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Systematic Review

Advances in Bacterial Cellulose Production: A Scoping Review

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Abstract: The versatility, contribution to sustainability, and diversity of applications of bacterial cellulose require large-scale production processes and new alternatives in terms of biological systems that, under controlled conditions, favor the growth and production of this biomaterial. This review article describes the technologies developed and the advances achieved in regard to the production of bacterial cellulose on a small and large scale, according to the findings evidenced in the scientific literature in the last ten years. A review, based on the guidelines in the PRISMA® methodology, of a selection of articles was carried out, with a Cohen's Kappa coefficient of 0.465; scientific databases, such as Web of Science, SCOPUS, PubMed, Taylor and Francis, and ProQuest, were considered. There is a wide variety of bacterial pulp production systems and the design of such a system is based on the type of cellulose-producing bacteria, oxygen requirements, mixing and agitation, temperature control, sterilization and cleaning requirements, and production scalability. The evolution in the development of bioreactors for bacterial cellulose has focused on improving the production process's efficiency, productivity, and control, and adapting to the specific needs of bacterial strains and industrial applications.

Keywords: bacterial cellulose; biomaterials; production technologies; bacterial cellulose applications

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Citation: Cruz, M.A.; Flor-Unda, O.; Avila, A.; Garcia, M.D.; Cerda-Mejía, L. Advances in Bacterial Cellulose Production: A Scoping Review. *Coatings* **2024**, *14*, 1401. https://doi.org/10.3390/coatings14111401

Academic Editors: Daniela Predoi, Carmen Steluta Ciobanu and Carmen Cîmpeanu

Received: 16 September 2024
Revised: 25 October 2024
Accepted: 30 October 2024
Published: 4 November 2024

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1. Introduction

Bacterial cellulose (B.C.) is a high-value polymer because it has a wide range of potential applications in multiple industry sectors [1,2]. Microorganisms synthesize this polymer, which exhibits distinct structural, physical, and mechanical properties compared to plant cellulose [3]. One of the promising applications of B.C. is its use as a coating material. Due to its biocompatibility, high water retention capacity, high purity, non-toxicity, and excellent mechanical strength, B.C. has been utilized as a coating in wound dressings, where it provides a protective barrier and accelerates healing [4]. B.C. is employed as an eco-friendly coating for packaging, which is ideal for food, offering a biodegradable alternative to plastic, while serving as a protective barrier against microbial growth [5,6]. Additionally, B.C. can be used as a coating for electronic components, such as flexible batteries and sensors, as it has excellent insulating and dielectric properties [7]. B.C. has demonstrated significant potential in the paper industry, enhancing both the physical durability and print quality of high-grade papers. When used as a surface coating agent, B.C. offers innovative solutions by expanding the achievable color gamut [8].

At present, the production of B.C. is developing and has attracted great interest, generating new methods and technologies for its production on a small and large scale [9].

The production of B.C. is performed using biotechnological processes that take advantage of the metabolic pathways of acetic acid bacteria, such as the genera *Acetobacter*, *Gluconobacter*, and *Komagataeibacter* (previously classified as *Gluconacetobacter*), resulting in a purer form of cellulose compared to plant-based cellulose [10].

Several technologies have been developed to optimize the conditions for production and improve its performance to achieve efficient and cost-effective production of B.C. Technologies that allow B.C. production should consider using specific culture media. These media employ sugars as a carbon source, providing the nutrients necessary for synthesizing B.C. and promoting its growth [2]. Specific fermentation conditions are carefully chosen to enhance B.C. production, optimizing variables such as the carbon source, pH, temperature, stirring conditions, and oxygen supply. [11,12].

Genetic engineering techniques have been used to improve the production of B.C. One such technique is the sequencing of genes responsible for B.C. synthesis [13], which can then be manipulated to improve the polymer's performance.

Advances in functional genomics have provided valuable information on the molecular mechanisms of B.C. synthesis, allowing the development of new strategies and further optimization of B.C. production, not only through the use of *Komagataeibacter xylinus* (*Acetobacter xylinum* or *Gluconacetobacter xylinus*) [14,15], but also via other bacteria and algae that are capable of synthesizing cellulose. Integrating new technologies, traditional methods, and advances in biotechnology, contribute to the yield and quality of B.C., increasing its importance and driving the growing global demand for B.C.-based products, which raises the need to develop sustainable production methods [16].

Figure 1 shows a map based on bibliographic data created from the most frequent terms: 2649 papers, studies published in the last 20 years on the SCOPUS database, and in which applications of B.C. are described.

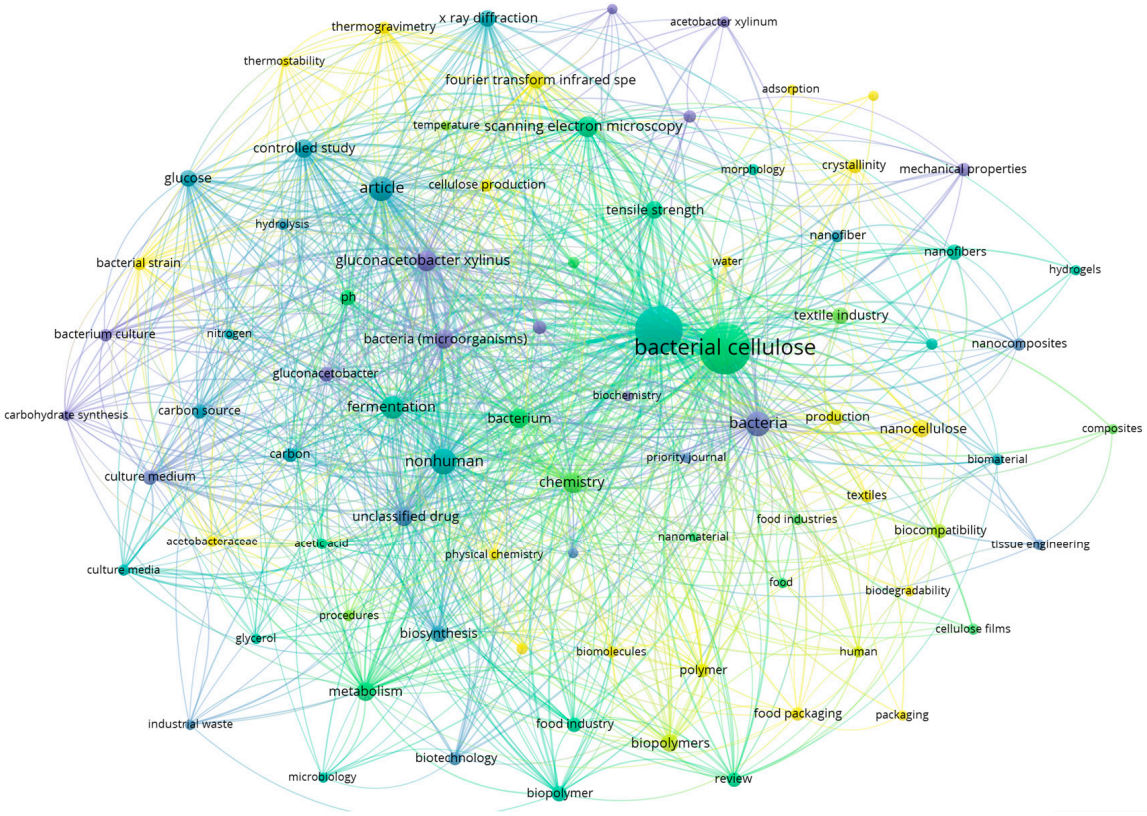


Figure 1. Bibliometric graph of the most frequent terms in related studies published on the SCOPUS database in the last 20 years; search carried out with string: "bacterial cellulose applications"; graph obtained with the VOSviewer® version 1.6.20 tool.

Figure 1 shows four areas of knowledge related to B.C. applications: biomaterials, biomedical applications, fermentation, and studies on the characteristics of this polymer. There is evidence of a greater number of studies on biomedical applications and the creation of biomaterials. A higher frequency is observed in regard to topics related to biocompatibility studies, tissue engineering, and fermentation.

Studies have addressed the impact of B.C. on promoting the Sustainable Development Goals. B.C. can contribute significantly to the United Nations Sustainable Development Goals (SDGs) due to its sustainable properties and its potential to address various environmental and social challenges [17,18]. Some of the contributions B.C. can make to implementing the SDGs (Figure 2) are described below.

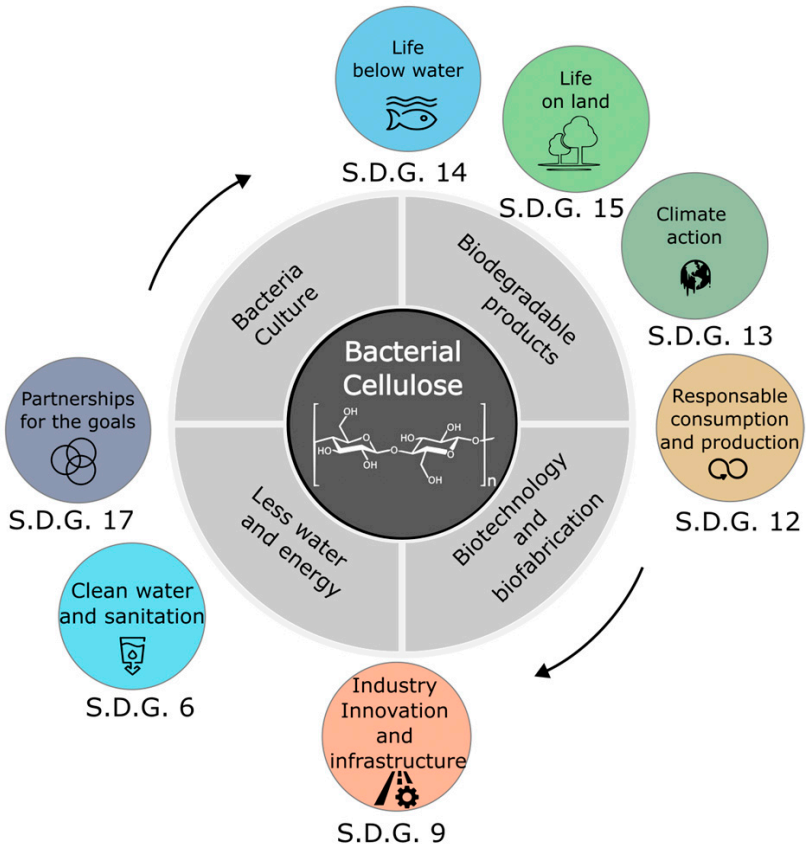


Figure 2. Contributions by bacterial cellulose to the Sustainable Development Goals.

Concerning industry, innovation, and infrastructure (SDG 9), using B.C. in industry represents an innovation in terms of the adoption of the most efficient production processes by obtaining sustainable materials as products, whose use generates more sustainable products, structures, or solutions. Regarding responsible consumption and production (SDG 12), producing biomaterials, such as B.C., promotes a more responsible approach to production and consumption by using renewable and biodegradable resources instead of non-renewable resources, such as oil. In addition, B.C. can help reduce textile waste and promote the circular economy by using waste from other industries as raw materials. B.C., its diffusion, and its use, contribute directly to combating climate change by generating a lower environmental impact (SDG 13).

B.C. production contributes significantly to the Sustainable Development Goal (SDG 12) on responsible production and consumption. This type of cellulose is generated from biotechnological processes, using bacteria, such as Gluconacetobacter, which synthesize cellulose under controlled conditions without the need for toxic chemicals or high amounts of energy. In addition, the B.C. production process can take advantage of agricultural or industrial waste, which contributes to waste reduction and the circular economy. Additionally, by using waste

as a source of nutrients and optimizing processes, waste generation is reduced and negative environmental impacts are minimized [19,20].

Promoting B.C. and its integration into the textile industry requires collaboration between various sectors, including governments, businesses, and organizations, to foster the adoption of sustainable technologies and knowledge transfer and generate partnerships to achieve the goals (SDG 17).

To improve B.C. production, government, companies, and organizations can collaborate through investment in research and development (R&D), the establishment of favorable public policies, and the creation of public–private partnerships. Both governments and non-profit organizations can provide funding for biotechnology research and investment and strengthen academic research centers that are working to optimize B.C. production processes, thus generating collaboration among institutions to develop and transfer new technologies.

In addition, all three actors can drive the creation of a circular economy by leveraging agricultural residues and industrial waste as materials in the production of B.C.. The government can support these efforts through incentive programs and regulations that promote the use of biodegradable materials. Organizations can promote cross-sector collaborations that contribute to a more efficient and responsible production cycle [21].

Collaboration between industry, academia, and government is critical to accelerate B.C. research, development, and commercialization [22]. Knowledge sharing can lead to faster breakthroughs and innovative applications [9]. The future of bacterial pulp production is shaping up to include process optimization, the diversification of raw material sources, the development of modification techniques, and the discovery of new applications.

This work provides a synthesized reference on the current advances in regard to the cultivation methods, strain selection, genetic modification, specific production technologies, optimization and improvement processes, sustainable production technologies, and agro-industrial waste used to produce biopolymers based on B.C., their applications, and innovations.

In the Methodology Section, this article describes the process of reviewing the scientific literature. In addition, the current applications of B.C., according to their use in industry, are described. The limitations and disadvantages in terms of B.C. production are specified. Finally, the expectations, different approaches, and challenges in regard to generating new technologies for B.C. production are addressed.

2. Methodology

The review detailed in this document was established through the use of a scoping review protocol, according to the guidelines in the PRISMA® methodology, and the details of the review that was carried out can be consulted in [23]. Scientific publications from the last ten years were included in the selection of documents; journal articles and conference papers from databases and repositories indexed on SCOPUS, the Web of Science, and PubMed, were considered.

The main research question was: What technologies have been developed to produce B.C.? The development of this review was divided into three phases: elaborating the research questions, defining the scope, and planning a comprehensive search to collect all the relevant documents. Subsequently, the articles were reviewed to identify the most relevant research and the documents were classified according to a predefined structure; finally, a process of extraction and review of the information used in preparing this document was carried out.

Four questions were posed to extract the information described below: RQ1. What are the potential applications of B.C.? RQ2. What technologies have been developed for the cultivation of B.C.? RQ3. What are the limitations and challenges in terms of B.C. production? RQ4. What is expected in the future in terms of bacterial pulp production technologies?

The scoping review checklist proposed by PRISMA® was used and the number of pages based on which relevant information can be found was specified to verify the

information provided in this document. The questions described in Table 1 were applied to assess the quality of the selected scientific articles.

Table 1. Quality assessment questions to assess the quality of the paper.

Quality Assessment Questions	Answer
Does the paper describe technologies used for bacterial cellulose production?	(+1) Yes/(+0) No
Does the paper describe the technical aspects of and methodologies for bacterial cellulose production?	(+1) Yes/(+0) No
Does the paper describe the limitations and disadvantages of bacterial cellulose production?	(+1) Yes/(+0) No
Is the journal or conference in which the paper was published indexed by the SJR?	(+1) if it is ranked Q1, (+0.75) if it is ranked Q2, (+0.50) if it is ranked Q3, (+0.25) if it is ranked Q4, (+0.0) if it is not ranked

Figure 3 shows the workflow used to select the documentation related to "technologies of bacterial cellulose production". A search was carried out on the specified scientific databases.

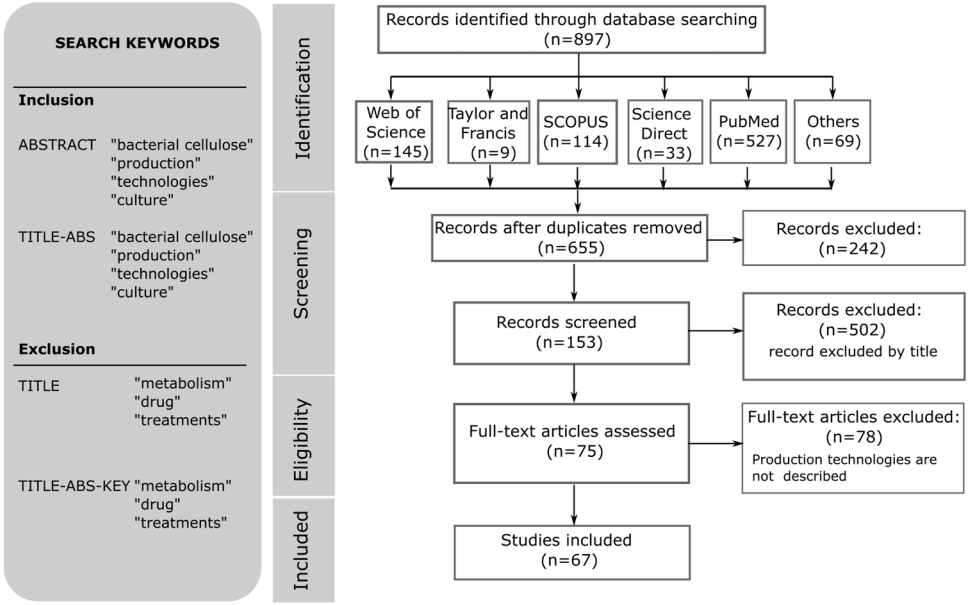


Figure 3. Workflow according to the guidelines in the PRISMA® methodology.

3. Potential Applications of Bacterial Cellulose

B.C. is a material of great relevance due to its unique properties, including its mechanical resistance, ultrafine fibers, biodegradability, high crystallinity, and purity, which makes it an attractive option for various applications [24] and which benefit multiple areas of industry (Figure 4).

In the food industry, B.C. is used as a thickening, stabilizing, and emulsifying agent in products such as sauces, dressings, and ice cream, improving the texture and stability of food [25]. The ability of B.C. to replace fat in baked goods and its use in edible packaging illustrates its value as an environmentally friendly alternative [26,27].

In the textile industry, B.C. is used as a base material for producing textile fibers and fabrics, driving the creation of clothing and fashion products [25]. Its versatility in shaping textiles is a crucial element of innovation within this industry [2,22].

In the last five years, B.C. has been applied in a variety of products that stand out for their sustainability and beneficial properties [3]. In the cosmetics industry, B.C. is used, for example, in facial masks, where it acts as a moisturizing material with high water

retention, providing deep hydration and better absorption of active ingredients, such as vitamin C, which helps to improve the skin. These masks are biocompatible, biodegradable, and more sustainable than synthetic alternatives, making them a popular choice in green cosmetics [28].

In the biomedical field, B.C. has been widely used in wound dressings, noted for its antimicrobial properties, fluid absorption, and ability to promote healing. It has also been used in the manufacture of vascular grafts and scaffolds for tissue regeneration, since its porous structure facilitates cell growth and the formation of new tissues [29]. Other products include B.C. as an emulsifier, specifically in the food industry, and its incorporation in batteries and electrical sensors, thanks to its flexibility and conductivity, which is enhanced with metal nanoparticles, such as graphene [28].

Medicine and pharmacology also benefit significantly from B.C. Bacterial cellulose has been used to produce biomedical materials, from dressings to implants, films, coatings, and drug delivery devices and vehicles. This material is biocompatible and promotes tissue regeneration [30]. Its use extends to tissue engineering, bone regeneration, and regenerative medicine [31,32]. Its high purity, water retention, tensile strength, biocompatibility, biodegradability, and three-dimensionality, make it especially attractive for medical applications, such as drug delivery, wound healing, and tissue engineering. The purity of B.C. makes it particularly valuable compared to plant-based alternatives, which can be contaminated with other polymers [1,33].

B.C. shows extraordinary potential in the biomedical field, from regenerating periodontal tissue to replacing blood vessels and nerves [34,35].

In the cosmetics industry, B.C. is used in the formulation of skin and hair care products, as well as being used as an emulsion stabilizer [25,36]. Its potential to provide innovative solutions in this area continues to be the subject of research.

Electronics finds an ally in B.C. It has been used to manufacture flexible displays and electronic devices, like capacitors, flexible electrode materials, and biosensors [9,36]. This application highlights its contribution to the technological forefront and its ability to adapt to changing demands.

In the construction field, B.C. is versatile and has been used for producing thermal and acoustic insulation materials and in manufacturing reinforcements for concrete and other sustainable building components [2,9].

The use and potential of B.C. has also been harnessed for biofuel production. In addition, its ability to capture and store carbon dioxide has been consolidated as an energy efficient and ecological solution. The potential of this material in environmental engineering has allowed the development and production of membranes for water treatment, with excellent results [37].

Developments exploring the application of B.C. in producing composite materials for papermaking have been evidenced. B.C. has proven valuable in fields such as restoring degraded paper in libraries and archives and producing proton exchange membranes [38,39].

The application of B.C. extends to nanotechnology, bioprocesses, and nanomedicine, promising areas for developing green chemistry products. In addition, its potential can be seen in engineering, biotechnological processes, materials science, and electronics [13].

The diversity of B.C.'s applications is impressive, spanning fields such as food production, electronics, textiles, paper, and more. Lourenço, 2023, highlights the potential of bacterial nanocellulose (BNC) as a valuable component in papermaking, enhancing both the physical properties and printing quality of fine papers. The authors have explored its application in both the wet-end process and as a coating material, paving the way for innovative advancements in the paper industry [8]. When used as a coating agent, BNC significantly improved the surface smoothness and light scattering coefficient of the paper. The study noted remarkable enhancements in the print quality, with improvements in the gamut area of over 25% compared to the base paper and over 40% compared to starch-only coated papers [8].

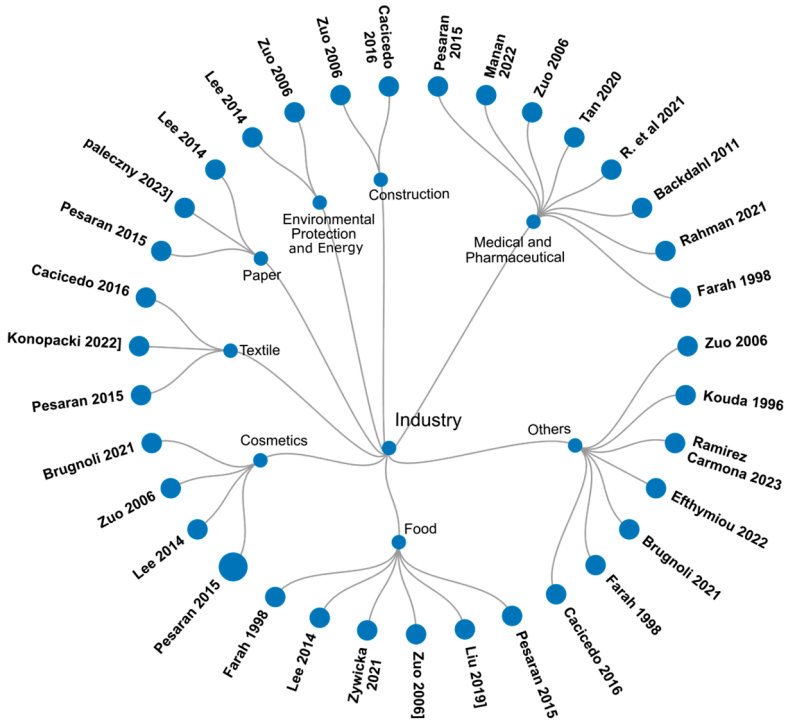


Figure 4. Some studies describing applications of bacterial cellulose in industrial areas [1,5,7,13,15,16,18,21,25–27,29,30,32–42].

4. Key Technologies for Bacterial Cellulose Production

This section describes the technologies and culture methods used to produce B.C. The technologies will be addressed considering the following categories: cultivation methods, strain selection and genetic modification, specific production technologies, optimization and improvement technologies, sustainable production and waste utilization technologies, biopolymers based on B.C., and specific applications and innovations.

4.1. Culture Methods

4.1.1. Culture Conditions

B.C. is obtained through fermentation in an aqueous medium, in a liquid environment containing specific nutrients. Bacteria synthesize cellulose chains in their extracellular matrix, as they reproduce and grow in the medium.

Factors such as the pH, temperature, nutrient availability, aeration, agitation, and oxygen levels, must be properly monitored to support microbial growth and cellulose synthesis.

Temperature control is crucial for B.C. production, with optimum temperatures averaging 30 °C, which may vary according to the bacterial strain used; outside this defined optimum temperature, the yield may be reduced [12].

Likewise, the pH has an impact on the product yield; it should be at a value of approximately 6, since any variation in this value diverts nutrients away from the metabolic pathways responsible for cellulose formation.

Aeration influences the availability of oxygen for the growth of the microorganism and the subsequent production of the product. In addition, in conjunction with agitation, the distribution of oxygen in the system is improved. However, there must be a balance in the system in this regard, so as not to affect the integrity of the cellulose by the agitation force [19,42]. The oxygen supply can be affected by traditional bioreactor designs, where oxygen transfer rates are insufficient for the growth of microorganisms, limiting their productivity.

Crystallinity is reduced because agitation causes the formation of irregularly shaped cellulose in the form of pellets, instead of uniform three-dimensional structures obtained in

static cultures. Mainly, at high agitation speeds, structural damage to the cellulose occurs due to the shear force in the system. This occurs mainly in stirred tank bioreactors [19,43].

4.1.2. Bioreactors

According to [26], various bioreactor technologies and culture conditions have been employed to produce B.C. on a large scale [42]. Bioreactors allow for more precise control of the culture conditions and can improve productivity [9]; however, the quality of B.C. is reduced as biofilm crystallinity decreases [43]. Several types of bioreactors are mentioned, such as stirred tank bioreactors [36], surface bioreactors, and flask fermenters [44].

Figure 5 presents diagrams of the multiple culture methods developed and used to produce B.C. The charts describe the input and output components and threads, specifying the required conditions, such as the temperature, stirring, and time control. As the output product of all the different methods, as shown in Figure 4, B.C. will be obtained.

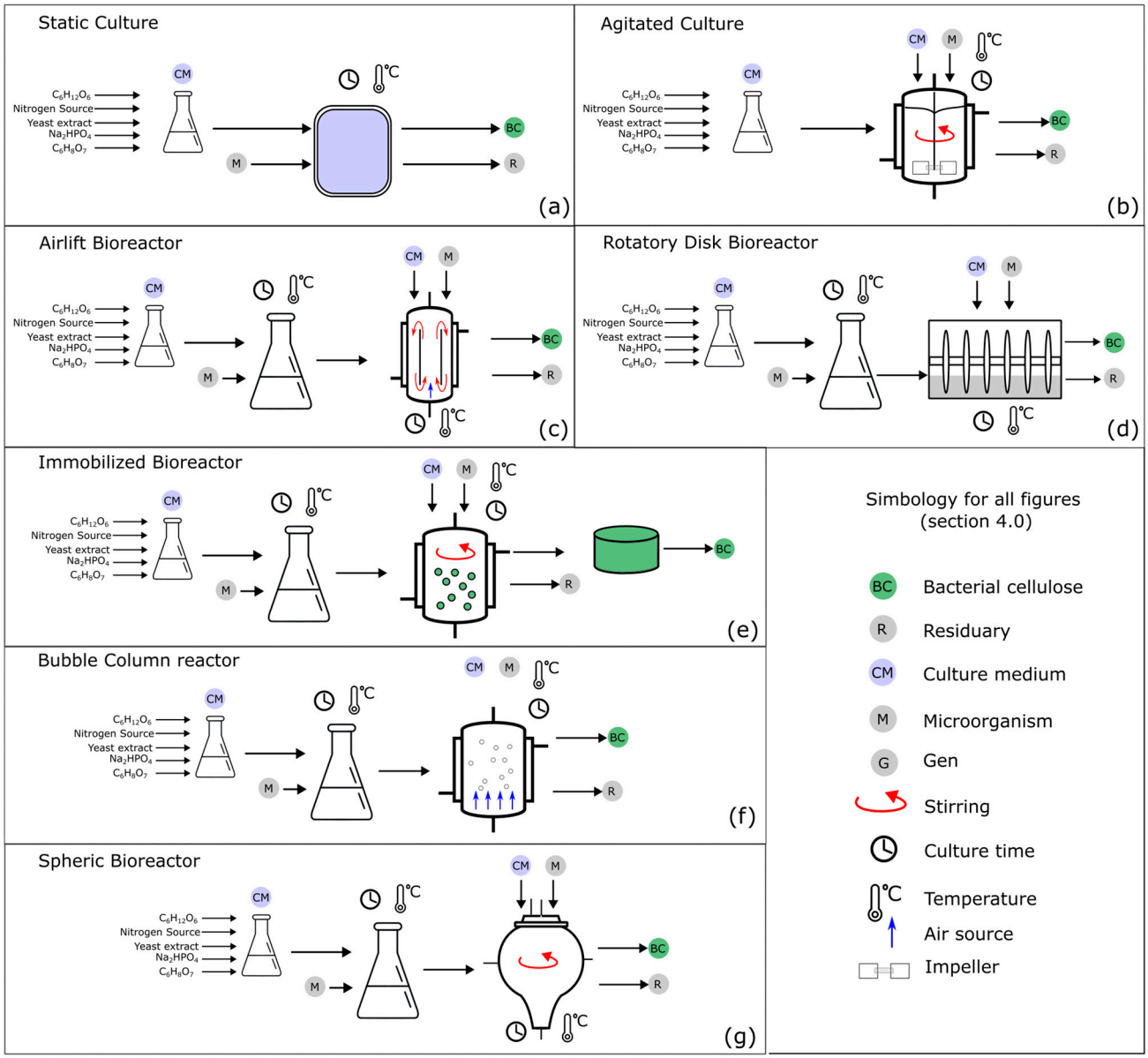


Figure 5. Different technologies and methods for producing bacterial cellulose: (**a**) static culture; (**b**) agitated culture; (**c**) airlift bioreactor; (**d**) rotatory disk bioreactor; (**e**) immobilized bioreactor; (**f**) bubble column bioreactor; and (**g**) spheric bioreactor.

Static culture is a production method for manufacturing B.C., where the bacteria are incubated in a liquid culture medium without movement or agitation. The cellulose obtained by this method is observed as a film (gel) at the air–liquid interface (Figure 5a). This culture system allows the production of B.C. on a small scale [24]. Although this method limits oxygen transfer and B.C. yield compared to stirred cultures, it also has benefits, such as the uniform formation of cellulosic films with high crystallinity, which are useful in specific applications, such as biomaterials [25]. As a measure to overcome the intrinsic limitations to non-agitated cultures, unconventional static culture systems with aeration on the biofilm surface or static serial cultures (SSCs) have been designed to successfully increase B.C. production yields by up to 25% [43,45].

Agitated culture is a widely used technology in the production of B.C., as it favors oxygen transfer and improves process efficiency, allowing greater control of the culture conditions and higher productivity (Figure 5b) [2].

An innovative technology for producing B.C. involves using an airlift reactor modified with wire mesh tubes (Figure 5c) [46]. An airlift reactor is a type of bioreactor that uses gas circulation to move the culture medium within the system, creating an upward flow in the inner zone (riser) and a downward flow in the outer zone (downcomer). This promotes better mixing and oxygen transfer without the use of moving parts [47]. Modified airlift-type reactors have been proven to be an innovative technology to improve B.C. production, addressing one of the main challenges in this process: limited oxygen supply.

These modifications to airlift reactors have the potential to increase the efficiency of industrial B.C. production, improving the quality of the final product and making it more suitable for specialized applications, such as biomaterials and medical products [46].

Airlift reactors are suitable for active bacterial strains, GMOs, and different carbon sources, because of their efficiency in regard to oxygen transfer, the absence of moving parts that can damage microorganisms, and their operational flexibility. In contrast, other types of reactors, such as stirred reactors, may present limitations in regard to oxygen transfer and may cause mechanical damage to cells [22].

The placement of B.C. culture in a rotating disk bioreactor causes cellulose-producing bacteria to be immersed in the culture medium and exposed to the atmosphere, allowing B.C. to form on the surface of the disks (Figure 5d). This method is beneficial for improving the transfer of oxygen and nutrients to the bacteria in the cellulose production process. Using rotating disks in the bioreactor helps maintain a larger contact surface area between the bacteria and the culture medium, improving the productivity and quality of the cellulose produced [46]. Moreover, this culture system allows the modification of the culture conditions that differ from conventional culture methods, such as the disk rotation speed, disk diameter, disk thickness, and distance between the disks [48].

This aspect is important because the larger the diameter of the disks, the greater the production of the B.C. film, and the speed can also have an important influence on the accumulation of B.C. The size of the disks affects the surface exposure to air and the culture medium. Larger disks increase the air–liquid contact area, which favors gas exchange and, thus, B.C. production. However, an excessive disk diameter can lead to inefficiencies, due to increased mechanical resistance [48].

The rotation speed helps control the mixing and oxygenation of the medium. Low speeds do not generate sufficient oxygen, while very high speeds can damage bacterial cells. Studies have shown that an optimal speed of 7 rpm is ideal for maximizing B.C. production in certain conditions.

As for the distance between the disks, adequate spacing allows for the proper flow of the medium and prevents stagnation, ensuring an even distribution of the nutrients and oxygen [49].

The culture and production of B.C. using cell immobilization systems (Figure 5e) involves a technique according to which cellulose-producing bacteria are kept attached to a solid support or matrix, improving the process's efficiency and facilitating the collection and separation of the product. This strategy seeks to overcome the limitations and

disadvantages of traditional methods, such as liquid and agitated fermentation. Within these systems, bacteria are immobilized in regard to the support [9], promoting the production process's productivity and stability. Various technologies have been developed to implement this immobilization, including the use of B.C. matrices, synthetic membranes, and other forms of support, such as silicone and wire mesh [31,46,50]. Also mentioned are bubble column bioreactors modified to improve oxygen transfer [51].

This process has been performed in different types of bioreactors, such as rotating disk reactors [50], modified aeration reactors [36], and biofilm reactors [42]. These systems allow for better control of the growing conditions, which can increase the productivity and quality of the B.C. produced. In addition, techniques for in situ and ex situ modification of B.C. [13] have been investigated, as well as the optimization of the culture conditions and the use of different media and carbon sources [44,52], using systems in which bacteria are immobilized in regard to the support to improve the productivity and stability of the process.

Most bubble column bioreactors (Figure 5f) tend to use uniform cylindrical geometry, such as a tube. This shape commonly results in the accumulation of B.C. at the recirculation points of the flow in the tank. The design proposed by Song et al. proposes the use of a spherical tank, which allows a better distribution of the air bubbles due to the uniformity of the tank surface, which avoids stagnation points in the flow, where air bubbles tend to accumulate. This also increases the interfacial area between the liquid and gas phase, which improves oxygen transfer [51].

The spherical design improves the oxygen transfer coefficient (kLa), by favoring a better gas–liquid interaction and bubble dynamics.

B.C. has been produced using a spherical bubble column bioreactor (Figure 5g). This modified bioreactor is used to grow *Komagataeibacter xylinus* and produce B.C. According to the study presented in [26], a spherical bubble column bioreactor features unique geometry that improves the oxygen transfer and mitigates problems related to limited oxygen supply during B.C. production. The bioreactor consists of a culture chamber filled with a slurry of bacteria and several rotating steel shafts covered by silicone tubes. This design enables efficient B.C. production in a controlled environment and even presents the possibility of scaling-up B.C. production [53].

Sequential fermentations have been used for the enrichment of the culture medium for B.C. production. This process consists of at least two fermentation processes. The first fermentation prepares the culture medium with nutrients and polysaccharides required for the second fermentation [54].

The production of B.C. through wells involves a static culture of bacteria from the genus *Komagataeibacter* in a liquid culture medium, contained in the wells. This method is based on forming a three-dimensional cellulose matrix at the air/liquid interface. During the process, bacteria grow on the surface of the liquid in the wells and secrete cellulose, which accumulates to form a film- or membrane-like structure [10]. The process involves different stages, such as preparing the medium, inoculating the bacteria, incubation, formation of the cellulose matrix, harvesting, and processing. After harvesting, the B.C. is purified and dried for further characterization and applications [38].

4.2. Strain Selection and Genetic Modification

4.2.1. Bacterial Strains

Symbiotic culture of bacteria and yeast (SCOBY) contain acetic acid bacteria capable of producing B.C. This symbiosis involves a series of interactions that benefit both bacteria and yeast growth. Invertase production from yeast allows sucrose hydrolysis to obtain monosaccharides and improve the substrate availability in the medium for bacteria consumption. This reduces the growth rate and enhances B.C. production. These bacterial communities are usually cultured in low-cost mediums, with a carbon source as the main component [55].

To enhance B.C. production, various strategies and technologies have been employed. One effective approach involves using bacterial strains, like *Komagataeibacter xylinus*, known for its high productivity and adaptability to both static and agitated culture conditions [56].

Several microorganisms, such as *Gluconacetobacter*, *Achromobacter*, *Acetobacter*, *Rhizobium*, and *Sarcina*, are known to efficiently produce B.C., and numerous studies have explored their potential in regard to industrial applications (Table 2 contains the details of such studies) [12,57].

Table 2. Bacterial strains for B.C. production; description of the principal microorganisms.

Microorganism	Description	References
Gluconacetobacter/Komagataeibacter	*Gluconacetobacter/Komagataeibacter xylinus* is one of the most efficient producers of B.C, often using various carbon sources like agro-industrial residues for large-scale production. B.C. from this bacterium is used in biomedical applications and nanocomposites.	[58–60]
Acetobacter	Similar to *Gluconacetobacter*, *Acetobacter* species are frequently studied in regard to fermentation processes for B.C. production, using bioprocess optimization to increase yields.	[58]
Achromobacter	Less frequently studied, but has potential in regard to B.C. production, especially when used in conjunction with other bacteria to enhance efficiency and adjust B.C. properties for industrial use.	[59]
Rhizobium	Shows promise in B.C. production and has been studied alongside other microorganisms to optimize B.C. yield and tailor it for specific industrial applications.	[61]
Sarcina	Known for producing B.C., though not as extensively researched as *Gluconacetobacter* or *Acetobacter*, it has potential for use in specific applications in industrial cellulose production.	[62]

The selection of microorganisms for the creation of a co-culture of cellulose-producing bacteria with a complementary microorganism has been tested to promote a symbiotic relationship between such microorganisms. *Komagataeibacter hansenii* co-cultured with *Aureobasidium pullulans* provides a supplementary pullulan polysaccharide and resulted in the production of B.C. with improved physical characteristics [63].

The culture of cellulose-producing bacteria, *Taonella mepensis,* has been tested using sequential fermentation with the fungus, *Trichoderma reesei*. The fungus carries out the first fermentation process, producing enzymes to hydrolysate polysaccharides from the culture medium. The hydrolysated medium is used by the bacteria in a second fermentation process for B.C. production [54].

4.2.2. Genetic Modification

Additionally, advancements such as the creation of modified bioreactors, the optimization of the culture conditions, and a potential genetic modification of the bacteria have been explored to further boost B.C. yields. These innovations aim to improve the scalability and reproducibility in industrial applications [2,42].

Genetic modification to produce B.C. in the laboratory employs genetic engineering techniques. This process aims to improve the efficiency and characteristics of B.C. production. The first stage consists of selecting the microorganisms. Another essential step in the genetic modification process is achieved by introducing specific genes into the selected microorganisms to improve their cellulose production capacities, according to which techniques such as gene editing [57], gene insertion (Figure 6), or gene deletion are used to manipulate the expression of the genes involved in cellulose synthesis [64]. It is crucial to

understand the genes and regulatory mechanisms involved in cellulose synthesis; with the identification and modification of genes, it is possible to optimize the B.C. production process. Bacterial strains can be modified to enhance the usage of certain carbon sources that are not part of the main metabolic pathways for B.C. production. The *K. xylinus* ATCC 23770 strain was modified to enhance the mannose metabolic pathway for the expression of mannose kinase, allowing mannose uptake as a carbon source for B.C. production [65]. The production process of B.C. using strain selection and genetic modification techniques requires an optimal environment for fermentation to maximize cellulose production.

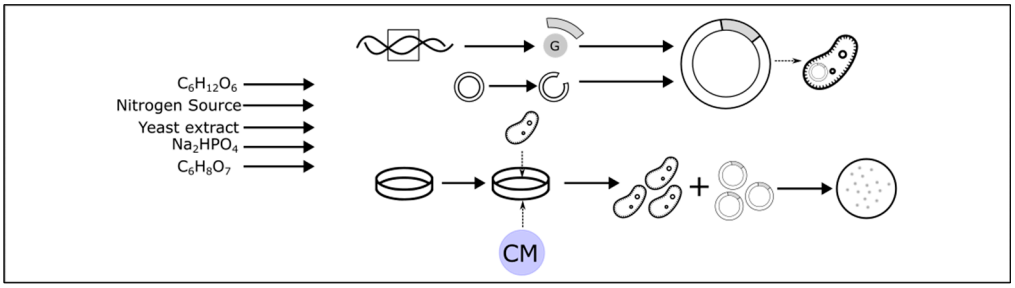


Figure 6. Diagram of the biotechnological process of genetic modification for bacterial cellulose production.

Genetic modifications make it possible to manipulate B.C.'s structural and physical properties to adapt its characteristics to specific applications by taking advantage of improvements in its characteristics, such as its chemical functionalization capacity, purity, crystallinity, biocompatibility, and biodegradability.

4.3. Optimization and Improvement Technologies

Developments have been made using artificial intelligence techniques, specifically an artificial neural network, to improve the efficiency and productivity of the B.C. production process. Fuzzy logic has been employed to [66] control and monitor the pH and temperature during the bacterial fermentation of cellulose, achieving optimal production conditions. This technology seeks to improve the growing conditions and other related factors to achieve better quality and quantity in terms of B.C. production [10]. This technique has significant implications for optimizing the growing conditions and maximizing the yield, although more detailed information is required to fully understand its specific applications and benefits in the context of B.C. production [24]. Improvements in fermentation consistency have been evidenced as a result of improved inoculum preparation [67]. In addition, the optimization of culture conditions has been achieved in order to improve B.C. production [50].

Statistical methods are the standard technique carried out for the optimization of bioprocesses, which includes an experimental component for verifying the purposes of the experiments. Plackett–Burman and the central composite design allow for the evaluation of the interaction between different factors that impact microorganism growth in a limited number of experimental runs. Furthermore, it enables the interpretation of the relationship between the said factors in order to predict their optimal interaction. These analyses aim to enhance the growing conditions for B.C.-producing bacteria and boost the overall product yield [68]. Optimization by Plackett–Burman and the central composite design revealed improved B.C. production of 31.7 g/L B.C. (in situ), with a 7.54-fold enhancement. This B.C. showed an excellent water retention capability, moisture content, water release rate, porosity, and thickness [68].

4.4. Sustainable Production and Waste Use Technologies

One of the biggest challenges when scaling B.C. production is related to the high costs of the culture medium. The Hestrin–Schramm medium is commonly used in the culture of acetic bacteria that produce B.C., which has a high requirement for glucose (20 g/L) as

the main source of carbon, as well as yeast extract (5 g/L), peptone (5 g/L), phosphates (2.7 g/L), and citric acid (1.15 g/L) [69]. This type of culture media can account for up to 30% of the cost of B.C. production [70]. Currently, the industry demands the development of culture media based on affordable carbon sources, which model microorganisms, such as *K. xylinus*, can ferment. Agro-industrial waste and its richness in terms of carbon nutrients has been harnessed to produce B.C. [16]. This technology is based on using byproducts and waste from the agricultural and food industries as substrates for the cultivation of cellulose-producing bacteria. Using agro-industrial waste as a carbon source can be a sustainable and economical strategy for producing B.C., by converting these byproducts into raw material for cultivating cellulose-producing bacteria. This technique provides advantages regarding the raw material costs and environmental sustainability, by repurposing byproducts that might otherwise be discarded. However, additional information is required to better understand how this process is carried out and the benefits and challenges associated with the utilization of agro-industrial residues in B.C. production [25].

B.C. production using agro-industrial waste has gained momentum in the last decade. B.C. production using enzymatic hydrolysates from sugar cane or corn cob bagasse [71], residues from wheat thin silage and dairy processing [72], residues from pineapple juice [73], grapes, citrus [3,74], cacao mucilage exudate [75], industrial fermentation wastewater [76], sugar cane and beet molasses [77], and mango bark [78], have been reported, using static, agitated, and intermittent cultures. The combination of agro-industrial residues with glycerol, which can also be a byproduct from biodiesel production [79], and ethanol, as a carbon source to stimulate cellulose biosynthesis, has also been reported [65,66,80,81]. The analyses of the physical, mechanical, and chemical properties of cellulose obtained through the use of hydrolysates from agro-industrial waste, determined by Fourier Transform Infrared Spectroscopy (FTIR), Scanning Electron Microscopy (SEM), and thermogravimetric analysis (DSC or TGA), have shown that the biopolymer has characteristics similar to those observed in B.C. biosynthesized from glucose and that, as such, it is suitable for numerous industrial applications. Occasionally, the B.C. obtained has shown a higher degree of polymerization, water retention, and a higher degree of crystallinity [74].

Agro-industrial waste stands out as a valuable input in the economically viable production of B.C. on a large scale, as it could become an ideal carbon source to produce the biopolymer through hydrolysis, extraction, and transformation processes (Figure 7), contributing to the reduction of waste and the creation of sustainable materials. The production of cellulose from agro-industrial waste can significantly impact the biopolymer and sustainable materials industry, as it takes advantage of byproducts that may otherwise be discarded [37]. Souza, et al., (2021) produced B.C. with *Komagataeibacter rhaeticus*, using coffee grounds, sugar cane molasses, and ethanol, achieving a maximum B.C. concentration of 11.08 $g \cdot L^{-1}$, and showing that different carbon sources are viable alternatives in terms of reducing the costs associated with B.C. production [82].

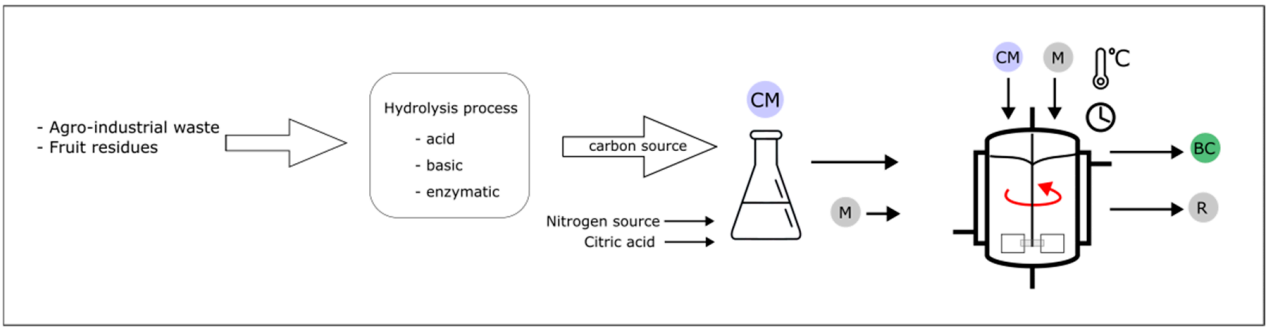


Figure 7. Diagram of the B.C. production process using agro-industrial waste.

The importance of sustainability is highlighted by using agro-industrial waste as a carbon source in order to achieve cost and production enhancement [26]. Implementing

these solutions improves the productivity and quality of B.C. production, with potential applications in various industries.

4.5. Production of Cellulose-Based Biopolymers

The production of cellulose nanofibers and their derivatives, as part of the leading technologies used in manufacturing cellulose-based biopolymers, have been developed for multiple applications in industry [3]. Cellulose nanofibers are microscopic structures with a high degree of versatility and are obtained from cellulose's mechanical or chemical decomposition (Figure 8). These nanofibers have potential applications in various industries, such as manufacturing composite materials, coatings, packaging, and medical products. Applications have been seen in the electronics industry, involving the construction of graphene supercapacitors for electronic devices that were complemented with B.C. nanofibrils, which showed enhanced flexibility and electrochemical performance [83].

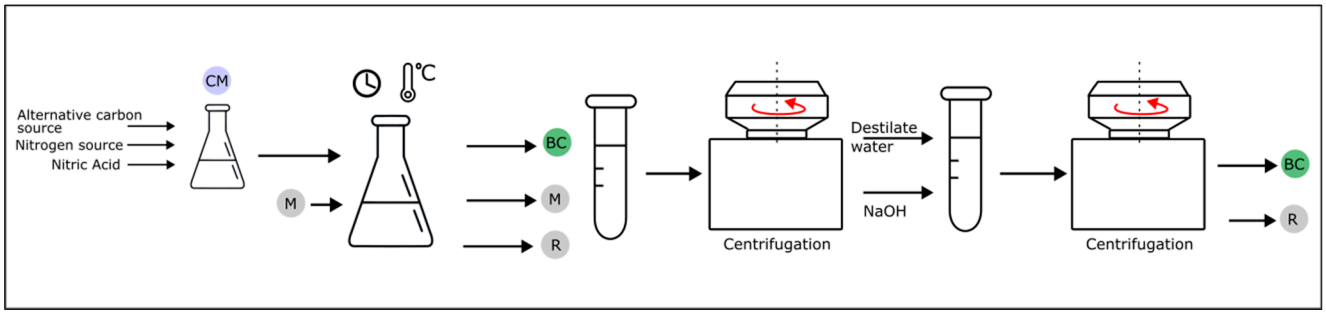


Figure 8. Downstream process involving cellulose-based biopolymers.

The food industry also utilizes cellulose fibers to change the physicochemical properties of products or as an edible matrix. It can be combined with different composites, such as xanthan gum, to obtain a product with more robust physical characteristics, with a higher yield and with lower production costs [84,85].

There are methods for the purification and characterization of B.C. that focus on how the quality of the material produced by the bacteria is obtained and evaluated [63]. Several methods for the purification of B.C. have been described. One of the simplest methods is the water washing process to remove water-soluble impurities, such as the production of media debris and bacterial waste products. However, the most used method involves a water wash, followed by a wash with 0.1 N sodium hydroxide at 60 °C. Again, a wash is carried out with water until the complete removal of the sodium hydroxide is achieved, which is then verified by the phenolphthalein test; finally, the washed B.C. is then stored in a 0.1% glacial acetic acid solution [86]. There are other processes, such as hydrogen peroxide bleaching, that are used to remove water-insoluble impurities, like proteins and pigments. Characterization is crucial to determine the purity and quality of the B.C. produced, affecting its potential applications in various industries [44].

4.6. Innovations and Specific Applications

One of the innovations used to sustain and promote cell growth and biofilm formation involves using B.C. as a scaffold for cultivating microbial fibroblasts and biofilms. B.C. has been used as a matrix according to which fibroblasts can attach and proliferate, making it a potentially useful scaffold in tissue engineering and regeneration applications [9]. The B.C. matrix can also be used to cultivate microbial biofilms, which could have implications in areas such as biofouling, bioremediation, and microbial engineering. Using B.C. as a scaffold for cells and biofilm culture takes advantage of its three-dimensional structure, high porosity, and biocompatibility, which could facilitate the development of various applications in biology and medicine [38].

The production of bioethanol, using a cellulose matrix for bacterial and enzyme immobilization, enhances the process by reducing the long turnaround and startup times.

Additionally, it maintains a relatively uniform cell concentration at the initial and final stages of the process, allowing repeated batch fermentation and saccharification and increasing the product yield [87]. It can be used with other support composites for immobilization, such as alginate beads, used in cultures of *Rhodopseudomonas faecalis* for the bioremediation of oil-polluted waters [42].

The production of vascular grafts using B.C., and a custom rotary bioreactor, are innovative aspects, which include the use of a bioreactor that has rotating steel shafts covered by silicone tubes, allowing the fermentation of B.C. in its tubular structure for the formation of vascular grafts. This technique involves fermenting B.C. in a culture medium containing glucose and other nutrients, taking advantage of the bacteria's ability to synthesize cellulose in controlled conditions [88]. Vascular grafts with a tubular structure can be generated with a wall thick enough to improve their mechanical strength and suitability for biomedical applications [89].

This cellulose matrix has also been used as a transdermal delivery system for active compounds and drugs. For example, it has been used with curcumin-embedded cellulose for wound and burn dressing and with α-mangostin from Mangosteen extract, which has been proven to effectively reduce cancer cell viability for B16 Melanoma and MCF-7 breast cancer cells [90,91].

4.7. Strategies to Improve Bacterial Cellulose Production

The production of B.C. has been optimized using various technologies and methods. A key strategy that has been proposed is the use of active bacterial strains, as explained in [26,67]. The strains from the *Komagataeibacter* group and its variant *xylinus*, are recognized for their high production capacity [32]. These strains are grown in specific media and in varied fermentation systems, which include solid-state fermentation, liquid-state fermentation, and the use of new and innovative bioreactors, enabling the efficient generation of B.C. [3].

Advances in the sequencing of genomes of strains from the genus *Komagataeibacter* have made it possible to implement genetic modification strategies to increase B.C. production through recombinant DNA techniques, such as homologous recombination, heterologous expression, and gene editing using CRISPR/Cas9 [13] (Figure 6). These modifications aim to regulate the expression of genes that are part of the biosynthetic pathway of B.C. It has been shown that the incubation of *K. xylinus* in agitated systems can irreversibly induce a B.C.-producing mutant phenotype by introducing an insertion sequence (IS) into the *bcsA* gene encoding the catalytic subunit that synthesizes the conversion of UDP-glucose to cellulose. Modifying recognition sequences to introduce an IS into the *bcsA* gene has prevented the loss of the biosynthetic function and promoted the production of 1.7 times more cellulose compared to the wild-type strain [92]. Likewise, the GD-I variant of *K. xylinus*, deficient in the enzyme glucose dehydrogenase, by disrupting the *gdh* gene, shows a greater ability to convert sugars into cellulose using glucose or a saccharified solution obtained from sweet potato pulp in the presence or absence of ethanol [93].

The transformation of *K. xylinus* through the introduction of the *crdS* gene of *Agrobacterium* sp., involved in the biosynthesis of Curdlan (β-1,3-glucan), has allowed the extracellular production of Curdlan/cellulose biomixtures that do not require additional structural modifications and that have excellent physical and chemical characteristics for biomedical applications [94]. Similarly, the overexpression of the glucose enzyme 6-phosphate isomerase from *E. coli* in regard to a transformed *K. xylinus* DSM 2325 variant, by introducing the *pgi* gene, produced 2.15 times more B.C. than the control strain [95]. These advances demonstrate the significant potential for improvement of the production yield and in terms of the better use of carbon sources that B.C.-producing strains can achieve through genetic engineering. Combining active bacterial strains with appropriate culture and fermentation technologies is key to improving productivity in regard to bacterial pulp production [10]. These optimized techniques are essential to achieving efficient, high-quality generation of B.C., for use in diverse industrial applications.

More processes can be enhanced to optimize B.C. production, for example, immobilized cell cultivation and the creation of biofilms on the matrix, are preferable over conventional cultivation. Biofilm formation takes place during fermentation, where the microorganism becomes attached to the surface of the support naturally through microbial immobilization. As mentioned previously, support materials like synthetic membranes have been used for this purpose, such as silicone and wire mesh. Rahman, et al. (2021) studied the production of B.C. using *Gluconacetobacter kombuchae* immobilized on *Luffa aegyptiaca,* introducing more sustainable support materials for bacterial immobilization [40].

Otherwise, another strategy to improve B.C. production was found in the study led by Ramirez et al., (2022), which investigated the production of B.C. using a symbiotic culture of bacteria and yeast (SCOBY) from a Kombucha beverage; this study aimed to develop active films based on the integral cellulosic material obtained from Kombucha fermentation on six different herbal infusions, taking advantage of the synergic metabolism of bacteria and yeast that enhance the yield and productivity of such cultures using low-cost media [55].

4.8. Limitations and Difficulties to Producing Bacterial Cellulose

This section describes some difficulties encountered in the multiple processes involved in B.C. production, considering the technologies mentioned earlier and their procedures.

During B.C. production in aerobic and agitated cultures, oxygen transfer has been reported to decrease in the last phase of the culture, especially after the glucose has been depleted; this is because the morphology of B.C. becomes fibrous and the broth becomes more viscous. The accumulation of fibrous B.C. within the culture increases the viscosity of the culture broth, making mixing more difficult and reducing the oxygen transfer rate [24,41].

The production of B.C. with the use of bacteria suffers from low yield and productivity, which increases the cost of production. Additionally, it requires the use of natural resources, such as water and energy, which can negatively impact the environment when major projects are considered [25].

B.C. production is a slow and expensive process compared to the production of other materials. Bacteria can be sensitive to culture conditions, affecting the productivity and quality of the B.C produced. B.C. produced by different strains of bacteria can have different properties and characteristics, can be difficult to handle and process due to its high degree of hydration and low density, and may be susceptible to microbial degradation and hydrolysis in certain conditions [9].

There is difficulty in controlling the mechanical properties of the B.C. obtained, which is why its use in some applications may be limited. B.C. may be less resistant to degradation than other materials, which may also limit its use in some applications [63].

The bacterial pulp production process can be affected by environmental factors, such as temperature and humidity, which can affect the quality and quantity of the B.C. produced. The production of B.C. can be affected by contaminants, such as other bacteria and fungi, reducing its quality [45].

The production time for B.C. can be limited because it requires specific growing conditions, such as an adequate carbon and nitrogen source, optimal temperature and pH, and adequate agitation [31,38]. Some of the main constraints in regard to B.C. production is the low yield and the need for large volumes of growth media [3].

Cellulose-producing bacteria have specific nutritional requirements, which can limit their production on a large scale. In addition, during production, the bacteria used can undergo genetic mutations, decreasing the volume of the B.C. produced [36].

Some of the limitations are the need for specific culture conditions for each bacterial strain, the production of unwanted byproducts, low productivity, and high production cost compared to other materials, the lack of acetate that reduces the viscosity of the culture medium and increases the coagulation of bacterial cells and cellulose, and the high crystallinity of cellulose that limits its degradation in biomedical and biomass conversion applications [42].

4.9. Evaluation of the Economic Aspects of the Preparation or Production of Bacterial Cellulose

According to 2020-2021 export data from the Observatory of Economic Complexity (OEC), the global cellulose market is valued at approximately USD 6.53 billion, with an annual growth rate of ~17% [96]. Leading producers include the United States (USD 1.45 billion), Germany (USD 1.21 billion), China (USD 870 million), Japan (USD 363 million), and South Korea (USD 353 million). Currently, the primary sources of cellulose are derived from plant biomass, such as wood, cotton, bamboo, African palm, banana, cassava peel, and sugar cane. However, concerns have been raised that increasing cellulose production could threaten food security by encouraging the cultivation of non-edible species and potentially increasing deforestation through agricultural expansion [97]. B.C. continues to capture a growing share of the global market each year due to its superior properties compared to PC and its lower environmental impact, due to bioreactor-based production. In 2022, the global B.C. market was valued at approximately USD 500 million, with a compound annual growth rate (CAGR) of 16%. By 2031, the market is projected to surpass USD 1.5 billion [96]. Leading B.C. producers include the United States, Canada, Japan, and China [97]. B.C. is primarily used in the production of food, medical supplies, textile fibers, and nanocomposites for eco-friendly packaging materials and electronic components. Key market segments include the manufacture of paper and cardboard, food products, nonwoven absorbent nets, and composite materials [96].

The expansion of the B.C. market has been heavily influenced by the cost, availability, and quality of raw materials, which directly impact the scalability and economic feasibility of production. Demonstrating the economic viability of B.C. production compared to plant cellulose is crucial. The high cost of the culture media, the variability in regard to the B.C. biosynthesis capacity among the different bacterial strains, the low B.C. yields from static cultures, and challenges in terms of scalability, are major obstacles to B.C. production. These issues have been actively addressed in recent years. For instance, utilizing alternative, low-cost substrates, such as agricultural byproducts, can substantially lower production costs. The cost derived from glucose (the main carbon source in the HS medium) can be reduced to a fraction of the cost when using the reducing sugars released from agro-industrial waste hydrolysates [19]. There are significant opportunities for innovation in optimizing the related production techniques, particularly through innovations in bioreactor design, fermentation methods, and strain engineering. Labor is a major expense that can be reduced through process automatization and training. Finally, targeting a high-value/low-volume market could be critical for setting competitive pricing and achieving high revenues [98].

5. Physical and Mechanical Properties of Bacterial Cellulose

The general physical and mechanical properties of B.C. are presented in Table 3. Evidence suggests that the use of alternative carbon sources, such as agro-industrial hydrolysates or wastewater from biological processes, can negatively affect some of these properties. Deviations in the morphology, porosity, crystallinity, and tensile strength of B.C. are commonly observed compared to B.C. produced using a HS medium. However, the chemical properties of B.C. remain unchanged regardless of the substrate used [76,99,100]. Moreover, it has been shown that the mechanical properties of B.C. are influenced by several factors, including the culture conditions (static or agitated), the culture media composition, and the presence of additives during fermentation. Downstream processes also influence the final properties of the B.C. For example, newly synthesized B.C. contains minerals, melanoidins (which give B.C. its brown color) and other bacterial exudates, and components from the culture medium, resulting in B.C. with low crystallinity (37%) and low purity (21%). These properties can be significantly improved, reaching up to 87% crystallinity and 97% purity, through alkaline washing (using NaOH) and drying [101]. Varying the NaOH concentration and treatment duration can result in B.C. with distinct characteristics, including a time-dependent reduction in tensile stress and an apparent Young's modulus. This behavior is likely due to the degradation of B.C. nanofibrils, proteins, and alkali-labile molecules [102]. This effect can be further enhanced through post-biosynthesis processes, such as microfluidization and shearing techniques, like ultrasonication [101,103].

Table 3. General physical and mechanical properties of bacterial cellulose.

Property	Value	Reference
Fibril size (bundle of nanofibrils)	<100 nm wide, 2 μm length	[57,101]
Elementary nanofibril size	7-8 nm wide	[57]
Crystal size Static culture Agitated culture Trickling bed reactor	 11. 95 nm 7.91 nm 10.07 nm	[104]
Crystallinity Static culture Agitated culture Trickling bed reactor	 84–91% 64% 69%	[57,104]
Purity	96–98%	[104]
Thermal properties Onset degradation temperature (T_{on}) Temperature at the maximum degradation rate (T_d)	 253.9 °C 273.9/328.3 °C	[101]
Porosity	83–86%	[104]
Initial water-holding capacity	98–99%	[57]
Rehydration ratio	72–83%	[104]
Flexibility (Young's modulus)	15–35 GPa	[57,102,105]
Stiffness	53.7–64.9 GPa	[106]
Tensile strength	200–300 MPa	[105,107]
Elongation	1.5–5.6%	[105,107]
Compressive modulus	7–8 kPa	[108]
Intrinsic viscosity	411 mL/g [a]	[8]
Degree of polymerization	1765 [b]	[8]
Hydrophilicity	1 g B.C.:100 mL water	[101]

[a] Intrinsic viscosity in cupriethylenediamine. [b] Based on the intrinsic viscosity values.

B.C. applications are strongly determined by the physical and mechanical properties of the polymer. A clear example is the effect of B.C. as a reinforcing agent in papermaking. The tensile and tear indices increase up to 49% and 140% when comparing paper produced with and without 10% B.C. [109]. In combination (1:1 ratio) with other polymers, like carboxymethyl cellulose (CMC), coating the surface of an uncoated office paper can increase the gamut area by >25% [8]. In the textile industry, the hydrophilicity of B.C. remains a significant challenge, limiting its applicability in the dry state. Although methods exist to increase the hydrophobicity of B.C. membranes, further studies are needed on this and other properties to enable the commercial introduction of B.C. into the textile sector (clothes, flooring, and interior design materials). The hydrophobic nature and high water retention capacity of B.C. are influenced by its crystallinity, the surface area per unit of mass, and exposed OH groups that could potentially bind to water molecules [110,111].

B.C. is often referred to as bacterial nanocellulose (BNC) due to the natural nanoscale structure of its fibrils, with some applications requiring cellulose particles of specific sizes. The particle size of B.C. is typically controlled through physical, chemical, or fermentation techniques, used independently or in combination. Physical methods include ultrasonication [112], high-pressure homogenization [113], microfluidization [114], and grinding [115]. Acid hydrolysis involves treating B.C. with strong acids, such as sulfuric acid (H_2SO_4) or hydrochloric acid (HCl). The acid breaks down the amorphous regions of the cellulose, which yields crystalline nanocellulose structures [116]. The fermentation regimen can influence the size of B.C. particles [117]. For instance, agitated and trickling bed reactors tend

to produce smaller B.C. crystals compared to those generated in static cultures (Table 3). In addition, the introduction of CMC (1% w/v) in the culture media induces bacteria to produce B.C. fibrils with a smaller diameter [118].

6. The Future of Bacterial Cellulose Technology

In the field of B.C. production, a series of developments and future perspectives are on the horizon that seek to improve the efficiency, quality, and potential applications of this polymer. This section presents aspects of interest that require further research and future developments.

The need to continue researching and optimizing the culture conditions to improve the productivity and quality of B.C. has been evidenced [42]. It has been proposed that the efficiency and profitability of B.C. production can be improved by optimizing the culture media and production conditions [3,34]. It is essential to study industrial production methods and techniques in order to improve the efficiency of bioreactors, as well as to better control solid-state culture systems [36,53].

Some studies propose further exploration and experimentation with the use of new strains of cellulose-producing bacteria, which may offer specific properties and characteristics for new and diverse applications [1,35].

Using alternative carbon sources, such as agro-industrial and organic waste, to produce B.C. has become an area of interest [25]. This diversification can not only reduce the costs, but also improve the sustainability of the process [40]. Developments in this area are expected to enable the adoption of more environmentally friendly practices, such as the increased use of renewable energy sources, with the respective reduction of waste and emissions [36,53].

It has been proposed that the genetic modification of B.C.-producing bacteria could be a key strategy to improve and drive greater material production and quality [35]. Research in molecular biology can also provide a deeper understanding of production mechanisms [89].

Exploring new applications that can be incorporated into new market niches is an area of industrial interest, as the potential of B.C. includes contributions in industry areas such as food, medicine, tissue engineering, and nanoelectronics [3,22]. Research and development in these areas could further benefit from using this material and may benefit from its commercial value [42].

The physical and mechanical properties of structures generated from B.C. may be better suited to various applications, including in regard to building materials and medical devices [45,47]. It is important, within the area of materials development, to evaluate the safety and toxicity of B.C., especially in regard to biomedical applications [38,87].

In order to optimize the results from the B.C. production process, it is considered essential to develop new and more efficient purification and processing technologies that can contribute to the quality and purity of the final product [53].

7. Patents

Over the past ten years, several innovative patents have been filed regarding B.C. production, focusing on diverse applications. These include improvements in the efficiency of cellulose production processes using various microorganisms, like Gluconacetobacter and Komagataeibacter [29]. Notable innovations include the use of nanocellulose–polymer composites for enhancing the flexibility and conductivity of materials for use in medical, electronics, and food packaging sectors. Many of these patents also explore sustainable, low-energy methods, utilizing waste products and bio-derived polymers to support circular economy initiatives [119].

Table 4 highlights key innovations in regard to bacterial cellulose production patents, focusing on sustainability, medical uses, and electronic applications.

Table 4. Recent patents related to bacterial cellulose production.

Patent Title	Summary	Filed Year	Applications	Ref.
20170191100	To provide a B.C. that is highly dispersible in liquid, shows excellent molding properties, and high miscibility with other materials when applied to materials and, therefore, has high applicability as a practical material and a bacterium which produces the B.C.	2017	Better B.C. production	[119]
20220315760	B.C.–polyurethane composite material, preparation method, and use are described. The preparation method comprises performing organic solvent exchange on B.C. microfibers and obtaining a B.C. microfiber composite.	2022	B.C.–polyurethane	[119]
20130211308	Nanosilver-coated B.C. nanofiber and a method of producing the nanosilver-coated B.C. nanofiber. The nanosilver-coated B.C. nanofiber is produced by preparing a suspension of B.C. fibers and oxidizing the B.C. fibers.	2013	Medical textiles, tissue engineering, wound healing applications	[119]
EP2331699	Describes a production method for cellulose synthesized by bacteria, enabling the large-scale production of homogeneous materials.	2019	Textiles, biopolymer production	[28]
CN103481720A	Outlines a method for manufacturing decorative designs using B.C., involving dyeing and molding processes.	2013	Textiles, decorative products	[28]

8. Discussion

B.C. has burst onto the scientific and technological scene as a material with revolutionary potential in terms of various applications, from tissue engineering to nanoelectronics. B.C.'s ability to act as a scaffold for the culture of microbial cells and biofilms makes it a promising option in tissue engineering and regeneration [4]. Its three-dimensional structure, high porosity, and biocompatibility make it attractive for various applications in biology and medicine [38].

Several technical and environmental challenges have been observed that need to be addressed to enable B.C. to achieve a suitable sustainable production and application level. As mentioned in [42], B.C. production can be slow and expensive compared to producing other materials. Large-scale production presents difficulties due to the specific nutritional requirements of cellulose-producing bacteria and the necessary culture conditions [36]. Using natural resources and energy sources in production raises concerns about their environmental impact, especially in large-scale projects. In search of solutions to these challenges, researchers have proposed various strategies. Diversifying carbon sources in terms of agro-industrial and organic waste could reduce production costs and increase the process's sustainability [25,40]. The genetic modification of cellulose-producing bacteria presents an opportunity to boost production and improve the quality of the materials [35]. Collaboration between industry, academia, and government is essential to accelerate B.C. research, development, and commercialization [22].

The safety and toxicity of B.C. in biomedical applications is a crucial aspect that requires rigorous studies in order to develop its future applications in this area [38,87]. Optimization of the growing conditions and further molecular biology research are critical steps to overcome the technical challenges and improve the quality of the materials [34,89].

Exploring new applications is also an area where significant growth is expected, especially in food, medicine, and tissue engineering [3,22].

The production and application of B.C. presents a rapidly growing field with transformative potential. It is imperative to address the technical, environmental, and application-related challenges between different industrial sectors, and continuous research and innovation projects are needed to boost the efficiency and sustainability of bacterial pulp production and explore new and exciting applications in various fields.

9. Conclusions

B.C. has garnered significant attention from the scientific and technological communities due to its versatility in terms of its applications to different sectors, such as tissue engineering, nanoelectronics, and beyond. Its biocompatibility, high porosity, and three-dimensional structure make it a promising material for biomedical use, particularly as a scaffold for microbial cells and biofilms. In addition to these applications, B.C. is being explored as a coating material for various surfaces. Its excellent barrier properties, antimicrobial activity, and biodegradability make it a potential candidate for applications in food packaging, medical devices, electronic components, and papermaking. However, realizing its full potential is accompanied by significant technical and environmental challenges. Slow and expensive production, the need for specific growing conditions, and the environmental impact of using natural resources present obstacles to large-scale adoption.

Overcoming the challenges to large-scale production and generating further applications of B.C. require an interdisciplinary approach. Strategies such as genetic modification and the exploration of new applications are critical to improving the efficiency of the production process and product quality. Another important strategy involves diversifying the carbon sources; utilizing agro-industrial and organic waste could potentially reduce production costs and make the process more sustainable.

Innovation is crucial when addressing these challenges. Optimizing the culture media and developing new purification technologies are key steps toward improving the production process and the quality of the materials. Furthermore, continuous research in the molecular biology field will help enhance the efficiency of B.C. production by introducing more efficient GMOs for B.C. production. Such innovations are essential to unlocking wider and more effective uses of this biopolymer across various sectors.

Despite the current challenges, the future of bacterial pulp production and its application across various industries is promising. With sustained research focused on optimizing the growing conditions, improving production efficiency, and addressing environmental concerns, the material has the potential to make a significant impact in medicine, technology, and beyond. The search for technical and environmental solutions and constant innovation is critical to making the most of this material and contributing to significant advances in fields ranging from medicine to technology.

Author Contributions: Conceptualization, M.A.C., O.F.-U. and A.A.; methodology, M.A.C. and O.F.-U.; software, A.A.; validation, M.A.C., M.D.G. and L.C.-M.; investigation, M.A.C., O.F.-U., A.A., M.D.G. and L.C.-M.; resources, O.F.-U. and A.A.; writing—original draft preparation, M.A.C. and O.F.-U.; writing—review and editing, M.A.C., M.D.G. and L.C.-M.; visualization, O.F.-U. and A.A.; supervision, M.A.C., M.D.G. and L.C.-M.; project administration, M.A.C. and O.F.-U.; funding acquisition, M.A.C. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by Universidad de Las Américas-Ecuador as part of the internal research project BIO.MCS.23.01.

Acknowledgments: Thanks are given to the Ecuadorian Corporation for the Development of Research and the Academy (CEDIA), the Technical University of Ambato, and the Universidad de las Américas (Ecuador) for the funding and technical support during the research process.

Conflicts of Interest: The authors declare that there are no conflicts of interest.

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