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Applications of bacterial cellulose in food, cosmetics and drug delivery

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Abstract

Bacterial cellulose (BC) is a versatile biopolymer with better material properties, such as purity, high degree of porosity, relative high permeability to liquid and gases, high water-uptake capacity, tensile strength and ultrafine network. This review explores the applications of BC and its hydrogels in the fields of food, cosmetics and drug delivery. Applications of BC in foods are ranging from traditional dessert, low cholesterol diet, vegetarian meat, and as food additive and dietary aid to novel applications, such as immobilization of enzymes and cells. Applications in cosmetics include facial mask, facial scrub, personal cleansing formulations and contact lenses. BC for controlled drug delivery, transdermal drug delivery, dental drug delivery, protein delivery, tissue engineering drug delivery, macromolecular produg delivery and molecularly imprinted polymer based enantioselective drug delivery are also discussed in this review. The applications of BC in food and cosmetics provide the basis for BC-based functional foods, nutraceuticals, cosmeceuticals and medicated cosmetics. On the basis of current studies, the BC-based drug delivery could be further fine-tuned to get more sophisticated control on stimuli-responsive drug release. Along with the currently available literature, further experiments are required to obtain a blueprint of drug *in vivo* performance, bioavailability and *in vitro-in vivo* correlation.

Keywords

Bacterial cellulose
Cosmetics
Cosmeceuticals
Dercemization
Drug delivery
Food
Nutraceuticals
Protein delivery
Tissue engineering

Introduction

Biomaterials play a vital role in the daily life of humans (Czaja et al. 2007; Hubbell 1995; Ratner and Bryant 2004; Shoichet 2009). The importance of biopolymers in our food applications, and personal and medical care cannot be ruled out (Ellis and Smith 2008; Murphy 2001; Jay et al. 2008). Cellulose is the most abundant biopolymer on the surface of earth with 1.5×10^{12} tons annual production (Czaja et al. 2004; Klemm et al. 2005), and most commonly it is obtained from plants (Siro and Plackett 2010).

In addition to plant cellulose (PC), cellulose is also obtained through *in vitro* synthesis with the help of enzymatic pathways, the chemical synthesis from glucose derivatives and the biosynthesis by various microorganisms, such as algae and fungi (Klemm et al. 2005), as well as various aerobic non-pathogenic bacteria of the genera *Agrobacterium*, *Sarcina*, *Rhizobium* and *Acetobacter* (Dufresne 2013; Khan et al. 2007; Shezad et al. 2010). While studying acetic fermentations in 1886, Brown reported the bacterial cellulose (BC) in the form of a strong white gelatinous pellicle on the surface of a liquid medium, which had a thickness up to 25 mm. The microbe responsible for this BC membrane (BCM) was called *Bacterium xylinum* that was later on renamed as *Acetobacter xylinum* (*A. xylinum*) and at the moment is recognized as *Gluconacetobacter xylinus* (*G. xylinus*) (Brown 1886a, b).

G. xylinus is the most extensively used microorganism in the basic and applied studies for BC production because of its higher productivity, and capability to consume different sugars and other compounds as sources of carbon (Ross et al. 1991; Saxena and Brown 2012). *G. xylinus* cultivated under controlled conditions with suitable nitrogen and carbon sources, produces highly porous BC network structures in the form of sheets or pellicles, subject to the culturing approach (Lin et al. 2013; Pircher et al. 2014). The culturing conditions may be agitated or static, and batch, semi-continuous or continuous cultivation (Lin et al. 2013, 2014; Pircher et al. 2014; Sulaeva et al. 2015). Typically, the synthesis of BC occurs in four enzymatically catalysed steps: (a) glucose is phosphorylated to glucose-6-phosphate; (b) glucose-6-phosphate is isomerized to glucose-1-phosphate; (c) glucose-1-phosphate is converted to uridine diphosphate glucose (UDP-glucose); and (d) finally glucan chains are synthesized from UDP-glucose (Ross et al. 1991). After this, the parallel glucan chains are aggregated and crystallized to form microfibrils followed by aggregation of the latter to discontinuous bundles of cellulose fibres (Iguchi et al. 2000; Lin et al. 2013). After removal of the culture medium and complete washing, colourless, odourless and tasteless BC is obtained in the form of a gel. This gel finds several applications in our life (Lin et al. 2013). The biosynthetic pathway of BC in *G. xylinus* is shown in Fig. 1.

Fig. 1
Biosynthetic pathway of BC in *G. xylinus*.
Adapted with permission from Lin et al. (2013)

The auspicious properties associated with BC, such as exceptional mechanical characteristics, stress-strain behaviour, good light transmittance, *in situ* moldability, porosity, stability, biocompatibility, low immunogenic potential, and capability for cell adhesion, migration and proliferation (Helenius et al. 2006; Millon and Wan 2006; Qiu and Netravali 2014; Svensson et al. 2005) make it appropriate biomaterial for tissue engineering applications. These applications include, but are not limited to [artificial cartilage \(Nimeskern et al. 2013; Svensson et al. 2005\)](#), [artificial bone \(Zimmermann et al. 2011\)](#), [artificial cornea \(Hui et al. 2009\)](#), [heart valve prosthesis \(Millon and Wan 2006\)](#), [artificial blood vessels](#), [artificial cartilage \(Nimeskern et al. 2013; Svensson et al. 2005\)](#), [bone \(Zimmermann et al. 2011\)](#), [cornea and blood vessels \(Hui et al. 2009; Klemm et al. 2001; Wan et al. 2011\)](#), [heart valve prosthesis \(Millon and Wan 2006\)](#), [nerve surgery \(Klemm et al. 2001; Wan et al. 2011\)](#), [meniscus implant \(Bodin et al. 2007\)](#), [artificial skin and skin tissue repair \(Fu et al. 2012; Qiu and Netravali 2014\)](#).

Some of these BC-based applications are shown in Fig. 2.

Fig. 2
Applications of BC in biomedicine

However, in the current review, we have focused mainly on the applications of BC in various fields, ranging from conventional food to modern functional foods, cosmetics, nutraceuticals, cosmeceuticals and drug delivery. This review will provide the readers an understanding of the role of BC as a functional additive, formulation stabilizer, biocatalysts platform, and ingredient for food, cosmetics and drug delivery systems. Furthermore, the review will be helpful for academic researchers and formulation scientists in food, cosmetics and pharmaceutical industries to give new insights to BC in terms of designing some novel BC-based functional foods, nutraceuticals, cosmeceuticals and drug delivery systems.

Better material properties of BC for food cosmetics and drug delivery applications

Although similar in chemical structure, BC has different and superior physical, mechanical and biological features to PC. Due to these superior properties, it finds applications in food, cosmetics, biomedicine and drug delivery (Lin et al. 2013). BC is biosynthesized in its purest form, which is entirely devoid of pectin, hemicelluloses and lignin (Chawla et al. 2009). Hence, BC is capable to be easily refined in comparison to PC (Shi et al. 2014b). As-synthesized, innate or pristine BC is highly porous in nature with high permeability to liquid and gases, and possesses high water-uptake capacity (more than 90 % of its weight) (Klemm et al. 2001). These characteristics of BC are due to the ultrafine network of the ribbon-shaped micro- and nanofibrils (Chawla et al. 2009), which are about 100-fold more thinner than the PC fibres. Such properties of BC make it suitable for application as formulation stabilizer, thickener, and for scrubbing and exfoliation without damaging the skin due to its soft texture of small fibres (Lin et al. 2015; Shi et al. 2014b). Moreover, the biocompatibility, low immunogenic potential and *in situ* moldability further enhance the applicability of BC in the field of biomedicine (Lin et al. 2016). These properties together with tensile strength (Campano et al. 2015) make BC a suitable candidate for dermal applications in cosmetics, and topical and transdermal drug delivery. Due to high water holding and ion exchange capacities, BC is an appropriate material for laxative effects and low cholesterol diet, respectively. Similarly, the transparency (Campano et al. 2015), along with high permeability to liquid and gases, makes BC an appropriate agent for facial mask, contact lenses and drug delivery to wound with ease of wound inspection (Czaja et al. 2006). The individual fibre strength of BC is almost comparable to that of Kevlar and steel (Yano et al. 2005), making it suitable candidate for applications, where high tensile strength is required, e.g., drug loaded bone cement. Several material characteristics of BC for applications under the scope of the current review are depicted in Fig. 3.

Fig. 3
Better material properties of BC

The material properties of BC can be further tailored by using various *in situ* techniques, such as addition of various substances, change in culturing conditions and the use of genetically modified strains, and *ex situ* strategies like physical and chemical modification, specialized drying conditions and electromagnetic irradiation (Krystynowicz et al. 2002; Lin et al. 2013, 2016; Olyveira et al. 2013; Petersen and Gatenholm 2011; Stoica-Guzun et al. 2007; Sulaeva et al. 2015; Yadav et al. 2010).

Applications of BC in food, cosmetics and drug delivery

Due to the abovementioned properties, BC finds various applications in foods, cosmetics and drug delivery. These applications are discussed with details in the following sections and are summarized in Fig. 4.

Fig. 4
Food, cosmetics and drug delivery applications of BC

Food applications

Being a dietary fibre, BC is considered "generally recognized as safe" (GRAS) by the Food and Drug Administration (FDA) since 1992 (Shi et al. 2014b; Park et al. 2009). BC possesses manifold potentialities in food industries owing to its high purity, a variety of textures and shapes (e.g., particles, spheres, filaments, multi-shaped pulps, films and whiskers), capability to acquire *in situ* changes, such as colours and flavours of culture medium, and easy production process (Shi et al. 2014b). Keeping in view the abovementioned properties, BC can be used as adjuvant in foods and food industry.

Traditional dessert

One of the first uses of BC is the manufacturing of a Filipino traditional dessert with a smooth mouth feel that is called 'nata de coco', whereby coconut water is fermented for the biosynthesis of BC, then the BC is chopped into minute sections and immersed in syrup of sugar. This 'nata de coco' is used as a sweet candy dessert (Iguchi et al. 2000; Klemm et al. 2005, 2006). The 'nata de coco' has turned into a very well-liked food and is now quickly spreading worldwide in the form of a dessert or candy (Gama et al. 2012; Phisalaphong and Chaiaparakobkij 2012).

Low cholesterol diet

BC possesses higher water-holding and cation-exchange capacities than PC with significant serum lipids and cholesterol lowering effect. Thus, fat free, low-cholesterol and low-calorie food commodities can be made with BC (Chau et al. 2008). It might also be employed as a potential candidate to replace the fat in emulsified meat products (Lin and Lin 2004). BC has decreased the quantity of cholesterol in *in vitro* tests through absorption or binding (Stephens et al. 1990). Moreover, the BC gel itself is too tough for biting, but it may become edible by processing it with alginate and calcium chloride or with sugar alcohol. The textures of such BC resemble molluscs and fruit, such as squids and grapes, respectively. The addition of abovementioned substances make BC edible by holding the water in the gelatinous BC, thus making the BC gel easy for cutting off with the teeth. These facts make BC a new material for processed foods, low-calorie desserts and salads (Okiyama et al. 1992).

Vegetarian meat

Vegetarian meat may be prepared by using BC in combination with *Monascus* extract obtained from a natural red pigmented mould (Parwadaria et al. 2010). The composite is stable against changes in colour and morphology, and its flavour is much like natural meat (Jůzlová et al. 1996; Wangmu and Konguang 2010). The vegetarian meat adds cholesterol-lowering effect to the other advantages of BC dietary fibres (Ng and Shyu 2004). Moreover, due to non-animal origin, this meat could be a suitable substitute to animal-based products for certain consumers with dietary restriction.

Food additive and dietary aid

BC has also been explored for its use as a potential gelling, thickening, suspending and stabilizing agent in the food industry (Shi et al. 2014b). BC also acts as a heat-stable suspending agent, and as a filler for the reinforcement of fragile food hydrogels, improving the worth of pasty foods by decreasing their stickiness (Okiyama et al. 1992). Moreover, BC (0.2–0.3 %) significantly increases the gel strength of Tofu (food made by coagulating and pressing soy milk), providing firmness and better texture. BC has also endowed Kamaboko (processed Japanese seafood) with better stiffness and brittleness, almost eliminating the springiness. This modified Kamaboko could better endure the aging process and human demand for sensory evaluation was still satisfied (Okiyama et al. 1993). Likewise, addition of BC, synthesized in agitated culture conditions, to chocolate drink prevented the precipitation of the cocoa due to the retention properties of BC mesh. There was a greater heat stability as the viscosity remained unchanged after the heat sterilization (Okiyama et al. 1993). Upon addition of BC into creamy condiment, the stickiness of the latter could be noticeably improved so that it would be easier to serve it quantitatively using a spoon (Shi et al. 2014b). Similarly, food items having BC can maintain their humidity for minimum storage period of 1 month. The contour of ice-cream having BC was maintained for at least 60 min after it was removed from freezer, which would otherwise melt over the same time in the absence of BC (Shi et al. 2014b). Hence, it is evident that BC could be extensively used in processed foods to improve the stability over a wide range of temperature, pH and freeze-thaw environments. These findings further clarify that BC could be widely applicable to processed foods to improve their quality and storage conditions.

Enzymes and cells immobilization

The production of high amount of food needs the use of modern technologies. Immobilization of enzymes and cells is one of such technologies. In case of certain food items, fermentation industry has been greatly assisted by the application of immobilized enzymes that can change several of their functioning parameters (Kilara et al. 1979; Fernandes 2010).

In the last decade, there has been a growing interest in the use of cellulose materials as an emergent interest in the use of cellulose biomaterials in bioprocessing technologies (Koutinas et al. 2012). Pure BC has exclusive material properties differing from PC and has therefore been the focus of attention as a new functional biomaterial (Petersen and Gatenholm 2011). In a research conducted by Wu and Lia (2008), glucoamylase was immobilized on BC beads. The BC beads in wet form having smallest size (500–1500 µm) were best for immobilization of enzyme in comparison to other types of BC beads. The stability of enzyme was increased against changes in lower temperature and pH values (Wu and Lia 2008). Likewise, the activity of immobilized enzyme via periodate oxidation method was increased by ca. 40 %. Being pH- and temperature-dependent, there was still ca. 46 % of the activity after 14 times of repeated use (Wu et al. 2013). Some other researchers used yeast for repeated batch fermentation for wine-making that was immobilized on BC. The immobilized yeast promoted the cost effectiveness of the manufacturing process by reducing the expenses for preparation of inoculum, whereby the yeast was recovered by simple separation at the end of the fermentation process (Nguyen et al. 2009; Ton and Le 2011). No significant difference was found for ethanol yield by yeast immobilized either on BC or calcium alginate (CA) (Monteleagre et al. 2012). However, in another study, Kirdponpattara and Phisalaphong (2013) immobilized yeast using composites of BC with CA (BC-CA) with high chemical, thermal and mechanical stability, suitable porosity, pore size and hydrophilicity. Thus, in terms of ethanol production, the yeast immobilized on BC-CA substrate was more efficient than the suspended culture and culture immobilized on CA matrix. The efficient ethanol production can be ascribed to the water uptake capacity and properly interconnected porous structure responsible for appropriate mass transfer during the process (Kirdponpattara and Phisalaphong 2013).

BC-based composites can be used for various important enzymes and cells immobilization. Similarly, the immobilization of *Corynebacterium glutamicum* using BC as a support was carried out by adsorption and subsequent incubation for the synthesis of L-lysine (Tam and Huang 2014). The immobilized cells were used eight times for repeated fermentation. The lysine yield was 95 % in the eighth repetition of reusing immobilized cells. Regarding stability and cell viability, the immobilized cells had 80 % cell survival in sterile water (pH 7) stored at 40 °C for 30 days (Tam and Huang 2014).

Laccases obtained from different sources are extensively used in food industry (Osma et al. 2010). These laccases find applications in improving the organoleptic properties of foods, such as the colour of tea-based products, the stability of the beer and wines, the taste and flavour of cacao nib, and the flavour and colour of some vegetable oils. Laccase may also improve the quality of certain foods, such as sauces, pastes, purees, concentrates, and soups by the process of deoxygenation (Osma et al. 2010). Likewise, it has been used to decrease the bitterness and darken the colour of chopped olives (in olive-water mixture), control malodour of cysteine, and stabilize the colour and flavour of fruit juices. Using laccase, the mechanical, textural and bread-making properties of flour can be altered, and the elegance of dough can be enhanced (Osma et al. 2010). In a study, Chen et al. (2015) immobilized laccase from fungus, i.e., *Trametes versicolor* on the BC sponge via cross-linking with glutaraldehyde and physical adsorption. The immobilized laccase through cross-linking showed wider pH range for good catalytic activity and higher stability in comparison to free as well as adsorbed one. The immobilized laccase retained 69 % of its original activity after 7 cycles (Chen et al. 2015).

Furthermore, BC has been used for immobilization of enzymes, such as horse radish peroxidase, glucose oxidase and laccase for biosensors, bioanalysis and enzymatic biofuel cell (Chen et al. 2011; Lv et al. 2016; Wang et al. 2010; Zhang et al. 2010), which is beyond the scope of this review.

From the aforementioned literature, it is evident that BC beads and cubes have potential for the immobilization of enzymes and cell systems for improving yield, quality and stability of food product in food industry. Moreover, these studies show the potentials of BC for the immobilization of other enzymes in techno-economically feasible manner for food production.

Food packaging

BC works as a food packing to confirm the safety and increase shelf-life of the products. Antimicrobial ingredients, ethylene and oxygen scavengers, and moisture and taint removers are all used in active BC-based packaging systems (Tomé et al. 2010). Moreover, modified BCM with tailored surface and barrier properties have been prepared by controlled heterogeneous esterification with hexanoyl chloride (Tomé et al. 2010). The esterified BCM showed an increased hydrophobicity, while maintaining the bulk structure of the pristine BC. The barrier properties were measured by its permeability to water vapour at different relative humidity, and humidified nitrogen, oxygen and carbon dioxide. About 50 % decrease in both water and gas permeability through modified BCM was observed. Permeability was observed for the modified BCM (Tomé et al. 2010).

Furthermore, Jipa et al. (2012) designed biodegradable BC and sorbic acid (BC-SA) based monolayer and multilayer films by incorporation of SA as antibacterial agent. The study showed that concentration of both BC and SA affected the sensitivity to water, rate of SA release, and antibacterial activity of BC-SA mono- and multilayer film. There was no SA degradation during film preparation (Jipa et al. 2012). Faster SA release rate was observed at lower concentration, but it became significantly slower at higher SA concentration due to slower dissolution rate of the formed SA crystals. Moreover, SA release rate was faster from the monolayer films compared to the multilayer films. The antimicrobial effect of BC-SA was tested against *Escherichia coli* K12-MG1655, which indicated that the new BC films possess promising antimicrobial properties (Jipa et al. 2012).

Similarly, composite materials with antimicrobial activities were designed, whereby poly(vinyl alcohol) (PVA) acted as polymeric matrix and grinded BC as reinforcing fibres (Dobre et al. 2012). SA was used as an antimicrobial agent due to its recognized preservative function in the food industry. The designed film showed antibacterial effect against *Escherichia coli* (Dobre et al. 2012), which revealed that new composite film could be promising antimicrobial material for food packaging.

From the above discussion, it is evident that BCM is a promising and interesting biopolymer for the development of materials with potential applications in the packaging industry with antimicrobial property and durability.

Studies related to applications of BC in food and food industry are summarized in Table 1.

Table 1

BC applications in food

Food, related item or process	Form of BC	Purpose of BC	References
Nata de coco	BC slices	Main structure	Iguchi et al. (2000)
Low cholesterol diet	Powdered BC	Fat adsorbent	Chau et al. (2008), Lin and Lin (2004), Stephens et al. (1990)
Vegetarian meat	BC sheets	Structural component, fat adsorbent	Jázlová et al. (1996), Purwadaria et al. (2010), Wongsu and Kongruang (2010)
Pasty food and jams	Aqueous paste	Heat-stable suspending and bulk forming agent	Okizama et al. (1992)
Tofu	Aqueous paste	Gelling agent	Okizama et al. (1993)
Kambo	Aqueous paste	Hardening agent, texture modifier	Okizama et al. (1993)
Chocolate drink	Aqueous paste	Stability against heat	Okizama et al. (1993)
Ice-cream	Aqueous paste	Hardening agent, stability against freeze-thaw process	Okizama et al. (1993)
Glucosylase	Beads	Solid support to increase enzymatic activity	Wu and Lia (2008), Wu et al. (2013)
Wine	BC pieces	Solid support to increase activity of yeast	Montelegre et al. (2012), Nguyen et al. (2009), Ton and Le (2011)
Fungal laccase	BC sponge	Solid support to increase activity of laccase	Chen et al. (2015)
L-lysine	BC cubes	Solid support to increase activity and cell viability	
Food packaging	BC sheets, film and powdered BC	Hydrophobic and antimicrobial packaging	Dobre et al. (2012), Jpa et al. (2012), Tomé et al. (2010)

Cosmetics applications

Cosmetics are substances that are used to improve some of the organoleptic properties of the human body (Hasan et al. 2012). Cosmetics include products that are applied to the human body for altering the appearance, enhancing the attraction, and cleansing or beautifying the body parts without affecting the normal body functions or structure (Hasan et al. 2012). Currently, the majority of the cosmetics are used by customers to boost their beauty without bearing in mind the ill-effects on body, for example, toxicity concerns associated with parabens (Nagel et al. 1977; Darbre and Harvey 2008). In order to avoid harmful effects to the consumers, natural skin-care products are recommended, which utilize herbal or natural ingredients (Hasan et al. 2012).

In this context, cellulose fibrils are applied in cosmetics to stabilize oil-in-water (O/W) emulsion without the addition of any of surfactant. Such formulations may not be irritant to sensitive skin due to the absence of any surfactant (Hasan et al. 2012). BC has also been reported to be an exceptional non-allergenic biopolymer for use in the cosmetics. The various application of BC in cosmetics are discussed in the following sections.

Facial mask

BC facial masks are of great interest as cosmetic devices to treat dry skin due to its biodegradability, low toxicity and ability to hydrate the skin (Annuakiti et al. 2011). In a study, one group of volunteers was asked to apply moist towels on the face for 25 min, while the second group was assigned to apply the translucent BC facial masks for the same period (Annuakiti et al. 2011). During the subsequent week, the groups were interchanged to the alternative treatment. Skin dullness, texture, elasticity, sebum content, moisture content and desquamation levels were evaluated using a system used for routine skin counselling before applying and after 5 min of removing the towels and trial product (Annuakiti et al. 2011). The user satisfaction about the BC mask was also investigated. The BC masks augmented the moisture contents of the skin significantly than moist towels upon a single treatment. No obvious effects on other characteristics of skin were observed. The cellulose-mask product BC facial masks rated around 4 out of 5 on the satisfaction rating scale (Annuakiti et al. 2011). The BC mask could be used as a natural cosmetic product for increasing moisture content of the skin can be used for increasing moisture content of the skin. The responses about user satisfaction in questionnaire-based study revealed that the BC facial mask was acceptable to consumer (Annuakiti et al. 2011).

Similarly, BC with and without glycerine was evaluated for skin irritation potential in human subjects (Almeida et al. 2014). There was no significant difference in terms of transepidermal water loss (i.e., absence of barrier disruption) and erythema with zero clinical score, except for few subjects with mild skin irritation. Moreover, addition of glycerine gave a significantly higher skin moisturizing effect, suggesting its potentials for moisturizing facial mask (Almeida et al. 2014).

In a patent, BC facial mask was fabricated with holes for eyes, mouth and nose (Zhong 2008). The author claimed that such mask may be suitable for repeated or prolonged use for skin beautifying purpose, skin nutrition, and moisturizing and cosmetic effects (Zhong 2008). Similarly, facial mask composed of BC membrane containing ginseng extracts has shown promising results in terms of moist feel, overall user satisfaction and skin elasticity in women over 30 years of age (Lee et al. 2011). In another study, BC facial mask with sodium bicarbonate (5 g), monohydrated citric acid (4 g), ascorbic acid (0.5 g) and salicylic acid (0.05 g) has been used for exfoliative and moisturizing purposes (Legendre 2008). In this study, the author has also claimed BC mask with thermal plankton as a constituent for its anti-wrinkle effects (Legendre 2008).

BC gel with controlled release of silk sericin were developed with improved moisture holding capability in comparison to commercially available paper mask (Aramwit and Bang 2014). Upon peel test using porcine skin, it was revealed that BC-based gel was biocompatible and less adhesive (peeled without pain) than paper mask (Aramwit and Bang 2014). The prepared gel may find potential applications in medicated cosmetics as anti-wrinkle, antiaging and moisturizing facial mask.

Keeping in view the above studies, it is worth mentioning that in addition to the aforementioned application, BC-based membranes could also be used for treating various skin conditions including xerosis, atopic dermatitis and psoriasis, whereby moisturizing effect is needed in addition to pharmacotherapy.

Facial scrub and medicated cosmetics

A facial scrub containing powdered BC and natural ingredients including olive oil, ascorbic acid (Vitamin C), Aloe vera extract and powdered glutinous rice was formulated (Hasan et al. 2012). Using plate-plate rheometer, both commercial and formulated facial scrubs showed shear thinning behaviour (non-Newtonian liquid). The formulated facial scrub possessed relatively higher viscosity at lower shear rates in comparison to the commercial one, but both possessed nearly comparable viscosities at higher shear rates. The tested samples were capable of drying out after 10 min at ~30 °C (room temperature). This novel formulated facial scrub containing BC as major ingredient engrosses the attention of cosmetics formulators for the development of facial scrub with natural ingredients, making it safe for skin. Moreover, Lin et al. (2015) claimed cosmetic containing fragments of BC film in the range of 0.05–1.0 % by weight. By adding the fragments of BC in the cosmetic not only improved the transdermal permeation of active ingredients present in the cosmetic, but also provided skin moisturizing function, sebum absorption and skin exfoliation (Lin et al. 2015). It has also been claimed that due to high water holding capacity and good gas permeability, BC is an appropriate carrier for cosmetically active ingredients including moisturizers, such as salicylic acid or hyaluronic acid whitening ingredients, such as kojic acid or ursolic acid, anti-wrinkling agents (e.g., polypeptides, and exfoliator), growth factors, enzymes, or a combination thereof (Lin et al. 2015). Moreover, according to authors (Lin et al. 2015; Tourmilhaac and Loran 2003), BC-based formulation can find extensive applications in designing the lip, skin and nail care products and long-lasting perfume.

Personal cleansing formulations

The purpose of personal cleansing formulations is remove dirt, reduce sebum and exogenous contaminants, and to control malodour and the skin microflora. In addition to hygienic benefits, surfactants in such formulations damage skin constituents and may entangle in the stratum corneum after washing (Kuehl et al. 2003; Walters et al. 2012). This can lead to allergic reactions and skin irritation, especially in case of sensitive skin (Draelos et al. 2013; Kuehl et al. 2003). In this regard, BC produced biosynthesized in agitated culture conditions (Ag-BC) showed exhibited the highest stabilizing effect for O/W emulsion among all the inspected cellulose-based materials (Ogiya et al. 1997). It was demonstrated that BC fine fibrils acted as a scaffolding structure and a mechanical barrier, interrupting the coalescence of oil droplets. Thus, the emulsion was stabilized without reducing the interfacial tension as occurs in the case of surfactants (e.g., sorbitan monolaurate). Due to its thinner fibrils, Ag-BC would protect a larger surface area of the droplets of oil in the form of mechanical barrier than any other cellulose-based material. Moreover, this emulsion was also stable against changes in temperature and pH, and against addition of salt in comparison with xanthan gum- and sorbitan monolaurate-based formulations. One of the potential applications of this O/W type emulsion could be the formulation of body parts cleansing products, especially for sensitive skin.

In a patent, a personal cleansing formulation consisting of liquid matrix, i.e., water, a lathering surfactant and an external structuring agent, comprising both BC network and a cationic polymer e.g., cationic starch derivatives and cationic cellulose derivatives or mixtures of these, was claimed to be formulated (Heath et al. 2012). The particles of these formulations were suspended in the liquid matrix with pH-values of less than ca. 4.0 or 7.0. Such compositions provided good lathering and easily rinse off properties without any unwanted filmy or slimy hand feel. The presence of particulate matters improve cleansing and exfoliation with conditioning benefits, and without any irritation or damage to the skin. A pH-value less than ca. 4.0 is especially preferred for salicylic acid formulations (Heath et al. 2012). Such formulation may be used for body cleansing for sensitive skin without any irritation, especially for body parts, where consumer's hand feel is important. Moreover, using compositions of such formulation at pH-value of less than ca. 4.0, salicylic acid formulation for personal cleansing can be formulated. Such formulations may be used to clear and prevent skin blemishes and pimples. These may also be used for the treatment of skin conditions with scaling or skin overgrowth (Heath et al. 2012).

Contact lenses

Other than optical indications, contact lenses find wide range of applications including cosmetic or decorative purpose (Rubinstein 2003; steinemann et al. 2005). BC is one of the potential candidates for fabrication of contact lenses due to its transparency, light transmittance, and permeability to liquid and gases. BC-based contact lens was fabricated by pouring high viscosity BC solution (in 1-butyl-3-methylimidazolium chloride) to a mould. Upon treating the solution with isopropyl alcohol followed by water, a clear BC membrane was precipitated, which spontaneously detached from the mould surface and the residual solvent diffused to the water. The hydrated BC contact lens retained its shape and transparency for a time of more than 8 weeks (Levinson and Glonek 2010). Similarly, transparent polymeric hydrogel was prepared by combining BC and 2-hydroxyethyl methacrylate polymer. The fabricated biomaterial possessed ca. 40 % (w/w) water content with good mechanical strength and integrity (Li et al. 2010) and had the ability to be used as contact lenses. Apart from optical and decorative purposes, these contact lenses can find potential applications for drug delivery to the cornea. Moreover, the ability of BC to take colour of the medium (Shi et al. 2014b) can be exploited for design of coloured and appealing contact lenses with transparent centre for the pupil, provided that the biocompatibility is not compromised by the colourant(s).

The applications of BC and BC-based products in cosmetics are summarized in Table 2.

Table 2

Applications of BC in cosmetics

Cosmetic product	Form of BC	Purpose of BC	References
Facial mask	BC sheets	Moisturizer	Annuakiti et al. (2011)
Facial mask	BC-glycerine composites	Moisturizer	Almeida et al. (2014)
Facial mask	BC membrane	Moisturizer	Zhong (2008)
Facial mask	BC-ginseng	Moisturizer and carrier	Lee et al. (2011)
Facial mask	BC with cosmetically substances	Moisturizer and carrier for the actives for exfoliative, brightening and anti-wrinkle purposes	Legendre (2008)
Facial mask	BC-sericin composites	Moisturizer and carrier for silk sericin	Aramwit and Bang (2014)
Facial scrub	Powdered BC	Viscosity enhancer	Hasan et al. (2012)
Facial scrub	BC fragments	Moisturizer, sebum absorbent and skin exfoliator	Lin et al. (2015)
Carrier for cosmetically active ingredients	BC fragments	Prolongs the contact time of the cosmetically active ingredient with the skin surface	Lin et al. (2015)
Foundation make-up	BC fragments	Stable make-up with less number of touch-ups and lesser amount required	Lin et al. (2015)
Personal cleansing product	BC fibres (synthesized in agitated conditions)	Surfactant free emulsion for sensitive skin	Ogiya et al. (1997)
Personal cleansing product	BC particles	Cleansing and exfoliation	Heath et al. (2012)
Contact lenses	Regenerated BC sheet	Film-forming agent	Levinson and Glonek (2010)
Contact lenses	BC-based hydrogel	Film-forming agent	Li et al. (2010)

Drug delivery applications

Drug delivery to wounds

Studies have suggested that fluid, particularly exudates from chronic wounds may inhibit healing process (Vowden and Vowden 2005). An excessively wet environment may lead to wound and skin maceration resulting in prolonged wound healing, whereas a dry wound will also heal more gradually due to lack of moisture required for cell migration (Benbow and Stevens 2010). Hence, exudates reduction looks like a key parameter for normal healing process (Sulava et al. 2015). Being an excellent absorbent (Gayathri and Gopalswamy 2014) and skin moisturizer (Annuakiti et al. 2011), BC can be an ideal candidate for lowering or removing the wound exudates, while at the same time maintaining a moist environment (Sulava et al. 2015). However, innate BC is devoid of antimicrobial activity against the wound deteriorating pathogens.

To achieve such goals, a BC film with antibacterial property was fabricated, whereby a lyophilized BC film was dipped in a benzalkonium chloride (BZK) solution followed by further lyophilization (Wei et al. 2011). Water uptake capacity, a feature important for wound dressing system, was also attained with a swelling ratio of 37.3 and 26.2 for saline solution and deionized water, respectively. A prolonged (at least 24 h) stable antibacterial activity was achieved against *Staphylococcus aureus* along with a higher water uptake capacity. Thus, BZK-loaded BC film may act as a potential functional wound dressing system for treatment of acute traumas.

Recently, Pavaloiu et al. (2014b) studied the release of the antibiotic amoxicillin (AMX) from BCM at nearly neutral (7.4) pH conditions. The concentration of AMX significantly influenced the drug release (Pavaloiu et al. 2014b). Among the other factors, there was a significant contribution of glycerol (as plasticizer) to *in vitro* drug release. The common topical drug delivery enhancer trimethyl ammonium bromide did not show any positive impact on the *in vitro* release of the drug. This system might provide a suitable way for antibiotic delivery to the wound.

The antimicrobial activity of antibiotics with prolonged drug release behaviour from BC was assessed *in vitro* using ampicillin (AMP) and gentamycin (GM) (Kaplan et al. 2014). For the assessment of exudate retention, the water uptake capacity of the BCM was found to be 65.6 ± 1.6 % in phosphate buffer saline (PBS). The drug loading was 99 and 48 mg/cm² for AMP and GM, respectively. The BCM released only trace amount (0.107 % of AMP and 0.113 % of GM) within 24 h. Thus, with no burst release, the amount of drug released within 7 days was 28 and 17 % for AMP and GM, respectively. Furthermore, due to sufficient amount of the drug in prolonged release manner, the antibacterial activity against *Pseudomonas aeruginosa*, *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Enterococcus faecalis* and *Escherichia coli* prevailed for as long as 3 days of incubation period (Kaplan et al. 2014). Furthermore, Rouabhi et al. (2014) covalently attached the GM to the surface of chemically modified BC, i.e., BC-RGDC-GM, where RGDC is a peptide composed of arginine, glycine, aspartic acid and cysteine. In addition to its bactericidal effect, BC-RGDC-GM was devoid of any toxicity for human skin fibroblasts (Rouabhi et al. 2014). Likewise, the *in vitro* release of tetracycline from BC was assessed as function of electron beam irradiation, which considerably decreased the diffusion of tetracycline (Stoica-Guzun et al. 2007). Hence, BC-based drug delivery to wound is a feasible way with its ability to absorb exudates as well. Furthermore, silver sulfadiazine (SSD) particles impregnated into BC revealed *in vitro* antimicrobial activity, human epidermal cells biocompatibility, and good epithelialization and wound healing activity in rat models with burns for burns in a rat model (Luan et al. 2012; Wen et al. 2015). A step further, a novel wound dressing system consisting of polyhexamethylene biguanide (PHMB) and the never dried BC (BC-PHMB) was evaluated for safety through *in vitro* cytotoxicity, haemolysis, sensitization in guinea pigs, irritation potential in rabbits and acute systemic toxicity (Serafica et al. 2010). In addition to good antimicrobial effects, wound healing in animal models showed that the BC-PHMB wound dressing rehabilitated 70 % of the wounds in comparison to 0, 20 and 50 % for the air-exposed, hydrogel treated and hydrocolloid treated wounds, respectively. Upon clinical effectiveness testing in humans, BC-PHMB showed promising results for wound healing of deep pressure wounds and venous leg ulcers (Serafica et al. 2010). Furthermore, in patient, this wound dressing system was more promising than the other commercial dressing in terms of bacterial load reduction and pain management (Haemmerle et al. 2012).

Purpose	Therapeutic candidate(s)	Strategy	Finding	References
Drug delivery to wound				
	BZK	Drug loaded BCM	Prolonged drug release and antimicrobial activity	Wei et al. (2011)
	AMX	Drug loaded BCM	AMX- and glycerol-dependent <i>in vitro</i> drug release	Pavlosin et al. (2014b)
	AMP, GM	Drug loaded BCM	Good water uptake capacity, no burst release and prolonged drug release with antibacterial effects	Kaplan et al. (2014)
	GM	Covalently attached to the surface of RGDC-modified BCM	Antibacterial effects without toxicity for human skin fibroblasts	Rouabhi et al. (2014)
	Tetracycline	Drug loaded BCM	Antibiotics release was sustained by electron beam-irradiation	Stoica-Guzun et al. (2007)
	SSD	BCM	<i>In vitro</i> antimicrobial activity, human epidermal cells biocompatibility, <i>in vivo</i> epithelialization and wound healing activity	Luan et al. (2012), Wen et al. (2015)
	PHMB	BCM	No <i>in vitro</i> cytotoxicity or haemolysis; no sensitivity, irritation potential or acute systemic toxicity in animals; good antimicrobial effects; promising for <i>in vivo</i> wound healing, and more pain reduction than the commercial dressing	Serafica et al. (2010), Haemmerle et al. (2012)
	Deacetylated chitosan, chitosan monomercaptoic	BCM	Antimicrobial effects	Buitrago et al. (2013), Wanling et al. (2012), Li-Kuan et al. (2013)
	Metallic nanoparticles (silver, copper, titanium dioxide)	BCM	Antimicrobial effects	Dobre and Stoica-Guzun (2013), Pinto et al. (2013), Khan et al. (2015)
Tissue engineering drug delivery				
	GM vancomycin	BC-based bone cement	Presence of BC in the bone cement prevented compression and fracture fragility; improved fatigue life and increased antibiotic elution The compression and fracture fragility were prevented, while the fatigue life and antibiotic elution were improved	Mori et al. (2011)

Purpose	Therapeutic candidate(s)	Strategy	Finding	References
Controlled drug delivery	BMP ₂	BC-based protein composite	Biocompatible, and capable of <i>in vitro</i> fibroblast differentiation and bone formation	Shi et al. (2012)
	Paracetamol	BC coated tablets	The flexible BC film sustained the drug release	Amin et al. (2012a)
	~	BC-based hydrogels with gelatine	Potentials for gastro-retentive drug delivery due to more swelling in acidic conditions	Pýřálová et al. (2015)
	Theophylline	BC-based hydrogels	Lesser drug release in SGF than SIP	Amin et al. (2014)
	IbuNa	BC-based hydrogels	pH-dependent sustained drug release	Pavaliou et al. (2014c)
	IbuNa	BC-based hydrogels	pH-dependent sustained drug release	Pavaliou et al. (2014a)
	Ibu	BC-based hydrogels	pH- and electro-dependent drug release	Shi et al. (2014a)
	Propranolol	MIP matrix	Selective transport and release of S-propranolol	Bodhibukkana et al. (2006)
	BSA	BC-based hydrogels without cross-linker	Devoid of cross-linker associated toxicity, protection of BSA from gastric conditions, <i>in vitro</i> sustained release of BSA, which was stable after loading and release	Ahmad et al. (2014)
	BSA	BCM	More BSA loading in never-dried BCM, and integrity and bioactivity of BSA was maintained after loading and release	Müller et al. (2013)
Dental drug delivery	BSA	BC-based hydrogels	Lower swelling and lower drug release in acidic pH in comparison to alkaline pH.	Amin et al. (2012b)
	Trypan blue	BC point	Greater drug release in comparison to paper point	Yoshino et al. (2013)
Transdermal drug delivery	Insulin	BCM	Gamma-irradiated BCM has slower insulin release than non-irradiated BCM	Otyveira et al. (2013)
	Tetracycline	Drug loaded BCM	Electron beam-irradiated BCM has slower tetracycline release than non-irradiated BCM	Stoica-Guzun et al. (2007)
	Ibu, LCH	Drug loaded BCM	Slower permeation of LCH than conventional formulations, faster permeation of Ibu than conventional formulations	Trovatti et al. (2012)
	DS	Drug loaded BCM	Permeation rate was comparable to commercial patches and significantly lower than commercial gel	Silva et al. (2014)
	Theophylline	BC-based hydrogels	Sustained release of theophylline	Pandey et al. (2013)
	Berberine	BCM	Drug release was slower in acidic pH, intermediate in alkaline pH and highest in neutral pH	Huang et al. (2013)
Macromolecular prodrg delivery				
	Ibu	pH-dependent ester conjugates	Sustained release of Ibu (faster in alkaline and acid pH, while slower at neutral pH)	Shi et al. (2013)

Conclusion and future prospects

The current review demonstrates that BC is a natural biomaterial with ‘GRAS’ status, biosynthesized by non-pathogenic bacteria. BC has great potential for application in food, cosmetics and drug delivery systems, in addition to the aforementioned biomedical applications. Nevertheless, there are a limited number of available studies in the field of foods and cosmetics, and there still exists adequate scope for the advanced research in these areas in more detail. For example, cholesterol lowering studies on animals and humans need further attention. Studies on food and cosmetics pave the way for potential applications of BC in nutraceuticals and cosmeceuticals. In terms of nutraceuticals, BC can be further employed in the form of fortified food by adding certain nutritional entities, such as vitamins and minerals to the existing and the new BC-based food items. The traditional dessert may also act as a sweetened vehicle for oral drug delivery, particularly for children. Moreover, due to its bulk-forming and water retention capacity, the fibrous nature of the BC-based food products can be assessed for its laxative effect in the treatment of constipation. BC can be used in O/W emulsion without surfactant, as a substitute to PC and PC-derivatives. This emulsion could be used for cleansing, makeup, and care or treatment of the lips, skin and the eyelashes, as well as treating certain medical conditions of the skin. Furthermore, a comparison between BC produced under static and aerated conditions should be carried out for pure BC in terms of water uptake for sweat retention in cosmetics, exudate retention in wounds, drug loading, drug release, and ~~few~~ physical and chemical modifications.

In the modern era, most of the people rely on cosmetics in one way or the other. By addition of antioxidants and therapeutic agents to BC-based cosmetics, a paradigm shift is expected from conventional cosmetics to cosmeceuticals and medicated cosmetics. It is noteworthy that due to its transparency, light transmittance and biocompatibility, BC and/or its hydrogels can be used for the fabrication of disposable and multiple use contact lenses for cosmetic purpose and optometry, and as ~~ocular~~ implants for ~~ocular~~ drug delivery.

BCM provides a good tool for delivery of antibiotics to the wound with potentials for exudates retention and moisturizing environment that are favourable for wound healing. These studies lack experiments on wound models to study the favourable properties of pristine and antibiotics loaded BCM for *in vivo* wound healing.

The fabrication of BC-based hydrogels has been tested with several polymeric matrices, such as PAA, PVA and PAM. However, many other polymeric biomaterials could be tested while considering specific interactions between carriers and drugs that might tailor the drug release. Despite of several studies regarding the oral delivery of proteins, only BSA as model protein has been studied. There still exists a space for research ~~on the~~about loading, release and stability studies of other proteins with therapeutic value.

Regarding transdermal drug delivery, BC-based delivery systems have shown promising results in term of biocompatibility (pure BC) with skin, and *in vitro* drug diffusion studies. However, further *in vivo* studies for skin irritation potentials of drug loaded BC and *in vivo* bioavailability of drugs from the BC-based delivery systems with and without penetration enhancer(s) are needed.

As discussed in some of the abovementioned studies, drug release is controlled by the process of pH-dependent diffusion, which could be further tailored by additional physical treatments or chemical modifications. Such approaches would enable a sophisticated control over the drug release, particularly in a response to body stimuli, such as temperature above normal, i.e., fever condition and tumour micro-environment. Moreover, BC-based nanogels would be helpful for invasive targeted delivery of proteinaceous and non-proteinaceous drug, provided that such nanogels are biodegradable *in vivo*. Such nanogels could also be used in the form of biomolecule-sensitive ~~hydrogels~~ delivery systems, e.g., glucose-sensitive hydrogels for delivery of insulin. Moreover, such biodegradable hydrogels can also be used for targeted drug delivery to tumour (acidic pH), provided that suitable nanogels are formed that are more sensitive to slight changes for invasive drug delivery. In addition, due to the presence of several-OH groups on its surface, BC has also potential for the formation of macromolecular prodrg by covalent conjugation. The Ibu conjugates can be further tested *in vitro* in the presence of enzymes (microbial esterases and cellulases) and in ~~in vivo~~ animal models to predict the *in vivo* performance. Moreover, this approach can be further tailored for pH-dependent (more stable in acidic environment) sustained release of other therapeutic candidates associated with gastric irritation (e.g., NSAIDs). The abundant surface free -OH groups can also be used for surface functionalization of BC for targeted drug delivery, for example, colon-specific drug delivery.

BC alone or in composite form with biocompatible polymer(s) may also find interesting applications in subcutaneous implantable devices for the delivery of therapeutic candidates, where prolonged therapy is desired, such as hormonal replacement therapy and contraception.

In case of MIP, the technique could further be tailored by designing specific MIP ~~to attain~~for enantioselective drug delivery ~~for~~with better patient's outcomes, and for enantiomer differentiation and deracemization. Moreover, MIP-based nanoparticulate columns with improved surface area can be designed for efficient enantiomer separation, analysis and deracemization.

In case of all drug delivery systems, discussed in this review, there is a need for further ~~in vivo~~ studies using various animal models and/or human volunteers for getting a clearer idea about the *in vivo* performance, bioavailability and *in vitro-in vivo* correlation (IVIVC) of the prepared delivery systems.

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References

Ahmad N, Anin MCIM, Mahali SM, Ismail I, Chuang VTG (2014) Biocompatible and mucoadhesive bacterial cellulose-g-poly (acrylic acid) hydrogels for oral protein delivery. Mol Pharm 11:4130–4142

Almeida IF, Pereira T, Silva NH, Gomes FP, Silvestre AJ, Freire CS, Sousa Lobo JM, Costa PC (2014) Bacterial cellulose membranes as drug delivery systems: an *in vivo* skin compatibility study. Eur J Pharm Biopharm 86:332–336

Anin MCIM, Abadi AG, Ahmad N, Katas H, Jamal JA (2012a) Bacterial cellulose film coating as drug delivery system: physicochemical, thermal and drug release properties. Sains Malays 41:561–568

Anin MCIM, Ahmad N, Halib N, Ahmad I (2012b) Synthesis and characterization of thermo- and pH-responsive bacterial cellulose/acrylic acid hydrogels for drug delivery. Carbohydr Polym 88:465–473

Anin MCIM, Ahmad N, Pandey M, Xin CJ (2014) Stimuli-responsive bacterial cellulose-g-poly (acrylic acid-co-acrylamide) hydrogels for oral controlled release drug delivery. Drug Dev Ind Pharm 40:1340–1349

Amnuakit T, Chusuit T, Raknam P, Boonme P (2011) Effects of a cellulose mask synthesized by a bacterium on facial skin characteristics and user satisfaction. Med Devices 4:77–81

Aramwit P, Bang N (2014) The characteristics of bacterial nanocellulose gel releasing silk sericin for facial treatment. BMC Biotechnol 14:104

Benbow M, Stevens J (2010) Exudate, infection and patient quality of life. Br J Nur 19:S32–S36

Bodhibukkana C, Srichana T, Kaewnopparat S, Tangthong N, Bouking P, Martin GP, Suedee R (2006) Composite membrane of bacterially-derived cellulose and molecularly imprinted polymer for use as a transdermal enantioselective controlled-release system of racemic propranolol. J Control Rel 113:43–56

Bodin A, Concaro S, Brittnberg M, Gatenholm P (2007) Bacterial cellulose as a potential meniscus implant. J Tissue Eng Regen Med 1:406–408

Brown AJ (1886a) XIX.—The chemical action of pure cultivations of *bacterium aceti*. J Chem Soc Trans 49:172–187

Brown AJ (1886b) XLII.—On an acetic ferment which forms cellulose. J Chem Soc Trans 49:432–439

Bruno BJ, Miller GD, Lim CS (2013) Basics and recent advances in peptide and protein drug delivery. Ther Deliv 4:1443–1467

Butchosa N, Brown C, Larsson PT, Berglund LA, Bulone V, Zhou Q (2013) Nanocomposites of bacterial cellulose nanofibers and chitin nanocrystals: fabrication, characterization and bactericidal activity. Green Chem 15:3404–3413

Campano C, Balea A, Blanco A, Negro C (2015) Enhancement of the fermentation process and properties of bacterial cellulose: a review. Cellulose 23:1–35

Chau C-F, Yang P, Yu C-M, Yen G-C (2008) Investigation on the lipid- and cholesterol-lowering abilities of biocellulose. J Agric Food Chem 56:2291–2295

Chawla PR, Bajaj IB, Survasse SA, Singhal RS (2009) Microbial cellulose: fermentative production and applications. Food Technol Biotechnol 47:107–124

Chen X, Chen Z, Zhu J, Xu C, Yan W, Yao C (2011) A novel H₂O₂ amperometric biosensor based on gold nanoparticles/self-doped polyaniline nanofibers. Bioelectrochemistry 82:87–94

Chen L, Zou M, Hong FF (2015) Evaluation of fungal laccase immobilized on natural nanostructured bacterial cellulose. Front Microbiol 6:1245

Czaja W, Romanovicz D, Brown RM (2004) Structural investigations of microbial cellulose produced in stationary and agitated culture. Cellulose 11:403–411

Czaja W, Krystynowicz A, Bielecki S, Brown RM (2006) Microbial cellulose—the natural power to heal wounds. Biomaterials 27:145–151

Czaja WK, Young DJ, Kawecki M, Brown RM (2007) The future prospects of microbial cellulose in biomedical applications. Biomacromolecules 8:1–12

Darbre PD, Harvey PW (2008) Paraben esters: review of recent studies of endocrine toxicity, absorption, esterase and human exposure, and discussion of potential human health risks. J Appl Toxicol 28:561–578

De Groot AS, Martin W (2009) Reducing risk, improving outcomes: bioengineering less immunogenic protein therapeutics. Clin Immunol 131:189–201

Dobre ML, Stoica-Guzun A (2013) Antimicrobial Ag-poly(vinyl alcohol)-bacterial cellulose composite films. J Biobased Mater Bioenergy 7:157–162

Dobre L-M, Stoica-Guzun A, Stroeescu M, Jipa I, Dobre T, Ferdeş M, Ciupmilac Ş (2012) Modelling of sorbic acid diffusion through bacterial cellulose-based antimicrobial films. Chem Pap 66:144–151

Draclous Z, Hornby S, Walters RM, Appa Y (2013) Hydrophobically modified polymers can minimize skin irritation potential caused by surfactant-based cleansers. J Cosmet Dermatol 12:314–321

Dufresne A (2013) Nanocellulose: from nature to high performance tailored materials. Walter de Gruyter, Berlin

Ellis B, Smith R (2008) Polymers: a property database. CRC Press, Boca Raton

Fernandes P (2010) Enzymes in food processing: a condensed overview on strategies for better biocatalysts. Enzyme Res. ~~862537~~Article ID 862537

<http://dx.doi.org/10.4061/2010/862537>
AQ3

- Fu L, Zhang Y, Li C, Wu Z, Zhuo Q, Huang X, Qiu G, Zhou P, Yang G (2012) Skin tissue repair materials from bacterial cellulose by a multilayer fermentation method. *J Mater Chem* 22:12349–12357
- Gayathry G, Gopalaswamy G (2014) Production and characterisation of microbial cellulosic fibre from *Acetobacter xylinum*. *Indian J Fibre Text Res* 39:93–96
- Haemmerle G, Signer M, Mintlboeck M (2012) Comparison of PHMB-containing dressing and silver dressings in patients with critically colonised or locally infected wounds. *J Wound Care* 21:13–19
- Harris JM, Chess RB (2003) Effect of pegylation on pharmaceuticals. *Nat Rev Drug Discov* 2:214–221
- Hasan N, Biak DRA, Kamarudin S (2012) Application of bacterial cellulose (BC) in natural facial scrub. *IJASEIT* 2:1–4
- Heath BP, Coffindaffer TW, Kyte III KE, Smith III ED, McConaughy SD (2012) Personal cleansing compositions comprising a bacterial cellulose network and cationic polymer. US patent, US 8097574 B2
- Helenius G, Bäckdahl H, Bodin A, Nannmark U, Gatenholm P, Risberg B (2006) *In vivo* biocompatibility of bacterial cellulose. *J Biomed Mater Res A* 76:431–438
- Huang L, Chen X, Nguyen TX, Tang H, Zhang L, Yang G (2013) Nano-cellulose 3D-networks as controlled-release drug carriers. *J Mater Chem B* 1:2976–2984
- Hubbell JA (1995) Biomaterials in tissue engineering. *Nat Biotechnol* 13:565–576
- Hui J, Yuanjuan J, Jiao W, Yuan H, Yuan Z, Shiru J (2009) Potentiality of bacterial cellulose as the scaffold of tissue engineering of cornea. In: Biomedical engineering and informatics, 2009. 2nd international conference, IEEE, Tianjin, China, pp 1–5
- Hussain MA, Badshah M, Iqbal MS, Tahir MN, Tremel W, Bhosale SV, Sher M, Haseeb MT (2009) HPMC-salicylate conjugates as macro/molecular prodrugs: design, characterization, and nano-rods formation. *J Polym Sci Part A Polym Chem* 47:4202–4208
- Iguchi M, Yamataka S, Budhiono A (2000) Bacterial cellulose—a masterpiece of nature's arts. *J Mater Sci* 35:261–270
- Jay JM, Loessner MJ, Golden DA (2008) Modern food microbiology. Springer, New York
- Jipa IM, Stoica-Guzun A, Stroescu M (2012) Controlled release of sorbic acid from bacterial cellulose based mono and multilayer antimicrobial films. *LWT Food Sci Technol* 47:400–406
- Júzová P, Martinková L, Křen V (1996) Secondary metabolites of the fungus *Monascus*: a review. *J Ind Microbiol* 16:163–170
- Kaliyaperumal A, Jing S (2009) Immunogenicity assessment of therapeutic proteins and peptides. *Curr Pharm Biotechnol* 10:352–358
- Kaplan E, Ince T, Yorulmaz E, Yener F, Harputlu E, Laçin NT (2014) Controlled delivery of ampicillin and gentamycin from cellulose hydrogels and their antibacterial efficiency. *J Biomater Tissue Eng* 4:543–549
- Khan T, Park JK, Kwon J-H (2007) Functional biopolymers produced by biochemical technology considering applications in food engineering. *Korean J Chem Eng* 24:816–826
- Khan S, Ul-Islam M, Khatat WA, Ullah MW, Park JK (2015) Bacterial cellulose-titanium dioxide nanocomposites: nanostructural characteristics, antibacterial mechanism, and biocompatibility. *Cellulose* 22:565–579
- Kilara A, Shahani KM, Shukla TP (1979) The use of immobilized enzymes in the food industry: a review. *Crit Rev Food Sci Nutr* 12:161–198
- Kirdponpattara S, Phisalaphong M (2013) Bacterial cellulose-alginate composite sponge as a yeast cell carrier for ethanol production. *Biochem Eng J* 77:103–109
- Klemm D, Schumann D, Uthardt U, Marsch S (2001) Bacterial synthesized cellulose—artificial blood vessels for microsurgery. *Prog Polym Sci* 26:1561–1603
- Klemm D, Heublein B, Fink HP, Bohn A (2005) Cellulose: fascinating biopolymer and sustainable raw material. *Angew Chem Int Ed* 44:3358–3393
- Klemm D, Schumann D, Kramer F, Heßler N, Hornung M, Schmauder H-P, Marsch S (2006) Nanocelluloses as innovative polymers in research and application. *Adv Polym Sci* 295:49–96
- Koochi MK, Hejazy M, Asadi F, Asadian P (2011) Assessment of dermal exposure and histopathologic changes of different sized nano-silver in healthy adult rabbits. *J Phys Conf Ser* 304:012028
- Korami M, Rezaayat SM, Bidgoli SA (2013) Sub-chronic dermal toxicity of silver nanoparticles in guinea pig: special emphasis to heart, bone and kidney toxicities. *Iran J Pharm Res* 12:511–519
- Koutinas AA, Sypas V, Kandyli S, Michelis A, Bekatorou A, Kourkoutas Y, Kordulis C, Lycourghiotis A, Banat IM, Nigam P, Marchant R (2012) Nano-tubular cellulose for bioprocess technology development. *PLoS ONE* 7:e34350
- Krystynowicz A, Czaja W, Wiktorowska-Jezińska A, Gonçalves-Miśkiewicz M, Turkiewicz M, Bielecki S (2002) Factors affecting the yield and properties of bacterial cellulose. *J Ind Microbiol Biotechnol* 29:189–195
- Kuehl BL, Fyfe KS, Shear NH (2003) Cutaneous cleansers. *Skin Ther Lett* 8(3):1–4
- Lee CK, Hsu KC, Cho JC, Kim YJ, Han SH (2011) Cosmetic bio-cellulose mask pack sheet and method for manufacturing same. US patent, US 20130244977 A1
- Legendre JY (2008) Assembly comprising a substrate comprising biocellulose, and a powdered cosmetic composition to be brought into contact with the substrate. US patent, US 20090041815 A1
- Levinson DJ, Glonek T (2010) Microbial cellulose contact lens. US patents, US 7832857 B2
- Li X, Wan W, Panchal CJ (2010) Transparent bacterial cellulose nanocomposite hydrogels. US patent, US 8940337 B2
- Lin K, Lin H (2004) Quality characteristics of chinese-style meatball containing bacterial cellulose (nata). *J Food Sci* 69:SNQ107–SNQ111
- Lin SP, Calvar IL, Catchmark JM, Liu JR, Demirci A, Cheng KC (2013) Biosynthesis, production and applications of bacterial cellulose. *Cellulose* 20:2191–2219
- Lin SP, Hsieh SC, Chen KI, Demirci A, Cheng KC (2014) Semi-continuous bacterial cellulose production in a rotating disk bioreactor and its materials properties analysis. *Cellulose* 21:835–844
- Lin Y-C, Wey Y-C, Lee M-L, Lin P-C (2015) Cosmetic composition containing fragments of bacterial cellulose film and method for manufacturing thereof. US patent, US 20150216784 A1
- Lin SP, Liu CT, Hsu KD, Hung YT, Shih TY, Cheng KC (2016) Production of bacterial cellulose with various additives in a PCS rotating disk bioreactor and its material property analysis. *Cellulose* 3:367–377
- Lu W, Senapati D, Wang S, Tovmachenko O, Singh AK, Yu H, Ray PC (2010) Effect of surface coating on the toxicity of silver nanomaterials on human skin keratinocytes. *Chem Phys Lett* 487:92–96
- Luan J, Wu J, Zheng Y, Song W, Wang G, Guo J, Ding X (2012) Impregnation of silver sulfadiazine into bacterial cellulose for antimicrobial and biocompatible wound dressing. *Biomed Mater* 7:065006
- Ly P, Feng Q, Wang Q, Li G, Li D, Wei Q (2016) Biosynthesis of bacterial cellulose/carboxylic multi-walled carbon nanotubes for enzymatic biofuel cell application. *Materials* 9:183
- Malik NN (2008) Drug discovery: past, present and future. *Drug Discov Today* 13:909–912
- Manning MC, Patel K, Borchardt RT (1989) Stability of protein pharmaceuticals. *Pharm Res* 6:903–918
- Manning MC, Chou DK, Murphy BM, Payne RW, Katayama DS (2010) Stability of protein pharmaceuticals: an update. *Pharm Res* 27:544–575
- Millon L, Wan W (2006) The polyvinyl alcohol–bacterial cellulose system as a new nanocomposite for biomedical applications. *J Biomed Mater Res B Appl Biomater* 79:245–253
- Montealegre CM, Dionisio ER, Sumera LV, Adolacion JR, De Leon RL (2012) A comparison between the performance of *S. cerevisiae* cells immobilized in nata de coco biocellulose and calcium alginate during continuous bioethanol production. *Int J Chem Eng Appl* 3:237–242
- Mori R, Nakai T, Enomoto K, Uchio Y, Yoshino K (2011) Increased antibiotic release from a bone cement containing bacterial cellulose. *Clin Orthop Relat Res* 469:600–606
- Müller A, Ni Z, Hessler N, Wesarg F, Müller FA, Kralisch D, Fischer D (2013) The biopolymer bacterial nanocellulose as drug delivery system: investigation of drug loading and release using the model protein albumin. *J Pharm Sci* 102:579–592
- Murphy O (2001) Non-polyol low-digestible carbohydrates: food applications and functional benefits. *Br J Nutr* 85:S47–S53
- Nagel JE, Fuscaldo JT, Fireman P (1977) Paraben allergy. *JAMA* 237:1594–1595
- Ng C-C, Shyu Y-T (2004) Development and production of cholesterol-lowering *Monascus*-nata complex. *World J Microbiol Biotechnol* 20:875–879
- Nguyen LA, He H, Pham-Huy C (2006) Chiral drugs: an overview. *Int J Biomed Sci* 2:85–100
- Nguyen DN, Ton NMN, Le VVM (2009) Optimization of *Saccharomyces cerevisiae* immobilization in bacterial cellulose by 'adsorption-incubation' method. *Int Food Res J* 16:59–64
- Nimeskern L, Avila HM, Sundberg J, Gatenholm P, Müller R, Stok KS (2013) Mechanical evaluation of bacterial nanocellulose as an implant material for ear cartilage replacement. *J Mech Behav Biomed Mater* 22:12–21
- Okiyama A, Motoki M, Yamataka S (1992) Bacterial cellulose II. Processing of the gelatinous cellulose for food materials. *Food Hydrocoll* 6:479–487
- Okiyama A, Motoki M, Yamataka S (1993) Bacterial cellulose IV. Application to processed foods. *Food Hydrocoll* 6:503–511
- Olyveira GM, Costa LMM, Basimji P (2013) Physically modified bacterial cellulose as alternative routes for transdermal drug delivery. *J Biomater Tissue Eng* 3:227–232
- Osm JF, Toca-Herrera JL, Rodríguez-Couto S (2010) Uses of laccases in the food industry. *Enzyme Res*. [948761](https://doi.org/10.4061/2010/918761)Article ID 918761
- <http://dx.doi.org/10.4061/2010/918761>
- Ougiya H, Watanabe K, Morinaga Y, Yoshinaga F (1997) Emulsion-stabilizing effect of bacterial cellulose. *Biosci Biotechnol Biochem* 61:1541–1545
- Pandey M, ~~Mohd~~ Amin MCIM, Ahmad N, Aber MR (2013) Rapid synthesis of superabsorbent smart-swelling bacterial cellulose/acrylamide-based hydrogels for drug delivery. *Int J Polym Sci*. [905471](https://doi.org/10.1155/2013/905471)Article ID 905471
- <http://dx.doi.org/10.1155/2013/905471>
- Pandey M, Mohamad N, Amin MCIM (2014) Bacterial cellulose/acrylamide ~~pH~~^{pH}-sensitive smart hydrogel: development, characterization, and toxicity studies in ICR mice model. *Mol Pharm* 11:3596–3608
- Park JK, Khan T, Jung JY (2009) Bacterial Cellulose. In: Phillips GO, Williams PA (eds) Handbook of hydrocolloids. Woodhead Publishing Ltd., Abington, pp 724–739
- Pavaloiu R-D, Stoica-Guzun A, Stroescu M, Jinga SI, Dobre T (2014a) Composite films of poly(vinyl alcohol)–chitosan–bacterial cellulose for drug controlled release. *Int J Biol Macromol* 68:117–124
- Pavaloiu R-D, Stoica A, Stroescu M, Dobre T (2014b) Controlled release of amoxicillin from bacterial cellulose membranes. *Cent Eur J Chem* 12:962–967
- Pavaloiu R-D, Stroescu M, Parvulescu O, Dobre T (2014c) Composite hydrogels of bacterial cellulose-carboxymethyl cellulose for drug release. *Rev Chim Buchar* 65:948–951
- Pavaloiu R-D, Stoica-Guzun A, Dobre T (2015) Swelling studies of composite hydrogels based on bacterial cellulose and gelatin. *UPB Sci Bull Ser B* 77:54–62

- Peng Y-S, Lin S-C, Huang S-J, Wang Y-M, Lin Y-J, Wang L-F, Chen J-S (2006) Chondroitin sulfate-based anti-inflammatory macromolecular prodrugs. *Eur J Pharm Sci* 29:60–69
- Pepas NA, Wood KM, Blanchette JO (2004) Hydrogels for oral delivery of therapeutic proteins. *Expert Opin Biol Ther* 4:881–887
- Petersen N, Gatenholm P (2011) Bacterial cellulose-based materials and medical devices: current state and perspectives. *Appl Microbiol Biotechnol* 91:1277–1286
- Phisalaphong M, Chiaooprakobkij N (2012) Applications and products—nata de coco. In: Gama M, Gatenholm P, Klemm D (eds) *Bacterial nanocellulose: a sophisticated multifunctional material*. CRC Press, Boca Raton, pp 143–156
- Pinto RJ, Daina S, Sadocco P, Pascoal Neto C, Trindade T (2013) Antibacterial activity of nanocomposites of copper and cellulose. *Biomed Res Int*. [380512](https://doi.org/10.1155/2013/280512)[Article ID 280512](https://doi.org/10.1155/2013/280512)
- Pircher N, Veigel S, Aigner N, Nedelec JM, Rosenau T, Liebhner F (2014) Reinforcement of bacterial cellulose aerogels with biocompatible polymers. *Carbohydr Polym* 111:505–513
- Prabhu BM, Ali SF, Murdock RC, Hussain SM, Srivatsan M (2010) Copper nanoparticles exert size and concentration dependent toxicity on somatosensory neurons of rat. *Nanotoxicology* 2010:150–160
- Prausnitz MR, Langer R (2008) Transdermal drug delivery. *Nat Biotechnol* 26:1261–1268
- Prausnitz MR, Mitragotri S, Langer R (2004) Current status and future potential of transdermal drug delivery. *Nat Rev Drug Discov* 3:115–124
- Purwadaria T, Ganawan L, Agustini GW (2010) The production of nata colored by *Monascus purpureus* J1 pigments as functional foods. *Microbiol Indones* 4:6–10
- Qiu K, Netravali AN (2014) A review of fabrication and applications of bacterial cellulose based nanocomposites. *Polym Rev* 54:598–626
- Radi ZA, Khan NK (2006) Effects of cyclooxygenase inhibition on the gastrointestinal tract. *Exp Toxicol Pathol* 58:163–173
- Ratner BD, Bryant SJ (2004) Biomaterials: where we have been and where we are going. *Annu Rev Biomed Eng* 6:41–75
- Ray PC, Yu H, Fu PP (2009) Toxicity and environmental risks of nanomaterials: challenges and future needs. *J Environ Sci Health A* 27:1–35
- Ross P, Mayer R, Benizman M (1991) Cellulose biosynthesis and function in bacteria. *Microbiol Rev* 55:35–58
- Rouahbia M, Asselin J, Tazi N, Messaddeq Y, Levinson D, Zhang Z (2014) Production of biocompatible and antimicrobial bacterial cellulose polymers functionalized by RGDC grafting groups and gentamicin. *ACS Appl Mater Interfaces* 6:1439–1446
- Rubinstein MP (2003) Applications of contact lens devices in the management of corneal disease. *Eye* 17:872–876
- Sanberg ME, Oldenburg SJ, Monteiro-Riviere NA (2010) Evaluation of silver nanoparticle toxicity in skin *in vivo* and keratinocytes *in vitro*. *Environ Health Perspect* 118:407–413
- Saxena IM, Brown RM Jr (2012) Biosynthesis of bacterial cellulose. In: Gama M, Gatenholm P, Klemm D (eds) *Bacterial nanocellulose: a sophisticated multifunctional material*. CRC Press, Boca Raton, pp 1–18
- Serafica G, Mornino R, Oster GA, Lentz KE, Koehler KP (2010) Microbial cellulose wound dressing for treating chronic wounds. US patent, US 7704523 B2
- Shezad O, Khan S, Khan T, Park JK (2010) Physicochemical and mechanical characterization of bacterial cellulose produced with an excellent productivity in static conditions using a simple fed-batch cultivation strategy. *Carbohydr Polym* 82:173–180
- Shi Q, Li Y, Sun J, Zhang H, Chen L, Chen B, Yang H, Wang Z (2012) The osteogenesis of bacterial cellulose scaffold loaded with bone morphogenetic protein-2. *Biomaterials* 33:6644–6649
- Shi X, Zheng Y, Zhang W, Zhang Z, Peng Y (2013) A novel drug carrier based on functional modified nanofiber cellulose and the control release behavior. In: Fourth international conference on smart materials and nanotechnology in engineering. International society for optics and photonics, Gold Coast, Australia, pp 879304–879306
- Shi X, Zheng Y, Wang G, Lin Q, Fan J (2014a) pH- and electro-response characteristics of bacterial cellulose nanofiber/sodium alginate hybrid hydrogels for dual controlled drug delivery. *RSC Adv* 4:47056–47065
- Shi Z, Zhang Y, Phillips GO, Yang G (2014b) Utilization of bacterial cellulose in food. *Food Hydrocoll* 35:539–545
- Shoichet MS (2009) Polymer scaffolds for biomaterials applications. *Macromolecules* 43:581–591
- Silva NH, Rodrigues AF, Almeida IF, Costa PC, Rosado C, Neto CP, Silvestre AJ, Freire CS (2014) Bacterial cellulose membranes as transdermal delivery systems for diclofenac: in vitro dissolution and permeation studies. *Carbohydr Polym* 106:264–269
- Siró I, Plackett D (2010) Microfibrillated cellulose and new nanocomposite materials: a review. *Cellulose* 17:459–494
- Steinemann TL, Fletcher M, Bonny AE, Harvey RA, Hamlin D, Zloty P, Besson M, Walter K, Gagnon M (2005) Over-the-counter decorative contact lenses: cosmetic or medical devices? A case series. *Eye Contact Lens* 31:194–200
- Stenstad P, Andresen M, Tanem BS, Stenius P (2008) Chemical surface modifications of microfibrillated cellulose. *Cellulose* 15:35–45
- Stephens RS, Westland JA, Neogi AN (1990) Method of using bacterial cellulose as a dietary fiber component. US patent, US 4960763 A
- Stoica-Guzun A, Stroescu M, Tache F, Zaharescu T, Grosu E (2007) Effect of electron beam irradiation on bacterial cellulose membranes used as transdermal drug delivery systems. *Nucl Instrum Methods Phys Res B* 265:434–438
- Sulavea I, Henniges U, Rosenau T, Potthast A (2015) Bacterial cellulose as a material for wound treatment: properties and modifications. A review. *Biotechnol Adv* 33:1547–1571
- Svensson A, Nicklasson E, Harnah T, Panilaitis B, Kaplan D, Britberg M, Gatenholm P (2005) Bacterial cellulose as a potential scaffold for tissue engineering of cartilage. *Biomaterials* 26:419–431
- Tam TTM, Huang NT (2014) Optimization of *Corynebacterium glutamicum* immobilization process on bacterial cellulose carrier and its application for lysine fermentation. *IOSR JEN* 4:33–38
- Tang L, Persky AM, Hochhaus G, Meibohm B (2004) Pharmacokinetic aspects of biotechnology products. *J Pharm Sci* 93:2184–2204
- Tomé LC, Brandão L, Mendes AM, Silvestre AJ, Neto CP, Gandini A, Freire CS, Marrucho IM (2010) Preparation and characterization of bacterial cellulose membranes with tailored surface and barrier properties. *Cellulose* 17:1203–1211
- Ton N, Le V (2011) Application of immobilized yeast in bacterial cellulose to the repeated batch fermentation in wine-making. *Int Food Res J* 18:983–987
- Tournilhac F, Lorient R (2003) Composition in the form of an oil-in-water emulsion containing cellulose fibrils, and its uses, especially cosmetic uses. US patent, US 6534071 B1
- Trovatti E, Freire CS, Pinto PC, Almeida IF, Costa P, Silvestre AJ, Neto CP, Rosado C (2012) Bacterial cellulose membranes applied in topical and transdermal delivery of lidocaine hydrochloride and ibuprofen: in vitro diffusion studies. *Int J Pharm* 435:83–87
- Ul-Islam M, Khan T, Khattak WA, Park JK (2013) Bacterial cellulose-MMTs nanoreinforced composite films: novel wound dressing material with antibacterial properties. *Cellulose* 20:589–596
- Vermonden T, Censi R, Hennink WE (2012) Hydrogels for protein delivery. *Chem Rev* 112:2853–2888
- Vowden K, Vowden P (2003) Understanding exudate management and the role of exudate in the healing process. *Br J Community Nurs* 8:S4–S13
- Walters RM, Mao G, Gunn ET, Hornby S (2012) Cleansing formulations that respect skin barrier integrity. *Dermatol Res Pract*. [495917](https://doi.org/10.1155/2012/495917)[Article ID 495917](https://doi.org/10.1155/2012/495917)
- Wan Y, Gao C, Han M, Liang H, Ren K, Wang Y, Luo H (2011) Preparation and characterization of bacterial cellulose/heparin hybrid nanofiber for potential vascular tissue engineering scaffolds. *Polym Adv Technol* 22:2643–2648
- Wang LP, Wang JY (2014) Skin penetration of inorganic and metallic nanoparticles. *J Shanghai Jiaotong Univ (Sci)* 19:691–697
- Wang W, Li HY, Zhang DW, Jiang J, Cui YR, Qiu S, Zhou YL, Zhang XX (2010) Fabrication of biozymatic glucose biosensor based on novel gold nanoparticles-bacteria cellulose nanofibers nanocomposite. *Electroanalysis* 22:2543–2550
- Wang T, Long X, Cheng Y, Liu Z, Yan S (2014) The potential toxicity of copper nanoparticles and copper sulphate on juvenile *Epinephelus coioides*. *Aquat Toxicol* 152:96–104
- Wanling Z, Zhe L, Zerui Z, Bihui Z, Shiyun C, Huaping W, Wen Z (2012) Preparation method for anti-virus bacteria cellulose protective. CN patent, 102321261 A
- Wei B, Yang G, Hong F (2011) Preparation and evaluation of a kind of bacterial cellulose dry films with antibacterial properties. *Carbohydr Polym* 84:533–538
- Wen X, Zheng Y, Wu J, Yue L, Wang C, Luan J, Wu Z, Wang K (2015) *In vitro* and *in vivo* investigation of bacterial cellulose dressing containing uniform silver sulfadiazine nanoparticles for burn wound healing. *Prog Nat Sci* 25:197–203
- Wonganu B, Kongruang S. (2010) Red bacterial cellulose production by fermentation of *Monascus purpureus*. In: Chemistry and chemical engineering (ICCCE), international conference, IEEE, Kyoto, Japan, pp 137–141
- Wright JM (2002) The double-edged sword of COX-2 selective NSAIDs. *CMAJ* 167:1131–1137
- Wu S-C, Lia Y-K (2008) Application of bacterial cellulose pellets in enzyme immobilization. *J Mol Catal B Enzym* 54:103–108
- Wu S-C, Lia Y-K, Ho C-Y (2013) Glucoamylase immobilization on bacterial cellulose using periodate oxidation method. *IJSE* 3:1–4
- Yadav V, Panilaitis BJ, Shi H, Lee K, Cebe P, Kaplan DL (2010) Novel *in vitro*-degradable cellulose-chitin copolymer from metabolically engineered *Gluconacetobacter xylinus*. *Appl Environ Microbiol* 76:6257–6265
- Yang M (2015) Stress and protein instability during formulation and fill/finish processes. *BioPharm Int* 28:46–49
- Yano H, Sugiyama J, Nakagaito AN, Nogi M, Matsuura T, Hikita M, Handa K (2005) Optically transparent composites reinforced with networks of bacterial nanofibers. *Adv Mater* 17:153–155
- Yoshino A, Tabuchi M, Uo M, Tatsumi H, Hideshima K, Kondo S, Sekine J (2013) Applicability of bacterial cellulose as an alternative to paper points in endodontic treatment. *Acta Biomater* 9:6116–6122
- Zhang T, Wang W, Zhang D, Zhang X, Ma Y, Zhou Y, Qi L (2010) Bioteplated synthesis of gold nanoparticle-bacteria cellulose nanofiber nanocomposites and their application in biosensing. *Adv Funct Mater* 20:1152–1160
- Zhong CY (2008) Bacterial cellulose gel face mask. CN patent, 200610075040.8
- Zimmermann KA, LeBlanc JM, Sheets KT, Fox RW, Gatenholm P (2011) Biomimetic design of a bacterial cellulose/hydroxyapatite nanocomposite for bone healing applications. *Mater Sci Eng C* 31:43–49