biomedical applications due to its unique properties.[15,72] BC, with its high water content of 98%, serves as an excellent hydrogel, and methods like supercritical drying or freeze-drying are employed to transform BC hydrogels into aerogels.[73] Both states of BC, as hydrogel and aerogel, exhibit great potential for biomedical applications. Recent research has focused on creating BC-based composites by combining them with polymers and nanoparticles, leading to the development of innovative biomedical products. The chemical characteristics, biocompatibility, hemocompatibility, biodegradability, porosity, high mechanical strength, crystallinity, transparency, liquid absorption capabilities, and 3D fibrous structure of BC position it as a versatile material for diverse biomedical applications.[74] Additionally, the polysaccharide nature of BC contributes to its non-immunogenic or less immunogenic profile compared to proteins. BC composites have found utility in the development of various biomaterials, including wound dressings, blood vessels, dental implants, scaffolds for tissue engineering (cornea, heart valve, bone, and cartilage), and drug delivery systems.[75]

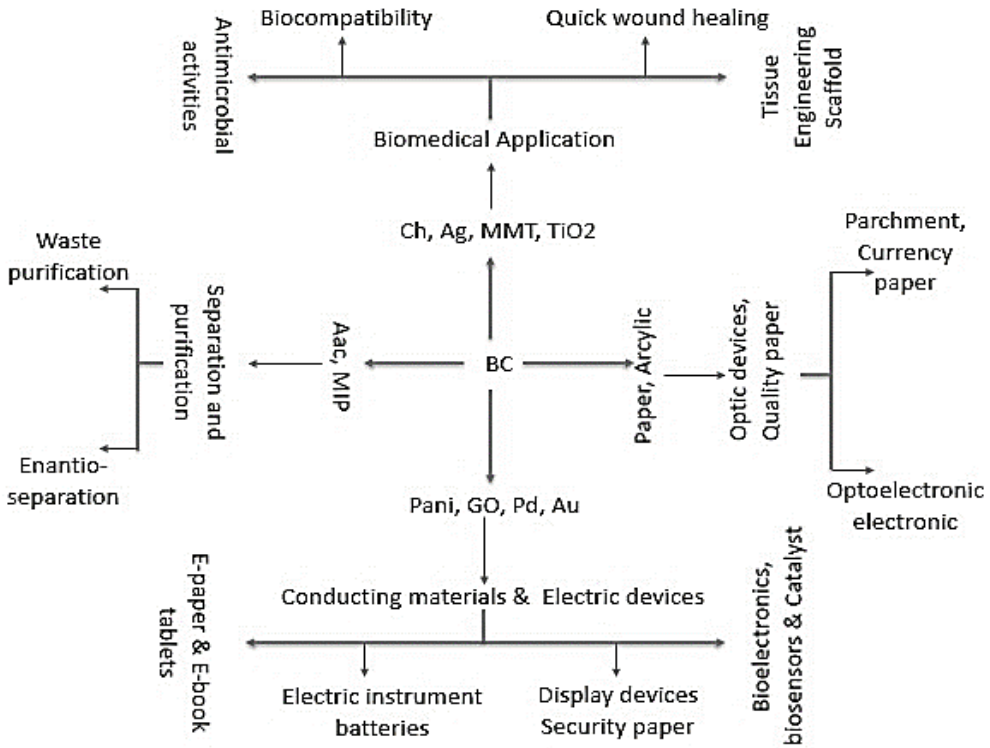

Figure 3: Depiction of BC composites formed from different components for specific applications in various sectors[3,15,72,102,117,127]

Wound dressings and skin regeneration

Bacterial cellulose (BC) has proven effective in wound dressings and skin tissue engineering, offering benefits, such as reduced pain, accelerated healing processes, and promotion of autolytic debridement.[76,77] Its hydrogel-like properties, stemming from high water uptake capacity, create an ideal environment for cell hosting and contribute to optimal wound healing. The *in-vivo* biocompatibility and 3D structure of BC provide a suitable substrate for cell attachment, growth, and rapid tissue regeneration in wounds, including chronic wounds and burns.[60,78] Despite the unique physical and chemical properties of BC as a scaffold for wound dressings, meeting all the required criteria for modern wound care involves addressing challenges, such as infections and inflammation. To enhance the wound healing capabilities of BC, researchers have explored composite materials. For instance, chitosan/bacterial cellulose (CS/BC) composite films reinforced with diamond nanoparticles have been investigated for their potential as wound dressings.[10,79] Electrospun CS/BC nanofibrous composites, incorporating graphene oxide (GO) nanosheets, demonstrated improved mechanical behavior and controllable water loss, which is essential for wound healing.[80] Antimicrobial properties have been imparted to BC through the incorporation of silver nanoparticles, contributing to the creation of antibacterial wound dressings. BC hydrogels containing montmorillonite (MMT) exhibited significant antibacterial activity, showing the versatility of BC in addressing microbial challenges in wound care.[81]

Recent developments include BC/TiO_2/GO nanocomposites with photocatalytic and photodynamic antibacterial activity, further expanding the potential applications of BC in wound care. The intrinsic wound-healing properties of BC, combined with various antimicrobial agents and nanomaterials, position it as a versatile material in the healthcare and biotechnology sectors.[78,81] The unique properties of BC align with the evolving needs of 21st-century wound care products, making it a promising material for advancing tissue and organ regeneration research and addressing challenges like antimicrobial resistance in healthcare. In summary, the efficacy of BC in wound care underscores its potential as a high-value material for achieving various objectives.[13]

Blood vessels

Bacterial cellulose (BC) has emerged as a versatile material for the synthesis of artificial blood vessels, addressing the need for both endothelialized lumens and mechanical strength crucial for physiological conditions. The foldability and moldability of BC make it an attractive option for synthetic prosthesis in blood vessel replacements. Tubular BC structures can be prepared through molding processes,[72,82] using cylinder glass molds, for atherosclerotic coronary replacement vessels. The molding involves inserting glass or silicon molds into culture media, allowing BC tubes to form around the molds. Alternatively, simple perforation of BC using a needle and subsequent freeze-drying has been employed to create tube-like structures without molds.[6] Tubular BC has proven effective in restoring blood circulation when coronary vessels are obstructed. BC, substituting synthetic materials like Teflon and Dacron, offers lower risks of blood coagulation and enhanced biocompatibility.[83] Its robust mechanical properties enable resistance against high circulatory system pressures. BC tubes, designed for small-diameter vascular grafts, exhibit morphology and mechanical characteristics crucial for optimal performance.[84] Functionalization of BC with peptides, such as the tripeptide Arg-Gly-Asp (RGD), promotes the attachment and growth of endothelial cells, enhancing the suitability of BC for blood vessel replacement.[85]

Artificial blood vessels, synthesized from BC, serve as substitutes for chemically synthetic materials, providing lower risks of blood clot formation and exhibiting high mechanical strength. The compatibility of BC with blood, lack of toxic effects, and support for cell growth make it an ideal element for creating viable artificial blood vessels.[39,86] The high tensile strength and flexibility of BC contribute to its ability to withstand the pressures generated by the circulatory system. BC-based nanocomposites, such as BC-PVA, demonstrate the necessary medical features for developing artificial blood vessels with desired properties, highlighting the potential of BC in the field of vascular prosthetics.[81,86]

Bone and cartilage tissue engineering

Bacterial cellulose (BC) exhibits immense potential for applications in bone and cartilage

tissue engineering due to its exceptional mechanical strength, crystallinity, ultrafine fibril network, and flexibility.[6,45] Electrospun nanofibers, which allow control over composition, fiber diameter, orientation, and pore size, provide an excellent substrate for use in bone tissue engineering.[87] BC, when incorporated with NFPCs (nano-fibrillated plant cellulose), supports the growth and proliferation of various cells, without inducing any toxic effects. For bone regeneration, porous structures are crucial to facilitate osteoblast ingrowth and the production of mineralized tissue.[88] Microporous BC scaffolds for bone regeneration have been successfully produced by incorporating paraffin wax microspheres into the fermentation process. Numerous BC composites have demonstrated enhanced osteogenic potential, promoting a quicker healing rate in bone regeneration due to the structural similarity of BC nanofibers to collagen, mimicking the bone matrix. The osteoconductive and mechanical properties of electrospun fibers can be further modified through the incorporation of bio-ceramics, such as hydroxyapatite.[89] Regarding cartilage regeneration, BC addresses the challenging clinical problem of low repairability. Poly(3-hydroxybutyrate)/BC scaffolds have been employed for cartilage regeneration, utilizing a compression molding/particulate leaching procedure. BC has been found to outperform materials like alginate and plastic in supporting chondrocyte migration and growth as a cartilage substitute.[10] However, the dense mesh of BC fibers can restrict cell infiltration, a challenge that has been addressed by incorporating pores into fibrous composites using porogens.[90] This approach opened new avenues for the development of BC-based grafts for damaged bone and cartilage.

Drug delivery

Nanocellulose materials, including bacterial cellulose (BC), have emerged as promising drug delivery systems for a wide range of clinical applications. BC exhibits excellent properties for drug delivery, providing a conducive environment for tissue repair through sustained release of therapeutic agents.[91] BC-based membranes and hydrogels have been investigated for various drug delivery applications, ranging from topical and transdermal delivery to verbal administration. Studies have demonstrated the feasibility of BC membranes for accurate drug delivery, preventing material loss and ensuring reproducibility of drug doses.[92] The characteristics of BC make it particularly suitable for transdermal drug delivery systems, offering simplicity in preparation and cost-effectiveness. Moreover, BC hydrogels, responsive to factors like temperature and pH, show promise as drug-release candidates with tailored properties.[2,34]

Table 4
Various bacterial cellulose-based biomaterials for biomedical applications

BC composite	Application	Function	Refs
BC films	Substitution of diseased arteries and blood vessel	Limitations on blood coagulation, significant water penetrability, high water-holding capacity, mechanical strength with enhanced biocompatibility, and low surface roughness	[84]
BC/chitosan	Scaffold, wound healing	Mechanical advantages, improved bio-compatibility, cell grasp, and expansion, profoundly nonporous, high water-holding, moderate water discharge highlights	[9,78]
BC/gelatin	Wound dressing	Attachment, multiplication, and tissue design platforms have all been improved	[56,93]
BC/MMT	Wound healing	Antimicrobial action, mechanical and thermal properties	[60]
BC/Go	Purification and separation of waste	Assimilation ability for hefty metals, restricting with metal particles, and partition of following metals, used for wastewater treatment	[79]
BC/chitosan and BC/silver nanoparticles	Electrical conductors and insulators	Antibacterial action, improved mechanical qualities and flexibility, and improved transparency	[94,111]

BC-based capsules have been explored as substitutes for gelatin capsules in oral drug delivery, displaying instant drug release, irrespective of drying methods or BC sheet thickness. Furthermore, BC has been utilized in the development of photodynamic therapy (PDT) systems for skin cancer treatment, as well as for the delivery of drugs like ibuprofen, showing its versatility in various therapeutic applications.[93] The biocompatibility of BC makes it an attractive candidate for drug delivery systems. Composite materials, such as polyvinyl alcohol (PVA)-BC and poly (vinyl alcohol)-chitosan-bacterial cellulose (PVA/chitosan/BC) have been developed to control drug release rates effectively. Additionally, surface-modified BC matrices have shown promise in enhancing drug release control and retention time.[15,94]

The FDA approval of BC-based medical devices and implants underscores its potential for drug delivery, transdermal applications, and tissue engineering.[95] BC structural properties, including fiber amount, thickness, and surface area, enhance drug incorporation efficiency and prolong drug retention time, aligning well with medical requirements. Moreover, BC modification strategies have been shown to further extend and regulate drug delivery, highlighting its continued relevance and potential in the field of drug delivery systems.[97,98]

Biosensors

Biosensors play a key role in detecting real-time biological signals, such as the release of antibodies or proteins in response to tissue injuries and infections.[98] Recent advancements highlight the potential of cellulosic materials, with bacterial cellulose (BC) standing out as a promising support for diagnostic devices.[2] BC offers stability, a large surface area, and high purity, making it a potential substitute for current biosensors. BC composites have found applications in various diagnostic sensors, contributing to cellular growth screening and the absorption of antibodies, enzymes, viruses, and polyelectrolytes. For example, researchers developed an electrically conductive biosensor using a BC/polyaniline/single-walled carbon nanotube (CNT) membrane.[10] Others explored the potential of Pd/BC hybrid nanofibers for dopamine detection,[99] or designed a smart wound-dressing substitute incorporating nanocellulose composites with a protease sensor for chronic wounds.[100] Another prominent development involved a biosensor based on horseradish peroxidase (HRP)/Au-BC nanocomposite, demonstrating excellent performance with a wider linear range, low limit of detection (>1 mm), and rapid response to hydrogen peroxide.[101]

Bacterial cellulose as bioink for 3D printing

The increasing global demand for organ replacement and tissue regeneration has driven advancements in tissue engineering and regenerative medicine, particularly through the development of 3D bioprinting.[122,123] This technology enables the creation of functional organs and tissues, with bioink serving as the critical component.[102] The selection of bioinks is essential, as they must meet various requirements, such as biocompatibility, printability, and mechanical stability, to ensure the successful development of 3D-printed tissue and organ structures. Enhancing the properties of bioinks through the combination of different materials and methods is necessary for advancing this field.[108] The current state-of-the-art in polymer-based bioinks used in 3D printing for tissue engineering and regenerative medicine. It emphasizes the key criteria for selecting effective bioinks, including biocompatibility, printability, and mechanical properties. Other crucial attributes for a bioink include high resolution during printing, *in situ* gelation, viscoelastic properties, affordability, availability, and scalability for industrial use. It should also mimic the internal structures of tissues, maintain mechanical integrity, require minimal post-printing maturation time, and offer immunological compatibility when implanted *in vivo*. Additionally, it should support a wide variety of different cell types. Also, the recent developments in bioink formulations have focused on materials like biomedical polymers, cells, and bio signals, and their roles in creating 3D tissues and organ structures.[129] Numerous bioink formulations have been developed, ranging from cell-biomaterial-based bioinks to cell-based bioinks, such as cell aggregates and tissue spheroids, for tissue engineering applications. Recent advancements in creating more tunable bioinks that are biocompatible, printable, and mechanically stable after printing are promising.[132] These innovations, often involving functional polymeric biomaterials and the blending of cells and hydrogels, demonstrate significant potential for producing more complex

tissue and organ structures through 3D bioprinting in the future.

Bacterial cellulose in cosmetology

Cosmetics play a significant role in enhancing various aspects of a person's appearance, covering the skin, face, nails, hair, and eyes.[15] With the increasing use of cosmetics for beautification, it is essential to consider potential side effects on the skin. For instance, certain cosmetic ingredients, like parabens, can lead to skin allergies.[117] Table 6 shows that there is a growing preference for natural skincare products, such as those made from bacterial cellulose (BC), which offers numerous applications in cosmetics, including facial masks, contact lenses, personal cleansing formulations, and facial scrubs.[15,118] BC stands out over plant cellulose due to its superior chemical purity, better hydrophilicity, increased water-holding capacity, stronger tensile strength, and enhanced polymerization. Its crystalline structure and unique ribbon-like microfibrils contribute to its porosity, making it an excellent choice for cosmetic applications.[119] The remarkable absorbency of BC, with the capability to hold liquid about ten times more than non-woven masks, positions it as an ideal material for skincare products.[18] The nano-fibers in BC provide good adhesion to irregular skin surfaces, ensuring that BC masks reach every contour of the face. The malleability, tear texture, and flexibility of BC, attributed to its nanostructure, make it highly suitable for skincare applications. Its thin thickness and nano-fibers, approximately 20 nm in diameter, enable BC masks to penetrate deep into fine lines and wrinkles, providing effective skincare where traditional sheet masks may fall short. The incredible soft touch of BC offers comfort, soothing effects, and hydration to the skin.[15,120]

However, BC, in its natural form, lacks inherent anti-aging, whitening, and cleansing properties. To maximize its potential in the cosmetics industry, BC is often impregnated with active substances, such as essential oils, herbs, plant extracts, algae extracts, panthenol, and more.[15] These active ingredients are selectively bound inside the BC matrix through hydrogen bonds, allowing for their gradual release into the skin during application. BC sheet-type mask packs, conforming to different facial areas, have gained popularity for their excellent skin moisturization and conditioning benefits.[121]

Additionally, the low toxicity and hydrating properties of BC make it of great interest for treating dry skin. Companies have invested in long-term research, developing various BC-based masks with functions such as moisturizing, cleansing, whitening, and anti-aging.[122] These products guarantee excellent moisturizing effects in a sterile and toxin-free environment, representing a novel skincare technology that combines innovation, comfort, and performance.

Table 6
Commercial BC-based cosmetic products with their properties[15,118]

Design	Properties	Products	Refs
Moisturizer BC mask	Effectively locks in skin moisture, keeping it silky and elastic for an extended duration	Royal Skin Brightening Bio-Cellulose Korean Beauty Mask in Korea	[131]
Anti-aging BC mask	Enhances skin elasticity and diminishes wrinkles and fine lines	Anti-ageing Bio-Cellulose Mask manufactured by Tech Nature Private Label in France	[120]
Smoothening BC mask	Provides soothing relief to the skin following aesthetic treatments and sun exposure	Aloe Bio-Cellulose Mask available in the U.S.A.	[116]
Whitening BC mask	Reduces dark pigmentation on the skin and evens out the skin tone for a bright and radiant appearance	DHC Bio Cellulose Mask from Japan	[125]
Oxygenizer BC mask	Exhibits anti-pollution and antioxidant properties, purifying, oxygenating, and safeguarding the skin	Laboratories esthetic Face Mask in France	[129]
Lightening BC mask	Illuminates and rejuvenates the skin while possessing anti-dark spot attributes	Bio-Cellulose Mask by Guangzhou Microcell Bio-Technology Co., Ltd. in China	[122]

As the cosmetics industry continues to evolve, the versatility and unique properties of BC position it as a valuable ingredient for advanced skincare solutions.[123]

A targeted approach is possible with these mask packs, since they are made to match the unique forms of the face and other places. The cellulose matrix of BC, which is based on hydrogen bonds, ensures the effective absorption and extended effects of active compounds on the skin.[124] Because of the gradual release, active ingredients can deeply affect the skin, providing superior skin conditioning and moisturization. Because BC face masks are so highly hydrating and low in toxicity, they are especially attractive for treating dry skin.[125] When compared to moist paper towels, research on customer satisfaction with BC masks has shown that they are successful in dramatically improving skin moisture content.[126]

Bacterial cellulose (BC) composites for electronic devices

Bacterial cellulose (BC) presents a distinctive three-dimensional fibril network reminiscent of paper upon drying. Recent investigations have explored the potential of BC composites-based optoelectronic and photonic devices, some of them are listed in Table 5.[32,102] While inherently non-conductive, BC can be transformed into electrically conductive sheets by incorporating specific conductive materials. These conductive or semi-conductive BC sheets are subsequently immobilized with electrochromic dyes and attached to electrodes.[103] The advantages of BC composites as electrodes are their high flexibility, biodegradability, excellent contrast of display devices, and high performance.[104,105]

Flexible bacterial cellulose membranes have already been employed in the development of organic light-emitting diode (OLED) devices.[106] Many researchers successfully fabricated OLED displays on cellulose and acrylic resin nanocomposites, demonstrating their utility in various applications, such as e-newspapers, e-book tablets, rewritable maps, dynamic wallpapers, and learning tools.[3,106] Numerous attempts have been made to synthesize BC composites containing various conductive materials with the ultimate aim of preparing electrical devices. These efforts include synthesizing BC composites with conducting polymers and conducting metals. The integration of BC into these composites opens up possibilities for diverse applications in the field of flexible and biodegradable electronics.[107]

Table 5
BC composite-based electronic devices/fabrication techniques applications with key findings

Composite material	Technique	Potential application	Key findings	Refs
PPY/BC/RGO		Flexible supercapacitors	Areal capacitance of 3.66 F cm^{-2} (at 1 mA cm^{-2}), 2.59 F cm^{-2} (at 50 mA cm^{-2}), areal energy density of 0.23 mWh cm^{-2}, maximal power density of 23.5 mW cm^{-2}, with 73.5% retained capacitance after 8000 cycles	[105]
GE/BC	CFLIC method	Electromagnetic interference shielding, batteries, supercapacitors	Electrical conductivity up to 101 S cm^{-1}	[109]
BC/GO	Vacuum-assisted self-assembly	Advanced biochemical and electrochemical devices	Increased Young's modulus by 10%, increased tensile strength by 20%, and enhanced electrical conductivity (6 orders of magnitude improvement)	[113]
BC/GE/PANI	*In-situ* membrane-liquid-interface technique	Shielding electromagnetic radiation, flexible electrodes	Electrical conductivity of 1.7±0.1 S cm^{-1}, and enhanced mechanical properties through uniform graphene dispersion	[126]
BC/CNF	C-based synthesis of CNF aerogels	Advanced biochemical and electrochemical devices	Lightweight, fire-resistant, absorbents, sensors, battery materials, catalyst supports. The density of CNF aerogels: is 4-6 mg/cm^3; Absorption capacity: Up to 310 times their weight; electrical resistance decreases linearly with increasing compressive strain	[124]

Flexible displays

BC has emerged as a promising substrate for flexible displays, but certain adjustments, such as enhancing surface smoothness and controlling hygroscopicity, are essential for its effective use in the fabrication of OLEDs.[4,39] Ummartyotin *et al*.[108] proposed a method involving the deposition of SiO thin films through plasma-enhanced chemical vapor deposition, serving as a transparent barrier to prevent water absorption.[108] This SiO layer not only protects against water absorption, but also contributes to surface smoothness. By combining SiO with a ferrofluid solution, the BC surface smoothness can be reduced to as low as 5 nm.[4] To further optimize BC for flexible OLED displays, composites with various compositions were prepared using a polyurethane (PU)-based resin. These composites, when utilized as substrates, demonstrated remarkably high visible light transmittance, reaching up to 80%.[39] In addition to outstanding transparency, these compounds exhibited significantly elevated thermal stability, withstanding temperatures up to 150 °C. When OLEDs were fabricated on these substrates, they displayed a maximum current efficiency of 0.085 cd/A and a power efficiency of 0.021 l m/W at 200 cd/m^2.[109] This study underscores the potential of BC nanocomposites as exceptional materials for flexible display substrates.

Optically transparent films

Bacterial cellulose (BC) produced through static cultures typically results in non-conductive films. To introduce conducting features into BC, composites with multiwalled carbon nanotubes (MWCNTs) have been synthesized by immersing a BC pellicle in an aqueous MWCNT dispersion containing a surfactant.[110] The electrical conductivity of the resulting BC pellicles, which contained well-dispersed and embedded MWCNTs, was approximately 1.4×10^{-1} S/cm.[111] Initially, these composites exhibited relatively low optical transparency, but this was enhanced by incorporating an aqueous silk fibroin solution into BC membranes.[112] The resulting composite films displayed good optical transparency, with a transmittance of 70.3% at 550 nm and electrical conductivity of 2.1×10^{-3} S/cm. In another study, graphene nanoplatelets (GNPs) were incorporated into pure BC membranes to confer electrical conductivity, with a BC membrane containing 8.7 wt% GNPs exhibiting an electrical conductivity of 4.5 S/cm.[113] Extensive research has focused on BC composites with polyaniline (PANi), a highly conducting polymer.[63-70] Previous research reported the *in-situ* synthesis of PANi in the BC matrix through the polymerization of aniline in the presence of ammonium persulfate as an oxidant, resulting in BC-PANi nanocomposites with excellent electrical conductivity of 5.5×10^{-2} S/cm and good mechanical properties.[114] Interfacial polymerization further improved the electrical conductivity of PANi/BC composites, raising it to 3.8×10^{-1} S/cm.[115] These BC conductive composite films combine the electronic characteristics of conducting polymers and nanomaterials with the excellent mechanical properties of the BC matrix, making them suitable for applications in optoelectronics, including flexible electrodes, flexible displays, and other electronic devices (Fig. 4).[4,39,116]

Composites with high mechanical strength for industrial applications

BC composites with enhanced strength open up avenues for diverse applications across various industries. Table 6 represents some of the approved BC-based products available on the market.[135-138] Some of the listed products for biomedical applications are FDA approved.

The incorporation of materials into BC growth media results in the assimilation of these materials into growing BC fibrils, contributing to improved mechanical properties.[21] An intriguing example involves the addition of scrap paper particles to BC growth media, where the embedded paper particles become integral to the growing cellulose.[2] This process enables the production of BC-paper composites with controllable quantities, surpassing the strength of traditional paper. This innovative approach, demonstrated by Mormino and Bungay,[127] shows the potential of BC composites in enhancing the mechanical properties of conventional materials. In a related study, BC was synthesized by introducing glucose phosphate along with glucose into the culture media.[3,128] The phosphate became incorporated into the BC gels, forming BC composites when combined with wood pulp during paper sheet formation. The addition of BC significantly enhanced the strength and fire resistance properties of the paper sheets. This breakthrough, explored by Basta and El-Saied,[129] suggests that BC composites play a pivotal role in the synthesis of high-quality and durable paper products.[130]

Table 6
Approved BC-based commercial products available on the market

Product	Type	Application	Company/agency	Refs
Basyc	Vessel implant (tubes)	CABG (coronary artery bypass surgery)	Jenpolymer Materials Ltd. & Co. (Germany)	[133]
Gengiflex	Non-resorbable cellulose membrane	Periodontitis	Biofill Produtos Biotechnologicos	[136]
OLEDs	Flexible and transparent composites	Eco-friendly biocompatible substrate for flexible electronics	MBRAUN (USA)	[138]
BioCelltrix	BC surgical mesh	Protection for miners from potential burns	Genesis (USA)	[134]
Cellulon	Binder	Medical applications including non-woven structures	CP Kelco (Atlanta, GA)	[135]
Nano-in Deep Cleaning	Nano micelles, Zinc oxide	Zinc oxide	Nano-Infinity Nanotech Co., Ltd (Taiwan)	[137]
VSonic	Speakers and headphones	Audio speaker diaphragm	Sony (Japan)	[138]
Securian	Tissue reinforcement matrix	Tendon repair	Xylos Corporation (US)	[137]

Due to the remarkable properties of BC, it also finds applications in the field of optoelectronic devices. BC composites serve as an excellent solution, providing significantly enhanced mechanical properties, without compromising optical transparency. Nogi *et al*.[131] reported BC nanocomposites were prepared with acrylic resins. In this process, BC sheets were impregnated in an acrylic resin solution, resulting in transparent composites, with tremendous potential for use in optoelectronic devices.[39] These BC-polymer composites not only exhibited superior strength, but also maintained stable transmittance, even with temperature variations. This demonstrates the versatility of BC composites, acting as reinforcing materials in optoelectronic applications, without compromising the optical properties of the polymer.[4,131] The incorporation of BC into composites holds promise for diverse industrial applications. Whether strengthening traditional materials like paper or enhancing the mechanical properties of optically transparent polymers for optoelectronic devices, BC composites showcase their adaptability and potential across various industries.[132] These innovations pave the way for the development of advanced materials with improved mechanical strength and versatile applications.

CONCLUSION

The potential applications of cellulose-based composites in various industrial and biomedical applications have been widely studied and discussed in this review article. The incorporation of different reinforcement materials to overcome the characteristic and functional limitations of BC has gained attention in recent years. Controlling the orientation of BC fibrils during biosynthesis may prove vital in improving the physicochemical characteristics of BC. BC-based materials have made significant advances in biomedical applications, the development of energy storage devices, wearable electronics, electrochemical biosensors, and drug delivery systems. However, it is still a challenge to develop innovative nano-scale BC-composites that can mimic the tissue completely. More research efforts are needed to improve the porosity of the BC based materials to enhance the cell seeding to expand the horizon of BC-based composites in other biomedical applications. Most of the current research on the development of BC-based composites is largely confined to the laboratory and needs to be scaled up to widen the application horizon as engineering biomaterials. The biggest obstacle faced in large-scale applications of BC-based materials is the high cost of production. There is an urgent need for the development of automated low cost and high scale production bioreactors in the future. Further research is needed to overcome the problems associated with BC composites on structure instability after chemical modifications, and improving physicochemical features.

ACKNOWLEDGMENTS: The authors are thankful to the Council of Science and Technology, UP (UPCST), for funding this research work, as well as to the Department of Biotechnology and the Department of Physics and Materials Science and Engineering (PMSE), JIIT Noida, India, for providing the necessary facilities to carry out this work.

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