

# Modifications of bacterial cellulose in wound care

## Modyfikacje bakteryjnej celulozy do stosowania w opatrywaniu ran

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### Abstract

Wound infection may occur in acute and chronic wounds, wounds resulting from surgery or traffic accidents, and burns. Regardless of the extent and cause of the wound, prompt treatment is essential in reducing the patient's pain and limiting the spread of contamination. Improper wound care and associated chronic diseases may hinder the therapeutic success. Bacterial cellulose (BC) is highly biocompatible and has no cytotoxic effect on cells engaged in wound healing, such as fibroblasts and keratinocytes. Its high hydration level guarantees the maintenance of a moist wound environment. High mechanical strength, flexibility and resistance to damage make BC a promising material for dressings. Unfortunately, it does not display an inhibitory effect on bacterial growth. Introducing antimicrobial agents into the structure of BC has been a subject of many studies. This paper aims to present the latest reports on the possibility of the absorption of bacteriostatic and bactericidal agents in BC, such as metal particles, essential oils, antibiotics, antiseptics, and wound irrigation solutions. Moreover, the modifications in BC culture and post-production treatments in order to improve its physical properties are discussed.

**Key words:** wound infection, wound, antiseptics, cellulose, biological dressings

### Streszczenie

Infekcja może rozwijać się w ranach ostrych, przewlekłych, powstałych na skutek operacji, wypadków komunikacyjnych czy oparzeń. Niezależnie od rozległości ran i przyczyn ich powstania konieczne jest szybkie zastosowanie odpowiedniego leczenia, celem zmniejszenia doznań bólowych pacjenta oraz ograniczenia rozprzestrzeniania się infekcji. Choroby towarzyszące oraz niewłaściwa pielęgnacja ran mogą przyczyniać się do opóźnienia sukcesu terapeutycznego. Celuloza bakteryjna charakteryzuje się dużą biogodnością oraz nie wykazuje działania cytotoksycznego względem komórek odpowiedzialnych za proces gojenia, takich jak fibroblasty i keratynocyty. Jej wysokie uwodnienie zapewnia utrzymanie wilgotnego środowiska rany. Wytrzymałość mechaniczna, elastyczność i odporność na uszkodzenia to cechy, dzięki którym celuloza bakteryjna rozważana jest jako potencjalny materiał do produkcji opatrunków. Niestety, bakteryjna celuloza nie wykazuje działania hamującego wzrost bakterii. Trwają badania nad możliwością wprowadzenia środków przeciwdrobnoustrojowych do struktury bakteryjnej celulozy. Celem pracy jest omówienie najnowszych doniesień dotyczących możliwości absorpcji środków bakteriostatycznych i bakteriobójczych w bakteryjnej celulozie, takich jak cząsteczki metali, olejki eteryczne, antybiotyki, antyseptyki oraz środki do przemywania ran. W niniejszej pracy omówiono również modyfikacje warunków hodowli bakteryjnej celulozy oraz zabiegi poprodukcyjne mające na celu ulepszenie właściwości fizycznych celulozy bakteryjnej.

**Słowa kluczowe:** zakażenia ran, rany, antyseptyka, celuloza, opatrunek biologiczny

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## Introduction

The skin functions as a protective barrier against pathogens, physical injury, ultraviolet radiation, and chemicals. It also regulates the body temperature and prevents excessive water loss and desiccation. Disruption of skin integrity, caused by burns, trauma, diabetes, and venous or pressure ulcers, leads to the impairment of its essential functions and can result in hard-to-heal wounds. The risk of developing chronic wounds increases in people with diabetes and obesity, as well as in elderly patients. Severe tissue damage with an infectious process is often difficult to control. It may result in an amputation or a life-threatening injury.<sup>1</sup> The treatment is a long, multistep process, involving wound and periwound skin cleansing, debridement, wound edges refashioning, treatment, and dressing.<sup>2</sup> However, although traditional dressings protect wounds from contamination and mechanical damage, they do not promote wound healing. In addition, dressing changes are often accompanied by damage of the regenerated wound surface and are associated with patient's pain.<sup>3</sup> Ideally, a wound dressing should maintain moisture, absorb exudate, reduce pain, and be non-adherent, airy, sterile and antimicrobial.<sup>3</sup> Recently, researchers have been focused on the properties and application of bacterial cellulose (BC). This biopolymer is applied in many industries, also in the medical field, and is considered to be one of the most promising wound dressing materials.<sup>4</sup>

The aim of this review was to discuss research focused on the physical properties of BC and the possibilities of its application in wound infection treatment.

## Properties of bacterial cellulose

Bacterial cellulose is produced by various bacterial species, such as *Rhizobium*, *Acetobacter*, *Sarcina*, *Pseudomonas*, and *Escherichia*.<sup>5</sup> Among them, *Acetobacter xylinus* spp., also named *Gluconacetobacter xylinus* spp. or *Komagataeibacter xylinus* spp., produces the most massive cellulose ribbon and is ubiquitous in BC production.<sup>6</sup> Presumably, cellulose provides an extra bacterial matrix, expanding the colonization and offering the advantage in the nutrient competition. Furthermore, researchers postulate that cellulose protects bacteria from unfavorable environmental conditions. For instance, BC forming on the liquid-gas interface provides a constant access to the aerobic conditions.<sup>7</sup>

Bacterial cellulose microfibrils are formed by  $\beta$ -1,4-glucan chains resulting from the polymerization of uridine diphosphate glucose. Consequently, these microfibrils aggregate into a fiber with a diameter from 10 nm to 100 nm and create a three-dimensional (3D) network with numerous pores due to hydrogen bonds.<sup>8</sup> Although the molecular formula  $(C_6H_{10}O_5)_n$  is the same for bacterial and plant cellulose, their physical and chemical features differ significantly. Contrary to plant cellulose, the BC

microfibrils are 100 times thicker and form a reticular structure. Plant cellulose contains lignin, pectin and hemicellulose, while BC is free of such impurities.<sup>5</sup> Due to its unique structure, it possesses high mechanical strength. Among its prominent features are 80–90% crystallinity, which, together with a high degree of polymerization (even up to 16,000 DPw), determines increased thermal stability and lower susceptibility to degradation.<sup>9</sup> Bacterial cellulose displays good flexibility, permeability, hygroscopicity, and hydrophilicity.<sup>8</sup> It is noteworthy that BC does not affect viability of fibroblasts and keratinocytes.<sup>10</sup>

There are 3 commonly applied BC production methods: static, agitation and bioreactor culture. In a static culture, BC film is produced on the gas-liquid interface in a span of 7–10 days and takes the shape of a flat gelatinous membrane. As a result of shaking, sphere-like or irregular cellulose shapes are formed. Agitation is intended to increase oxygen transport in the medium. However, according to the reports, shaking does not influence cellulose productivity.<sup>11</sup> Moreover, physical properties of cellulose, such as crystallinity or the degree of polymerization obtained by the agitation method differ from the properties of BC obtained in a static culture.<sup>12</sup> The bioreactor culture is applied in industrial bioreactors in order to reduce cultivation time and increase BC productivity. Bioreactors can be modified to provide various culture conditions such as oxygen-enriched air or rotating disks.<sup>13</sup> Regardless of the method, after harvesting, BC is purified in sodium hydroxide from bacterial cell debris and substances in the culture medium, and washed with water to obtain a neutral pH.<sup>12</sup> Interestingly, it was reported that the properties of BC produced in a commercial Hestrin–Schramm (HS) medium are comparable to those of BC cultured in different media. Therefore, obtaining BC can be inexpensive and eco-friendly.<sup>14</sup>

## Bacterial cellulose as an antibacterial dressing

Wound healing is a physiological process whose timing depends on the area and location of the injury. Unfortunately, therapeutic success may be delayed by several factors such as wound infection or an allergic reaction to the dressing.<sup>15,16</sup> Wound infection may be caused by Gram-positive and Gram-negative bacteria or fungi, including multidrug-resistant strains. Therefore, the selection of an appropriate dressing is crucial to patient safety.<sup>15</sup> Bacterial cellulose exhibits high biocompatibility and low cytotoxic effect, and does not induce allergic reactions.<sup>17</sup> These properties promote the healing process and tissue regeneration.<sup>18</sup> However, BC does not display antimicrobial properties. In order to impart antimicrobial properties to BC, the researchers decided to take advantage of its absorbance and release potential and incorporate antimicrobial substances into the cellulose.<sup>19</sup>

## Metals

Antibacterial activity of silver nanoparticles has been determined against Gram-positive and Gram-negative bacteria, but their mechanism of action is not well understood. It is speculated that silver ions inhibit bacterial growth by destroying the cell wall and repressing DNA transcription.<sup>20</sup> Jalili Tabaii and Emtiazi prepared a cellulose carrier with silver nanoparticles by soaking BC in an AgNO<sub>3</sub> solution. They reported that BC enriched with silver nanoparticles demonstrated an even 100% higher antimicrobial effect against *Staphylococcus aureus* spp. and *Escherichia coli* spp.<sup>21</sup> It was also reported that copper ions cause cell membrane damage and DNA impairment.<sup>22</sup> Copper nanoparticles incorporated into BC displayed long-term bactericidal efficacy against *S. aureus* spp. and *E. coli* spp., for up to 90 days.<sup>23</sup> Also, the antibacterial activity of BC chemisorbed with copper nanoparticles against *Bacillus subtilis* spp. and *Candida albicans* spp. was reported.<sup>24</sup> It is worth noting that BC chemisorbed with copper nanoparticles did not exhibit cytotoxicity to fibroblasts.<sup>23</sup> Additionally, BC chemisorbed with zinc oxide displayed antibacterial activity against *S. aureus* spp., *Pseudomonas aeruginosa* spp., and *E. coli* spp.<sup>25</sup> Its antimicrobial mechanism of action relies on bacterial cell disruption, cell membrane hydrophobicity change and genes downregulation. Moreover, zinc oxide generates reactive oxygen species (ROS) that induce oxidative stress, leading to damage of the cell components.<sup>26</sup> Additionally, zinc oxide incorporated in BC promotes wound healing and tissue regeneration.<sup>25</sup>

## Essential oils

Recently, the antimicrobial action of essential oils (EOs) has been of interest to some researchers.<sup>27</sup> Dudek-Wicher et al. studied the antibiofilm efficacy of 3 essential oils: tea tree, geranium and frankincense essential oils, incorporated in BC against Gram-positive (*S. aureus* spp., *Enterococcus faecalis* spp.) and Gram-negative (*Klebsiella pneumoniae* spp., *P. aeruginosa* spp., *E. coli* spp.) strains and 1 fungal strain (*C. albicans* spp.). All tested EOs exhibited antibiofilm efficacy against the tested strains, with efficacy of nearly 80–100%, exhibited by tea tree and geranium essential oils.<sup>27</sup> Unlike antiseptics or antibiotics, the volatile property of EOs allows them to reach the areas neighboring the areas of application. Bacterial cellulose enriched with thymol, a component of an essential oil, was successfully applied on a third-degree burn wound closure. Bacterial cellulose chemisorbed with thymol exhibited low cytotoxicity on fibroblasts and increased cell viability.<sup>28</sup> Junka et al. tested 3 essential oils, namely clove, eucalyptus and thyme, against *S. aureus* spp. and *P. aeruginosa* spp.<sup>10</sup> All essential oils were successfully impregnated and effectively released from BC discs. Two different methods were applied to assess their antimicrobial activity. In the disk

diffusion method, all tested EOs demonstrated very high efficacy. The 2<sup>nd</sup> method (Antibiofilm Dressings Activity Measurement (ADAM)), considered the penetrability index of the tested EOs. This method has demonstrated significant differences in EO activity. Minor bactericidal activity was observed for clove oil, while thyme and eucalyptus oils displayed a significantly higher activity. However, thyme and clove oils displayed a significantly higher cytotoxicity against fibroblasts than the eucalyptus oil.

## Antibiotics

The antibiotics most commonly applied in wound treatment are ceftriaxone, gentamycin, vancomycin, ciprofloxacin and tetracycline. Topical application of antibiotics in compresses previously immersed in an antibiotic solution is not recommended for wound infection treatment.<sup>29</sup> The reasons are the difficulties in determining the drug concentration and the uncontrolled rate of drug release to the infected skin, which may increase the percentage of resistant strains. Antibiotic incorporation in BC makes it possible to determine the amount of the drug bound and to control the drug release rate from the membrane.<sup>30</sup>

Lazarini et al. compared the release time of ceftriaxone from BC produced in media with different sugar compositions. Bacterial cellulose produced in the medium supplemented with sugarcane molasses displayed a higher fiber density.<sup>31</sup> Hence, the release time of ceftriaxone from chemisorbed BC was prolonged by 5 h, as compared to BC cultured in a standard HS medium.<sup>31</sup> Junka et al. successfully impregnated BC with gentamycin. The antibiotic concentration was 2 g/L, corresponding to the commercially available collagen gentamycin sponge.<sup>32</sup> The release rate of gentamycin from BC was lower than from the collagen sponge. Even after 48 h of incubation, a small amount of gentamycin was released from BC. In contrast, 90% of gentamycin was released up to 8 h during the experiment from the collagen sponge.<sup>32</sup> Bacterial cellulose dressings, chemisorbed with gentamycin in 2 concentrations of 2 g/L and 0.006 g/L, were administered on rat bones. Despite their uneven and porous surface, BC chemisorbed with gentamycin effectively inhibited the growth of *S. aureus* spp., restraining the bacterial biofilm development.<sup>32</sup> Furthermore, vancomycin and ciprofloxacin are widely applied in wound infection treatment. It was reported that BC dressings impregnated with these antibiotics effectively impede infection development.<sup>33</sup> A high bactericidal effect of vancomycin and ciprofloxacin was determined against *S. aureus* spp. and *K. pneumoniae* spp. strains. Nevertheless, a significant amount of the antibiotics was released from BC in the 1<sup>st</sup> hour of the experiment. The above may lead to low usefulness of vancomycin and ciprofloxacin in BC in long-term wound treatment.<sup>33</sup> However, Cacicedo et al. slowed the release rate of ciprofloxacin from BC by incorporating chitosan (Chi) into the cellulose structure.

Bacterial cellulose/Chi modification prolonged the release time by more than 6 h and exhibited antimicrobial activity against *S. aureus* spp. and *P. aeruginosa* spp. Adding ciprofloxacin to the hybrid significantly enhanced the bactericidal effect.<sup>34</sup> Shao et al. incorporated different tetracycline hydrochloride concentrations into BC.<sup>30</sup> The lowest concentration of tetracycline hydrochloride in BC (0.41 mg/dm<sup>2</sup>) was sufficient to restrain the growth of *S. aureus* spp., *E. coli* spp. and *B. subtilis* spp. However, the inhibition zone of *C. albicans* spp. was detectable only in the highest tested concentration (10.17 mg/dm<sup>2</sup>). The fast release stage of tetracycline was up to 1 h after the beginning of the experiment. Interestingly, the percentage of the antibiotics released from the cellulose was increased in the BC/tetracycline hydrochloride with higher concentrations of the incorporated antibiotic. Additionally, free tetracycline was released slower than when incorporated in BC, which suggests the BC usefulness for controlled drug dosage.<sup>30</sup>

## Antiseptics and wound irrigation solutions

In recent years, antiseptics have attracted considerable attention in wound care. The most commonly used wound healing agents include polyhexamethylene biguanide hydrochloride (PHMB), octenidine dihydrochloride (OCT), iodine povidone (PVP-I), and chlorhexidine gluconate (CHX).<sup>35,36</sup> Their broad spectrum of action includes both Gram-positive and Gram-negative bacteria in vegetative and spore forms, as well as fungi, viruses and multi-drug resistant strains. Most antiseptics are characterized by a high ability to eradicate the biofilm. Additionally, resistance mechanisms to these antimicrobials are not recorded.<sup>35</sup>

Dydak et al. presented the results of antimicrobial activity for all of the abovementioned antiseptics in the biocellulose disk diffusion method against Gram-positive (*S. aureus* spp., *Staphylococcus epidermidis* spp., *Enterococcus faecium* spp.), Gram-negative (*K. pneumoniae* spp., *E. coli* spp., *Acinetobacter baumannii* spp., *P. aeruginosa* spp., *Enterobacter cloacae* spp.) and fungal strains (*C. albicans* spp.). The most significant inhibition zones were found for PVP-I and CHX, followed by PHMB and OCT, against all tested bacteria. Also, the largest zone of inhibition of fungal strain growth was determined for PVP-I. Moreover, the high antifungal efficiency was shown for CHX and PHMB, whose inhibition zones were comparable.<sup>37</sup> Wiegand et al. reported that PHMB incorporated in BC exhibited a higher bactericidal activity against *S. aureus* spp. than PVP-I in BC. However, better biocompatibility in human keratinocytes was obtained for BC/PVP-I than for BC/PHMB.<sup>38</sup> The BC/OCT displays a similar antimicrobial activity against *S. aureus* spp. and *P. aeruginosa* spp. Its high growth inhibitory efficacy was assessed using the disk diffusion method, in which the inhibition zones were 22–23 mm and 20–22 mm,

respectively.<sup>39</sup> Also, Inoue et al. reported high inhibitory activity of BC/CHX against *S. aureus* spp., *E. coli* spp. and *C. albicans* spp., using the disk diffusion method.<sup>40</sup> Super-oxidized hypochlorite solutions are considered wound irrigation solutions. However, there are reports of their very low efficacy in growth inhibition and biofilm eradication.<sup>41,42</sup> The lack of antimicrobial efficacy of hydrochloride solutions has been demonstrated in microtiter plate studies and chemisorbed BC.<sup>37,41–43</sup> A wound irrigation product containing 0.004% of sodium hypochlorite and 0.004% of hypochlorite acid was evaluated in the research on the antimicrobial efficacy of antiseptics.<sup>37</sup> No growth inhibition was detected with the disk diffusion method for most of the strains of the tested species of *S. aureus* spp., *S. epidermidis* spp., *Enterococcus faecium* spp., *K. pneumoniae* spp., *E. coli* spp., *P. aeruginosa* spp., *E. cloacae* spp., *A. baumannii* spp., and *C. albicans* spp.

The antimicrobial efficacy of antiseptics increases with prolonged real-contact time.<sup>44</sup> The incorporation of antiseptics in BC makes it possible to extend the contact time of microorganisms exposed to antimicrobial agents. The insertion and release time depend on the molecular mass of the compound.<sup>38</sup> As the molecular mass of the compound increases, the time of its release from the cellulose also increases. The PVP-I release from BC was slightly delayed compared to PHMB, due to higher molecular mass of PVP-I. For both compounds, rapid release rate lasted up to 8 h. Furthermore, release with a slower rate continued up to 24 h for PHMB and 48 h for PVP-I.<sup>38</sup> The time of rapid release of octenidine was equal in the case for PHMB and PVP-I, the release with a slower rate continued even up to 96 h.<sup>45</sup> Moreover, 2 release stages of chlorhexidine from BC were observed by Inoue et al. The stage of rapid release took 15 min from the beginning of the experiment. After this time, the release rate slowed down and remained constant for 48 h.<sup>40</sup> The rapid release stage of 15 min was observed for PHMB and PVP-I by Krasowski et al.<sup>19</sup> Octenidine incorporated in BC maintains its activity for an extended period. The BC/OCT stored for over 6 months presented similar features (low cytotoxicity and high antimicrobial activity) as a freshly prepared dressing.<sup>45</sup> Alkhatib et al. supplemented BC with poloxamer to prolong OCT release time from BC. Poloxamer is a nonionic triblock copolymer which, when incorporated in BC, does not affect the bactericidal efficacy of BC/OCT. Moreover, BC/poloxamer is highly biocompatible. The incorporation of poloxamer into BC enables extending the release time of OCT up to 8 h which can be employed for long-term treatment of chronic wounds.<sup>39</sup>

Additionally, incorporating antimicrobial substances into BC may influence the material structure, thus improving its physical properties. Adding PVP-I caused structural changes of BC, which led to an increased comprehensive strength when compared to native BC. In contrast, adding PHMB and OCT did not cause any changes in the cellulose structure.<sup>38,45</sup>



**Table 1.** Effect of natural and synthetic polymers on selected physical properties of bacterial cellulose

Parameter	Modification	Value without modification	Value with modification	Reference
Temperature of thermal degradation	bacterial cellulose/chitosan	263°C	366°C	51
	bacterial cellulose/collagen	262°C	352°C	53
	bacterial cellulose/polyacrylonitrile	296°C	560°C	58
	bacterial cellulose/poly(ethylene glycol)	263°C	293°C	59
Young's modulus	bacterial cellulose/chitosan	6.0 GPa	1.8 GPa	51
	bacterial cellulose/collagen	4.5 GPa	9.5 GPa	53
	bacterial cellulose/poly(ethylene glycol)	6.35 GPa	4.12 GPa	59

## Modifications of physical properties of bacterial cellulose in order to improve dressing design

Bacterial cellulose exhibits excellent absorption properties. It consists of 99.9% water, which fills the pores formed by the nanofibrils structure. The pore size varies, depending on the cellulose culture time. As the culture time extends, the pore volume in the cellulose decreases, and thus, the surface area of the membrane is reduced.<sup>46</sup> Pore-forming agents added to the culture, such as agarose microparticles, can improve water holding capacity of BC.<sup>47</sup> Increased carrying capacity of BC and constant release of antibiotics from BC can also be obtained by changes in the culture medium carbon source.<sup>31</sup> Also, laser piercing can be applied to enhance the amount of water trapping sites.<sup>48</sup> The absorption ability of BC may involve exudate assimilation from the wound environment.

Bacterial cellulose can be functionalized with different natural and synthetic polymers to improve some of its mechanical properties. Chitosan is a biopolymer that adversely affects bacterial viability.<sup>49</sup> Its mechanism of action relies on bonding to teichoic acids in the Gram-positive bacteria cell wall or disrupting the nutrients intake in Gram-negative strains.<sup>50</sup> Cai et al. reported that BC supplemented with chitosan (BC/Chi) showed enhanced thermal stability (temperature of thermal degradation increased from 263°C to 366°C) and lower tensile strength (Young's modulus decreased from 6.0 GPa to 1.8 GPa).<sup>51</sup> One of the best-known natural polymers is collagen, whose drawbacks are high cost, poor mechanical properties and no antimicrobial effect. However, collagen is highly biodegradable and its surface offers excellent cell-binding properties. Therefore, collagen is studied as a scaffold for BC.<sup>52</sup> Zhijiang and Guang reported that combining BC with collagen (BC/Col) increased thermal stability (temperature of thermal degradation changed from 262°C to 352°C) and tensile strength (Young's modulus increased from 4.5 GPa to 9.5 GPa), and decreased crystallinity (from 87% to 75%). The BC/Col scaffolds

enabled fibroblasts to adhere and proliferate, contrary to native BC, on which fibroblasts did not show enhanced growth after being adhered to the surface.<sup>53</sup> Pasaribu et al. proposed a BC wound dressing functionalized with collagen and Chi in different configurations.<sup>54</sup> The BC/Col/Chi and BC/Chi/Col demonstrated similar moisture and antibacterial activity. However, BC/Chi/Col had smaller pores and displayed lower thermal stability than BC/Col/Chi (the temperatures of maximum mass-loss were 329°C and 338°C, respectively). According to the report, a higher chitosan-to-collagen ratio in the dressing provides a better potential for wound dressing. Gelatine, a collagen denaturation product, is an alternative to collagen as a BC matrix. The BC/gelatine shows good adhesiveness and biocompatibility, promotes cell adhesion and is inexpensive.

Poly(acrylic acid), which inhibits bacterial growth, is among the synthetic polymers considered for incorporation into BC for wound dressing.<sup>55,56</sup> Mohamad et al., who investigated burn wounds, reported significantly higher wound reduction in the group where BC with acrylic acid were enriched with fibroblasts and keratinocytes than in the control group including BC with acrylic acid only. Additionally, more significant collagen deposition was noted for BC loaded with cells, as compared with other treatments.<sup>57</sup> Another example of synthetic polymer incorporated in BC is polyacrylonitrile. Xiao et al. reported that BC/polyacrylonitrile in 25:75 ratio displays higher thermal stability (temperature at weight losses of 50% increased from 296°C to 560°C). Also, comparing dynamic contact angles, the BC/polyacrylonitrile composite has shown a high hygroscopicity property, playing a decisive role in exudate absorption.<sup>58</sup> The BC/poly(ethylene glycol) composite was characterized by better adhesion and proliferation of fibroblast than pure BC. In addition, this polymer improved the thermal stability of BC (from 263°C to 293°C), while tensile strength tended to decrease (Young's modulus decreased from 6.35 GPa to 4.12 GPa).<sup>59</sup>

The effects of natural and synthetic polymers on selected physical properties of bacterial cellulose are presented in Table 1.

## Other biomedical applications

The research on the use of BC does not finish with the development of skin wound dressings. The usefulness of BC has been studied by scientists from various fields of medicine. Its high flexibility, persistence and good biocompatibility allow BC to conform to uneven surfaces and treat infections in hard-to-reach areas. There are reports of potential use of BC in dental therapies, treatment of inflammatory lesions, or after dental procedures, like extraction, root canal treatment or mucosal transplantation.<sup>19,60,61</sup> Depending on the application, BC can be made stable or degradable, allowing it to be placed in the body permanently or temporarily.<sup>62</sup> Some studies were carried out on the application of BC in bone engineering and cartilage implants.<sup>63,64</sup> Due to the excellent biocompatibility and slow degradation, BC is considered a composite bone repair material.<sup>63</sup> Moreover, BC coated with hydroxyapatite displays enhanced mechanical properties.<sup>63</sup> It is excellently moldable, so that it can be applied in soft tissue reconstructions. It has frequently been reported that BC has potential to become a material for artificial blood vessels, for instance in replacement of atherosclerotic coronaries.<sup>64</sup> Innovatively, Binnetoglu et al. applied BC tubes in facial nerve repairment, which allowed for robust myelinated fibers regeneration.<sup>65</sup> An intriguing adaptation of BC was applied in eye therapeutics. Bacterial cellulose with convex shape can be used as contact lenses. Additionally, BC loaded with drugs may be applied in eyeball infections.<sup>66</sup>

## Conclusions

Bacterial cellulose displays high absorption capacity, which makes it suitable for the incorporation of many antimicrobial substances, both hydrophilic and hydrophobic. Small molecules, such as metal ions, as well as high-molecular compounds with bactericidal activity, are being tested. Numerous studies have shown that antibiotics and antiseptics applied in wound infection treatment display high antimicrobial effect within release time from BC. Moreover, BC seems to be a proper carrier for essential oils that consist of antibacterial compounds and which may be used in wound care. Additionally, its physical properties such as crystallinity, thermal stability and tensile strength can be easily modified by specific changes implemented in a culture method or incorporation of natural or synthetic polymers. The aforementioned advantages of BC make it a promising material for wound dressing development.

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