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Review

Functionalization of bacterial cellulose: Exploring diverse applications and biomedical innovations: A review

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Abstract

The demand for the functionalization of additive materials based on bacterial cellulose (BC) is currently high due to their potential applications across various sectors. The preparation of BC-based additive materials typically involves two approaches: *in situ* and *ex situ*. *In situ* modifications entail the incorporation of additive materials, such as soluble and dispersed substances, which are non-toxic and not essential for bacterial cell growth during the production process. However, these materials can impact the yield and self-assembly of BC. In contrast, *ex situ* modification occurs subsequent to the formation of BC, where the additive materials are not only adsorbed on the surface but also impregnated into the BC pellicle, while the BC slurry was homogenized with other additive materials and gelling agents to create composite films using the casting method. This review will primarily focus on the *in situ* and *ex situ* functionalization of BC then sheds light on the pivotal role of functionalized BC in advancing biomedical technologies, wound healing, tissue engineering, drug delivery, bone regeneration, and biosensors.

Introduction

Polysaccharides (ex. cellulose) are macromolecules that can form extensive networks of molecular interactions through intermolecular hydrogen bonding. They also can establish binding sites with proteins, lipids and metallic molecules, forming stable multicomponent systems. Additionally, these macromolecules serve as crucial components of membrane receptors [1]. Polysaccharides are the most prevalent macromolecular polymers found in nature, and are derived from multiple sustainable sources including algae, plants, and microorganisms like fungi and bacteria [2]. Structurally these polymers contain monosaccharides units linked by glycosidic bonds. Their classification (Fig. 1) based on their intracellular or extracellular localization or, according to their chemical structure, ex., which homopolysaccharides are homoglycans consisting of the same monosaccharides, whereas heteropolysaccharides are heteroglycans that consist of different monosaccharides [3,4]. Cellulose, a naturally occurring polysaccharide, is found extensively on our planet, reaching an estimated production of nearly 180 billion tons per year. Structurally, cellulose consists of glucose units linked together by β-1→4 glycosidic bonds, represented by the formula $[(C_6H_{10}O_5)n]$ [[5], [6], [7]]. Both plant and microbial (ex. algae, fungi, and bacteria) sources of cellulose have been reported. BC, is a glucose unit biopolymer and an extracellular polysaccharide, similar to plant cellulose. BC was accidentally discovered by Adrian Brown in 1886 while studying *Bacterium aceti*, when a solid mass formed in the fermentation medium. Once called the "vinegar plant" or "mother" and commonly used in homemade vinegar production, was later identified as cellulose and the name *Bacterium xylinum* was assigned to the microorganism responsible for its synthesis [8,9]. BC was later reported to be produced by several other microbes such as Gram-positive *Lactiplantibacillus plantarum* [10], *Rhodococcus* sp. [11], *Bacillus licheniformis* [12], and *Leifsonia* sp. [13], and Gram-negative *Komagataeibacter hansenii AS.5* [14], *Komagataeibacter diospyri* [15], *Komagataeibacter medellinensis* [16], and *Komagataeibacter hansenii* GA2016 [17]. These BC producing strains were isolated from diverse sources such as rotten apple [10,18], Kombucha [19,20], rotten mandarin [21], vinegar [22], and contaminated honey wine [23]. BC has unique characteristics including high water retention capacity, pure ultrafine network, high degree of crystallinity, strong mechanical properties, high degree of polymerization, good formability, hydrophilicity, biocompatibility, flexibility, non-toxicity, biodegradability, and useful mechanical properties such as Young's modulus value, tensile strength, compressibility, and elongation [[24], [25], [26], [27]]. BC itself has limited applications while the functionalization of BC, presents a common challenge in various sectors. In the past, to address this challenge numerous attempts have been made to functionalize BC through *in situ* and *ex situ* methods, resulting in a polymeric composite with unique applications. BC functionalization with hyaluronic acid [28], sodium alginate [29], graphene oxide [30], starch [31], chitosan [32] and metal nanoparticles [33] have been reported with resulting enhanced membrane characteristics. Therefore, the functionalized BC represents a promising biopolymer with several application in food packaging [34], wound healing [35], cosmetics [36], dye removal [37], and heavy metal removal [38]. This review aims to focus on the recent progress in functionalization of BC through *in situ* and *ex situ* approaches.

Section snippets

Functionalization of bacterial cellulose

The extensive number of hydroxyl groups in BC provide many opportunities for modifications to enhance its functionality, as reported by [39]. Two common methods have been used for mass production of BC. In static fermentation, BC was formed at the air-liquid interface and referred to as pellicles, due to its aerobic nature. In agitated conditions, BC was obtained in the form of randomly distributed pellets or suspended fibers [40]. The functionalization of BC by *in situ* modification depends on…

Applications of bacterial cellulose in biomedical applications

Functionalized BC (FBC) has emerged as a valuable tool in biomedical research and applications. Its versatility, biocompatibility, and ability to be functionalized make it a promising material for wound dressing, bone regeneration, drug delivery, and tissue engineering. As more research is conducted, the full potential of FBC in these applications is likely to become increasingly apparent, paving the way for the development of innovative and improved biomedical devices.…

Concluding remarks and future perspectives

This review explores the transformative potential of bacterial cellulose (BC) functionalization, emphasizing its broadening scope in numerous sectors, particularly in advancing biomedical technologies. BC's inherent characteristics like high water retention, mechanical strength, biocompatibility, and biodegradability render it a prime candidate for diverse applications and functionalization in wound healing, tissue engineering, drug delivery, bone regeneration, and biosensors. The increasing…

CRediT authorship contribution statement

Ahmed K. Saleh: Writing – review & editing, Writing – original draft, Supervision, Software, Project administration, Investigation, Formal analysis, Conceptualization. **Julie Basu Ray:** Writing – review & editing, Writing – original draft. **Mohamed H. El-Sayed:** Writing – original draft, Formal analysis, Revise the final form of the manuscript. **Adel I. Alalawy:** Writing – original draft. **Noha Omer:** Writing – original draft. **Mahmoud A. Abdelaziz:** Writing – original draft. **Ragab Abouzeid:** Writing –…

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article.…

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