

Present status and applications of bacterial cellulose-based materials for skin tissue repair

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ABSTRACT

Bacterial cellulose (BC, also known as microbial cellulose, MC) is a promising natural polymer which is biosynthesized by certain bacteria. This review focused on BC-based materials which can be utilized for skin tissue repair. Firstly, it is illustrated that BC has unique structural and mechanical properties as compared with higher plant cellulose, and is thus expected to become a commodity material. Secondly, we summarized the basic properties and different types of BC, including self-assembled, oriented BC, and multiform BC. Thirdly, composites prepared by using BC in conjunction with other polymers are explored, and the research on BC for application in skin tissue engineering is addressed. Finally, experimental results and clinical treatments assessing the performance of wound healing materials based on BC were examined. With its superior mechanical properties, as well as its excellent biocompatibility, BC was shown to have great potential for biomedical application and very high clinical value for skin tissue repair.

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1. Introduction

Cellulose is well known as one of the most abundant biodegradable materials in nature and has thus been the topic of extensive investigations in macromolecular chemistry. Over the past 30 years, developments in molecular biology and the application of cell systems *in vitro* have resulted in extensive exploration of the mechanisms underlying the biosynthesis of cellulose in nature. Cellulose based polymers have wide applications in tissue engineering, controllable delivery system, blood purification, sensor, agriculture, as well as water purification (Chang & Zhang, 2011). Bacterial cellulose (BC, also known as microbial cellulose, MC) is a promising natural cellulose synthesized by certain bacteria. The wide applications of BC are foreseeable.

Because of its unique structural and mechanical properties as compared with higher plant cellulose, BC is expected to become a commodity material in various fields. BC fibers have a high aspect ratio with a diameter of 20–100 nm. As a result, BC has a very high surface area per unit mass. This quality, combined with its highly hydrophilic nature, results in a very high liquid loading capacity. Moreover, its biocompatibility, hydrophilicity, biocompatibility, transparency and non-toxicity make it an attractive candidate for a wide range of applications in various fields, especially those related

to biomedical and biotechnology applications (Dahman, 2009). The fibrous structure of BC consists of a three-dimensional non-woven network of nanofibrils, sharing the same chemical structure as plant cellulose, which is held together by inter- and intra-fibrillar hydrogen bonding, resulting in a hydrogel state with high strength. The biosynthetic pathways of BC, including those involving enzymes and precursors, have previously been described in detail by Chawla, Bajaj, Survase, and Singhal (2009). Such biomedical devices are advantageous in terms of their high paper-like reflectivity, flexibility, contrast, and biodegradability (Klemm, Heublein, Fink, & Bohn, 2005). Much work has already focused on designing ideal biomedical devices from BC, such as artificial skin, artificial blood vessels, artificial cornea, heart valve prosthesis, artificial urethra, artificial bone, artificial cartilage, artificial porcine knee menisci, and deliveries of drug, hormone and protein (Halib, Amin, Ahmad, Hashim, & Jamal, 2009; Oshima, Taguchi, Ohe, & Baba, 2011; Petersen & Gatenholm, 2011; Wang, Gao, Zhang, & Wan, 2010). As an intuitionistic introduction, the prospects for the various biomedical applications of BC-based materials are shown in Fig. 1.

It is clear from previous research that the materials derived from BC can provide a promising future for biomedical application. This paper reviews the applications of BC as skin tissue repair material; specifically, we summarize the researches on BC for the application of BC in skin tissue engineering. Experimental results and clinical treatments have demonstrated the effectiveness of BC-based wound healing materials. Furthermore, all the results have indicated that BC as a skin tissue material in the biomedical field will have continuing importance in the future.

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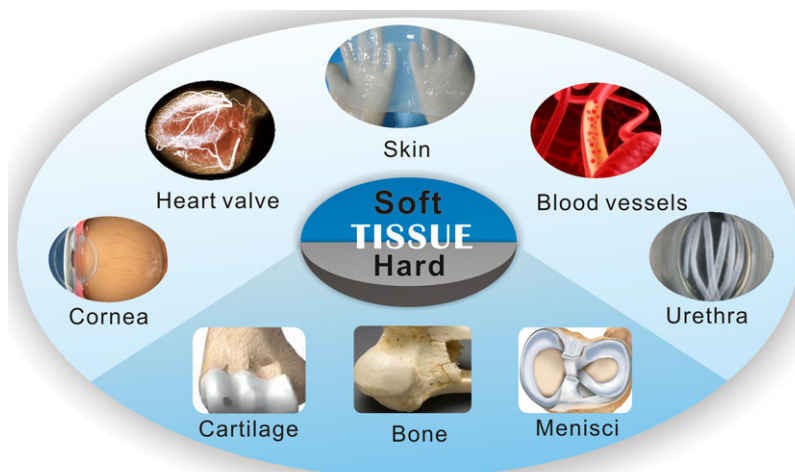


Fig. 1. Prospects for the various biomedical applications of BC-based materials.

2. Basic properties

The hydrophilic ability of BC is determined by its high water content, while only 10% out of the 99 wt% water presented in BC gels behave like free bulk water (Gelin et al., 2007). Recent studies have shown that atomic force microscopy can be used to measure the elastic modulus of suspended fibers through a nanoscale three-point bending test. Guhados, Wan, and Hutter (2005) measured Young modulus of BC fibers with diameters ranging from 35 to 90 nm at a value of 78 ± 17 GPa (Guhados et al., 2005). The value obtained (114 GPa) was higher than those previously reported, but lower than estimates from the modulus of crystalline cellulose-I (130–145 GPa) (Hsieh, Yano, Nogi, & Eichhorn, 2008).

A study by McKenna et al. showed that an increase in the fermentation time could lead to a decrease in mechanical strength, illustrated by Young's modulus first increasing and then decreasing after 96 h. BC behaves like a viscoelastic material; brittle failure has previously been reached at approximately 20% strain and 1.5 MPa stress under uniaxial tension (McKenna, Mikkelsen, Wehr, Gidley, & Menzies, 2009). Slightly enhanced tensile strength and deformation at break were obtained by increasing the molding compression pressure, while the modulus also decreased nearly linearly with increasing film porosity. This behavior was related to denser structure under increased mold compression, which reduced the interfibrillar space, thus increasing the probability of interfibrillar bonding (Retegi et al., 2010).

3. Bio-fabrication

The fabrication of a BC network sheet was attempted by heat-pressing in metal molds with a micro pattern to open a pathway to potentially versatile materials. To modify the surface of natural fibers, BC was utilized as a substrate for bacteria during fermentation of BC (Pommet et al., 2008). A structural hydrophobic similar to the "Lotus effect" was thus examined on this sheet, by introducing a micro-lattice pattern on to its surface. Indeed, the surface of the sheet was found to be more hydrophobic when the structural hydrophobic effect and the synergistic effects of heating and micro-patterning were combined (Tomita, Tsuji, & Kondo, 2009). Efficiency in the production of BC is indispensable in determining its potential applications. Carreira et al. (2011) evaluated several residues from agro-forestry industries as economic carbon and nutrient sources for the production of BC: namely grape skins aqueous extract, cheese whey, crude glycerol and sulfite pulping liquor. Agro-forestry residues were successfully used as carbon sources for

the production of BC. The most relevant results were attained with wine and pulp industries residues: 0.6 and 0.3 g/L of BC (Carreira et al., 2011).

3.1. Self-assembled and oriented bacterial cellulose

Potato and corn starch were added to the culture medium and partially gelatinized in order to allow BC nanofibrils to grow in the presence of a starch phase. The BC-starch gels were hot pressed into sheets with a BC volume fraction higher than 90%. During this step, starch was forced to further penetrate the BC network. The self-assembled BC-starch nanocomposites displayed coherent morphologies (Grande et al., 2009). Five separate sets of experiments were conducted to demonstrate the assembly of nanocellulose by *Acetobacter xylinum* (*Gluconacetobacter xylinus*) in the presence of electric fields in micro- and macro-environments, which demonstrated a new concept of bottom up material synthesis through a biological assembly process (Sano, Rojas, Gatenholm, & Davalos, 2010). The maximum water holding capacity value 92.21 g/g was measured for BC formed in reactors modified with 3.0% of agar. The maximum production rate was observed after the second day of cultivation as compared to the third day of cultivation in the case of the control experiment without agar (Shah, Ha, & Park, 2010).

BC gel can be produced on an oxygen-permeable substrate such as polydimethylsiloxane (PDMS). The optimum ridge size of $4.5 \mu\text{m}$ was related to the contour length of the bacteria cells. The fracture stress (σ) of uniaxially oriented BC gel under elongation was 4.6 MPa, which was 2.3 times higher than that of the BC-air material ($\sigma = 2$ MPa) (Putra et al., 2008). The extraction and refinement of high-strength crystalline microfibril bundles (15–20 nm thick) from BC networks was investigated, as well as their morphology prior to and post electrospinning. The diameter of the fibers decreased significantly with increasing cellulose content from about $1.8 \mu\text{m}$ (1 wt%) to about 100 nm (20 wt%). The results demonstrated a significant improvement in thermal stability for the composite material. The fibers were aligned into an anisotropic nanocomposite during spinning (Olsson, Azizi Samir, et al., 2010; Olsson, Kraemer, et al., 2010).

3.2. Magnetic bacterial cellulose

Bacterial cellulose, with its porous network structure, was also used as an accelerator to precipitate Ni nanoparticles through the room temperature chemical reduction of NiCl_2 hexahydrate.

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