

Cellulose-based Antimicrobial Composites and Applications: A Brief Review

Bo Sun^{1,2}, Fangong Kong³, Min Zhang², Weijun Wang²,
Birat Singh KC¹, Jimi Tjong¹, Mohini Sain^{1,*}

1. *Center for Biocomposites and Biomaterials Processing, Department of Mechanical and Industrial Engineering, University of Toronto, Toronto ON, M5S 3B3, Canada*

2. *Key Laboratory of Food Nutrition and Safety (Tianjin University of Science and Technology), Ministry of Education, Tianjin, 300457, China*

3. *Key Laboratory of Pulp & Paper Science and Technology of Shandong Province, Ministry of Education, Qilu University of Technology (Shandong Academy of Sciences), Ji'nan, Shandong Province, 250353, China*

Abstract: Cellulose-based antimicrobial composites, typically in the form of functional films and cloth, have received much attention in various applications, such as food, medical and textile industries. Cellulose is a natural polymer, and is highly biodegradable, green, and sustainable. Imparting antimicrobial properties to cellulose, will significantly enhance its applications so that its commercial value can be boosted. In this review paper, the use of cellulose for antimicrobial composites' preparation was discussed. Two different approaches: surface loading/coating and interior embedding, were focused. Three most widely-applied sectors: food, medical and textile industries, were highlighted. Nanocellulose, as a leading-edge cellulose material, its unique application on the antimicrobial composites, was particularly discussed.

Keywords: antimicrobial; cellulose-based; composites; nanocellulose

1 Introduction

Cellulose is the most abundant natural polymer in nature. Cellulose material and its derivatives have been used in a wide range of applications such as papermaking, textile industry, as well as in food and pharmaceutical fields^[1-2]. However, this polysaccharide-based material is prone to be biologically attacked by microbials upon storage or processing^[3]. Microbial growth on the cellulose substrates results in an unpleasant odour for the paper industry, and might initiate skin irritation as used



Bo Sun, PhD;
E-mail: sunbo.sun@utoronto.ca



*Corresponding author:
Mohini Sain, professor; research
interest: polymer compounding;
E-mail: m.sain@utoronto.ca

for textile fabrication. Some bio-chemical reactions on the cellulose chains would potentially cause toxicity or infection, especially when the product is used in food or pharmaceutical areas^[4-5].

One of the solutions for eliminating the aforementioned detrimental effects is modifying cellulose via the use of antimicrobial agents^[6]. The most commonly applied approaches in literature can be classified into surface modifications (e.g., loading or coating) and interior embedding. This paper aims to present different strategies of antimicrobial modification of cellulose material for the preparation of functional composites, and overview their various applications in the research and industrial communities. In particular, nanocellulose and its applications for the newly commercialized product, will be reviewed.

2 Classification of antimicrobial agents

The selection of antimicrobial agents has to account for their reaction mechanism, antimicrobial activities, cost and side effects^[7-8]. The most commonly-used antimicrobial agents for combining with cellulose materials can be classified into non-biobased and biobased agents. Of which, non-biobased agents include inorganic silver nanoparticles, povidone-iodine and polyhexamethylene biguanide^[9]. While chitosan and polyphenols, which are extracted from animals or plants, can be considered as typical biobased antimicrobial agents.

2.1 Non-biobased antimicrobial agents

Metals and their oxides, as classical non-biobased materials, are considered as promising antimicrobial agents because of their unique sterilization activities towards wide variety of microorganisms^[10]. Currently available inorganic metals include Ag, Au, Cu and Pt, and metal oxides of Ag₂O, TiO₂, SiO₂, CuO, ZnO, CaO, MgO and Fe₂O₃^[11]. They are usually present in the form of nanoparticles for antimicrobial purpose. Among these metal particles, silver and its oxides are given top consideration, due to their excellent antimicrobial activity against various bacterial strains. Silver nanoparticles can disrupt the unicellular membrane

of microbes to eliminate their instinct enzymatic activities. Different approaches have been adopted for the fabrication of silver nanoparticles, based on their end use. Moreover, silver-based composites have been rapidly developed in the last decade, such as *in-situ* assembly of silver-based metal organic framework (Ag-MOFs) for the preparation of surface functionalization membrane^[12], as well as the specialty membranes coated by polydopamine and immobilized with silver nanoparticles^[13]. Currently, solid active particles and semi-solid products, such as silver nitrate ointment and silver sulphadiazine cream are reachable in the market for packaging and wound treatment^[14].

Recently, certain efforts have also been focused on the synthesis of silver nanoparticles by using phytochemicals from plant materials as natural reducing and capping agents. The bioextracts from leaves or flowers contain various chemicals, such as phenolic acids, flavonoids, carbohydrates and amino acids. As substitutes for toxic chemicals, these bioextracts can therefore exhibit multiple functionalities for the fabrication of silver nanoparticles^[15]. Fig.1 depicts the use of various plant materials for eco-friendly synthesis of silver nanoparticles and their antimicrobial properties^[16].

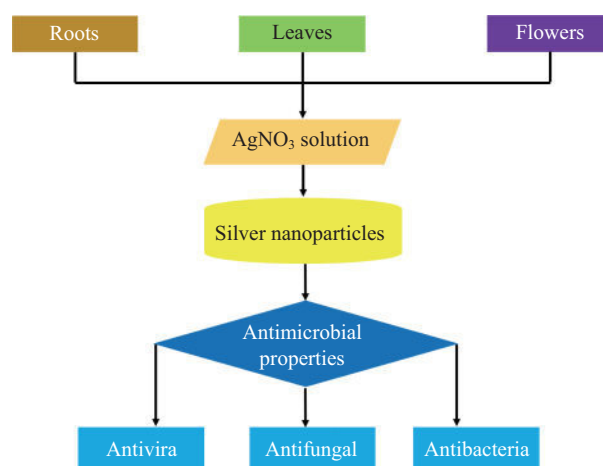


Fig.1 Various plant materials for eco-friendly synthesis of silver nanoparticles and their antimicrobial properties

In the presence of natural phytochemicals, nanosized silver particles (size of less than 50 nm) can be produced by the direct reduction of Ag⁺

ions. Three steps are generally involved during the phytochemical-mediated synthesis process: (1) solvent-extraction of phytochemicals, (2) the use of plant extracts for reaction, and (3) nucleation and growth of silver nanoparticles^[17]. Table 1 lists examples of phytochemicals which were used for the fabrication of silver nanoparticles, as well as their morphology and antimicrobials properties.

Besides the aforesaid metal nanoparticles, certain topical antimicrobials such as neosporin, mupirocin and tetracycline can also be used as non-biobased agents for antimicrobial purpose^[18].

2.2 Biobased antimicrobial agents

In recent years, natural resource based antimicrobial agents have attracted considerable attention due to the increasing concerns of environmental pollution and infectious diseases control^[19]. A large group of low molecular weight compounds have been isolated from animals or plants, such as phenolics, terpenes, bacteriocins, peptides, fatty acids (lipids), organic acids as well as their compounds. These active ingredients can be modified, or directly used as bio-based antimicrobials^[20]. Among them, peptides and

synthetic mimics of peptides have been recognized as promising candidates for the new generation of antimicrobial agents with enhanced specific activity against a variety of pathogens. This class of compounds includes peptides whose action mechanism involve interaction with microbial membranes to disrupt its structural stability, called antimicrobial peptides^[21], and proteins or enzymes that degrade the components of biofilms^[22], called biofilm-dispersing proteins or matrix-disruptive enzymes. Moreover, the antimicrobial mode of peptides can also exert immunomodulatory effects which lead to the microbial clearance via triggering of host immune response^[23]. It was reported that wound-dressings made from cotton cellulose loading with antimicrobial peptides exerted a significant reduction of *Staphylococcus aureus* and *Klebsiella pneumonia*. These cellulose-based wound-dressings were proven with no cytotoxicity to human dermal fibroblasts^[24]. In addition to the aforementioned advantages, certain challenges also exist as to apply these antimicrobial peptides for industrial use, such as high manufacturing cost, unwanted side effects and adaptive antimicrobial resistance^[25].

Chitosan, another category of antimicrobial,

Table 1 Morphology and antimicrobial properties of silver nanoparticles using phytochemicals as reagents

Phytochemical or plant extract	Silver nanoparticle size/nm	Antimicrobial activity	Inhibition concentration /($\mu\text{g}\cdot\text{mL}^{-1}$)
<i>Potentilla fulgens</i>	10~15	Cancer cell lines MCF-7 and U-87 cells	0.2~12
Tree oyster mushroom <i>Pleurotus ostreatus</i>	<40	<i>B. cereus</i> , <i>B. subtilis</i> , <i>S. aureus</i> , <i>P. aeruginosa</i> and <i>E. coli</i>	13~27
<i>Nigella arvensis</i> leaf extract	5~100	H1229 and MCF-7 cancer cell lines	10
Chinese herbal <i>Cornus officinalis</i>	11.7	Human gastric carcinoma, human prostate cancer and human liver cancer cells	25.54 and 21.46
Pod extract of <i>Cola nitida</i>	12~80	<i>P. aeruginosa</i> , <i>K. granulomatis</i> , <i>E. coli</i> , <i>S. aureus</i> , <i>A. flavus</i> , <i>Aspergillus niger</i> and <i>A. fumigatus</i>	50 and 150
Seed extracts of <i>Diospyros paniculata</i>	10~40	<i>Bacteria-B. subtilis</i> , <i>B. pumilis</i> , <i>Streptococcus pyogenes</i> , <i>P. aeruginosa</i> , <i>S. aureus</i> , <i>E. coli</i> , <i>Klebsiella pneumoniae</i> , <i>Proteus vulgaris</i> Fungal- <i>Aspergillus niger</i> , <i>Aspergillus flavus</i> , <i>Penicillium notatum</i> , <i>Saccharomyces cerevisiae</i> and <i>Candida albicans</i>	25~100
Crude extract of <i>Bergenia ciliata</i>	~35	<i>Micrococcus luteus</i> , <i>S. aureus</i> , <i>Bordetella bronchiseptica</i> , and <i>Enterobacter aerogens</i>	11.11, 33.33, 100 and 300
Liquor of <i>Eucalyptus</i> wood	25~30	Bacteria- <i>S. aureus</i> , <i>P. aeruginosa</i> , and <i>E. coli</i> Fungus- <i>P. chrysogenum</i> , <i>C. oxysporum</i> , <i>C. albicans</i> and <i>A. niger</i>	25~100

is a natural cationic polysaccharide with inherent biocompatibility property. Owing to its excellent nontoxicity and biodegradability, chitosan has been widely used in different scientific fields, including food-preservation, pharmaceutical and other biotechnology areas^[26]. Structured with hydroxyl and amino groups, chitosan can be subject to various chemical modifications, and its activity highly depends on its pH value. With a pH value of higher than pKa, chitosan is prone to exhibit antimicrobial activity due to the hydrophobic interaction and chelation effects^[27]. Ottenhall et al^[28] combined cationic chitosan/polyvinylamine with cellulose as for the fabrication of antimicrobial composite for insulating packaging. The prepared sample exhibited high water-stability and antimicrobial activities against both *Escherichia coli* (a common model bacteria) and *Aspergillus brasiliensis* (a sporulating mold). The use of this biobased packaging material can protect the items from both microbial and mechanical damage, while with no demanding of toxic strengthening additives. Vasile et al^[29] incorporated the gentamicin coated ZnO nanoparticles into chitosan matrix under different weight ratios, to yield a ZnO/gentamicin-chitosan gel (Fig.2). Test results showed that the prepared ZnO/gentamicin-chitosan gel significantly inhibited the growth of *Staphylococcus aureus* and *Pseudomonas aeruginosa* in both planktonic and surface-attached conditions. The finished product was proposed for cutaneous healing use, considering its excellent performance on the controlled release of

antimicrobials.

Polyphenol is a representative natural material which is non-toxic, biodegradable and sustainable. A large number of studies have revealed the antimicrobial efficacy of polyphenol extracted from different sources and used in various application areas, such as pharmaceutical or food products. Compared with other antimicrobials, polyphenol isolated from fruit or tea exhibits excellent water-solubility due to the existence of its surface hydroxyl groups. Gaikwad et al^[30] prepared the functional low-density polyethylene (LDPE) films by coating with different amounts of phenolic compounds, pyrogallol (PGL). The applicability of resultant LDPE/PGL films for packaging was investigated. The results showed that the barrier properties for water and oxygen increased from 0.78 and 0.32 g·mm/(m²·h·kPa) of neat LDPE film to (470±23.2) and (273±57.1) g·mm/(m²·h·kPa), respectively. Nevertheless, color stability tests showed that there was a decrease in L^* value for the coated LDPE films, which was in good agreement with their previously published results^[31]. The oxidation of functional groups of PGL during the film processing was proposed as a possible cause for the above phenomenon. Moreover, the LDPE/PGL films exhibited desirable antimicrobial activity against *Staphylococcus aureus* (Gram-positive) and *Escherichia coli* (Gram-negative), especially for *Staphylococcus aureus*. In another study, Han et al^[32] used sodium alginate (SA) and carboxymethyl cellulose (CMC) as matrix

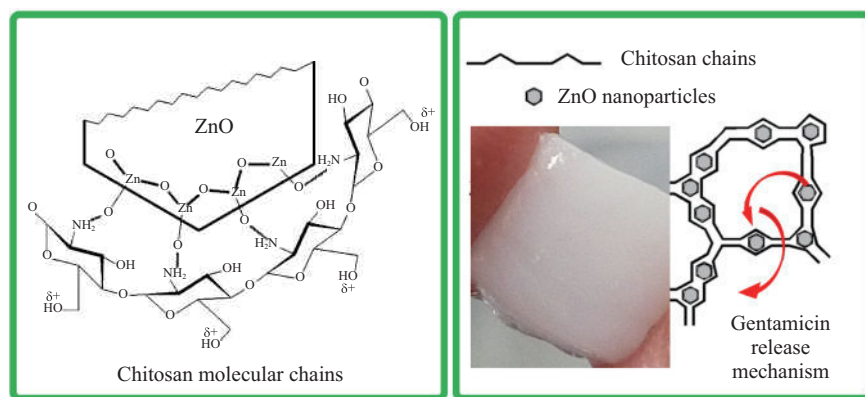


Fig.2 Morphology/molecular structure of ZnO/gentamicin-chitosan gel and its controlled release of antimicrobials

for incorporating with different concentrations of pyrogallol acid (PA). An antimicrobial film was prepared by adding glycerin and CaCl₂ as plasticizer and cross-linking agent, respectively. Fourier transform infrared (FT-IR) spectroscopy was used to investigate the microstructure of the generated film, and the results showed that PA interacts with SA/CMC matrix via hydrogen bonding. Compared with the control

(SA/CMC films), the SA/CMC/PA film showed an improvement in the barrier properties against ultraviolet light. Its moisture and oxygen permeability were enhanced as well. Upon PA loading of 40 g/kg, the increase of film elongation reached to 39.6%, accompanying with a decrease of color parameter L^* value. Moreover, SA/CMC/PA film, especially at high PA concentration, was effective against *Escherichia coli* and *Staphylococcus aureus*.

Despite its excellent performance, certain drawbacks have to be considered as for the scale-up applications of polyphenol. As revealed in the aforementioned two studies, undesired processing stability and acceleration of coloration upon weathering were commonly-exist issues, and numerous efforts have been put to overcome these bottlenecks. Sun et al.^[33] investigated the use of sulfated nanocellulose (SCNC) as emulsifiers for enhancing the stability of gelatin-encapsulated tea polyphenol (G-TPP). Well-entrapped SCNC-G-TPP capsules were obtained under an optimal processing condition, with particle size of (92 ± 1) nm. High performance liquid chromatography (HPLC) results showed that SCNC-G-TPP had a higher residual TPP of $(85.7 \pm 0.8)\%$ after storage for 6 days, which was distinct from $(44.9 \pm 0.5)\%$ of G-TPP. The free radical DPPH method revealed that after 40 min of storage at 121°C , the decrease of TPP was only $(8.9 \pm 0.3)\%$ for SCNC-G-TPP, while that of G-TPP was $(17.2 \pm 0.3)\%$. As shown in Fig.3, the potential contribution of SCNC may be attributed to the increased strength of gelatin capsule by SCNC via hydrogen bonding between

hydroxyl groups from SCNC and amino groups from gelatin. The abundant sulfate groups of SCNC might further enhance the structural stability of SCNC-G-TPP capsules.

Biobased surfactants which are prepared by enzymatic fermentation, can also be used as antimicrobial agents for practical applications. It is known that petroleum-based surfactants are facing challenges in terms of limited fossil fuel availability, harsh manufacturing conditions, undesired biodegradability and potential aquatic toxicity. Biobased

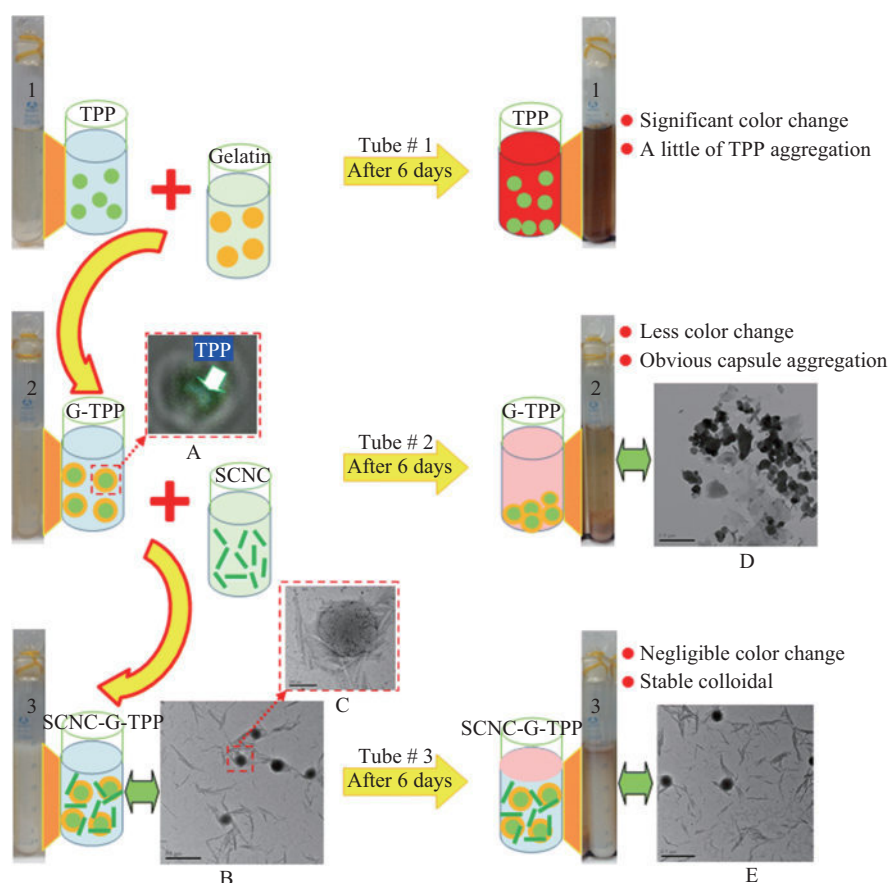


Fig.3 Understanding of different stabilities of TPP, G-TPP and SCNC-G-TPP (A) Confocal Laser Microscope (CLSM) image at 70 nm by argon laser, showing the typical core-shell structure of G-TPP; (B) Transmission Electron Microscope (TEM) image of SCNC-G-TPP, showing the formation of SCNC-stabilized TPP capsules (measuring bar of 0.5 μm); (C) TEM image of enlarged structures of SCNC-stabilized TPP gelatin capsule, showing that it was stable and intact (measuring bar of 100 nm); (D) TEM image of G-TPP (after storage for 6 days), showing the capsule aggregates (measuring bar of 0.5 μm); (E) TEM image of SCNC-G-TPP (after storage for 6 days), showing the stable SCNC-stabilized TPP capsules (measuring bar of 0.5 μm) (TPP concentration of 0.05 g/100 mL for all samples; initial pH value of 4 for all test tubes; end pH value of 3.9 for tube #1, 3.9 for tube #2 and 3.8 for tube #3, respectively)^[33] (Reprinted with permission from *Cellulose*)

surfactants, on the other hand, can address some of the above issues. Ren^[34] investigated the synthesis of biobased surfactants and evaluated their antimicrobial activities for potential food applications. Lipase was used for the preparation of glucose-fatty acid ester via the combination of glucose and fatty acids. The resulted glucose ester, in forms of glucose laurate, significantly inhibited the growth of *Escherichia coli* O157:H7, *Listeria monocytogenes* and *Salmonella Enteritidis* during 24 h under a concentration of 6.5 mg/mL. The finding of this work provided important information regarding the use of biobased surfactants as antimicrobial ingredients for food and agriculture industries.

Furthermore, as for the application of multi-compounds antimicrobials, Ngo et al^[35] prepared a novel type of poly-phenolic branched-chain fatty acids (poly-PBC-FAs) by using two streams of natural resources: phenolics (e.g., thymol, carvacrol and creosote) and fatty acids derived from oils. The finished products are odourless and in liquid form under room temperature. Test results showed that they had excellent antimicrobial activity against Gram-positive bacteria due to their unique amphiphilic properties.

3 Fabrication of antimicrobial cellulose composites

Fabrication of antimicrobial cellulose composites is of much interest to the scientific community and has been under intense studies during the past few decades. General approaches to bind the antimicrobial agents with cellulose involved a variety of methods based on two main categories: (1) surface loading/coating; (2) interior embedding.

3.1 Surface loading/coating

Surface loading/coating can be further classified as physical or physi-chemical methods depending on whether chemical reactions are involved in the preparation process. Physical surface loading/coating methods can be widely found in the

literature, such as electrostatic layer-by-layer (LBL) deposition. Electrostatic LBL is a well-developed coating method for the establishment of nanostructured multilayers on the surface of cellulose matrix. For example, the multilayers could be constructed through alternate deposition of polyanions and polycations via electrostatic interactions^[36]. Recent studies have been focused on the modification of cellulose by using electrostatic LBL polyelectrolyte/nanoparticles (antimicrobial agents) multilayers. Improvements on the physical properties, such as homogenous surface morphology and enhanced antimicrobial activities, could be obtained^[26].

As for the physi-chemical methods, they refer to certain types of high density or high bulk of composites which need to be prepared via multiple-steps involving both physical and chemical methods. Shown in Fig.4 is a previously reported example with two steps involved: (1) mixing cellulose with precursor solution for loading the silver particles on the cellulose surface, and the water washing/removing of the unattached silver ions; (2) transferring the cellulose-silver middle composites into a reducing agent solution to finalize the *in situ* reduction^[37]. During the reaction, the size of silver particle could be controlled through manipulation of the immersing time in reducing agent solution. In general, silver nitrate can be used as a precursor, and the reducing agent can be selected from varied substances, such as sodium citrate^[38] or sodium borohydride^[39].

3.2 Interior embedding

The interior embedding method for the preparation

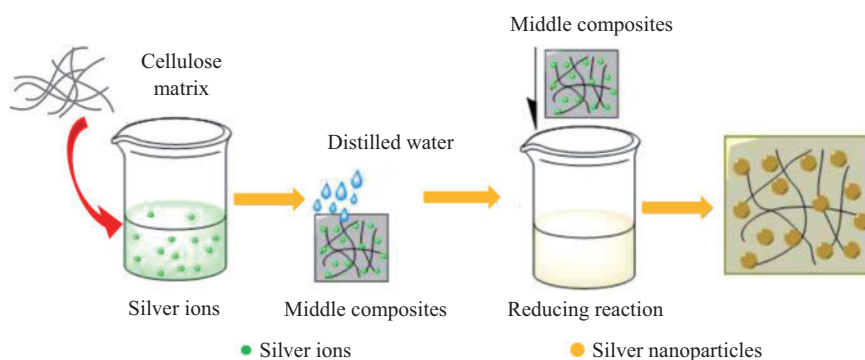


Fig.4 Two-steps preparation method for the antimicrobial cellulose-silver composite

of antimicrobial composite is usually involved during the cellulose regeneration process. Due to the rapid development of novel cellulose solvents, regenerated cellulose has captured extensive attention as for the use in ultrafiltration and forward/reverse osmosis process^[40]. As one specific example, silver nanoparticles, prepared by using Tollens' process, can be added into the melted cellulose-alkali/urea solution before casting of cellulose membrane. Upon uniformly mixing, silver nanoparticles can well disperse into the cellulosic matrix, and generate a composite film with thickness of approximate 0.5 mm during the following casting process^[41]. The finished product usually has extended antimicrobial capacity accompanied with sustained release behaviour.

Besides that, antimicrobial agents can also be loaded onto the regenerated cellulose after they are prepared. Benavente et al^[42] fabricated an regenerated cellulose membrane by dipping the regenerated cellulose into nano-silver colloids. X-ray diffraction (XRD) and SEM analysis confirmed the presence of silver nanoparticles on the surface of cellulose membrane. Elastic measurements showed that the binding of silver particles to composites could potentially increase their rigidity and chemical stability against oxidation. Moreover, silver nanoparticles rendered the composites good antimicrobial properties, thus reducing the undesired biofouling upon their application in wastewater treatment. Shen et al^[43] prepared the cellulose-based composite by incorporating the silica particles (SBA) into cellulose solution, which was later used to load the chloramphenicol for antimicrobial application. CaCO_3 was added as the coating material for SBA before they were mixed with the cellulose working solution (7 wt% NaOH, 12 wt% urea, 81 wt% deionized water), thus protecting the microstructure of SBA against the etching of alkali solution. Test results showed that a layer of CaCO_3 was effectively immobilized on SBA, which contributed to the preservation of mesoporous morphology of SBA in the finished cellulose composite. The high specific surface area and unique porous structure rendered cellulose-

SBA-chloramphenicol composite with a sustainable drug release behaviour. As reported, the initial release of chloramphenicol was rapid, then turned slow and constant after a stable phase. This phase could maintain for 170 h in a particular case of cellulose composites containing 20% and 30% of SBA, followed by a slow release process up to 270 h. Moreover, the antimicrobial test against *Staphylococcus aureus* and *Escherichia coli* showed that the developed composite exhibited persistent antimicrobial ability over 144 h. Its mechanical property, swelling behavior as well as water vapor transmission rate well complied with the recovery requirements of wound healing materials.

4 Typical application of cellulose-based antimicrobial composites

4.1 Food industry

Interest in cellulose-based food packaging materials is steadily growing to satisfy the need of replacing petroleum-based plastics with bio-resourced materials^[44]. Cellulose has many advantages in items' packaging due to its affordable cost and light weight. Moreover, it is easy to be recycled and decomposed under natural atmosphere. From an economic and industrial point of view, it would be of a great benefit to apply the cellulose-based packaging materials in a commercial scale. In such applications, antimicrobial function would be required.

Using antimicrobial agents in active food packaging is relatively recent and used to cause many concerns at consumers' side regarding the edible safety of antimicrobials. For this reason, there is a growing preference for bio-agents which are extracted from natural sources. Rollini et al^[45] investigated the combination of propolis glycolic extract and chitosan to develop a completely bio-based antimicrobial food packaging agent. CMC or microfibrillated cellulose (MFC) was added under two different pH values during the papermaking process. The results showed that the maximum wet strength of (7.4 ± 0.5) N·m/g and wet resistance of $(13.3 \pm 1.2)\%$ could be achieved at pH value of 7 by adding MFC and chitosan (the highest

molecular weight) into food packaging material. Tests on thinly sliced raw veal meat confirmed the antimicrobial activity against *L. innocua* of around 1 log cycle in 48 h at 4°C.

4.2 Medical industry

The surfaces of all medical devices, such as hygiene products made of cellulose pulp, are extremely susceptible to microbial infection, due to its moderate environment for microbial growth. It was reported that most hospital-acquired infections were originated from the insufficiently sterilized medical devices. The urging need to address these issues paved a way to the development of cellulose-based antimicrobial products for medical use, such as scaffolds and catheters.

El-Naggar et al^[46] loaded a reactive cyclodextrin (RCD)-based nanoemulsion with coconut oil in the presence of Tween 80 as emulsifying agent, and developed an antimicrobial medical cotton fabric. The entrapment efficiency of coconut oil loaded RCD-based nanoemulsion after centrifugation was calculated as more than 93%. TEM and SEM analysis confirmed the nano-sized scale of coconut oil loaded RCD nanocomposite. The obtained RCD-based nanoemulsions were applied to the bleached cotton fabrics by using “pad-dry-cure” technique. The finished fabrics before and after being submitted to 20 washing cycles were measured against different types of bacteria and fungi via inhibition zone method. The results showed that treated cotton fabrics exhibited excellent antimicrobial activity even after 20 washing cycles. The above prepared product was proposed to be used as super antimicrobial medical textile for protecting human beings against pathogenic microbes.

Gomes et al^[24] incorporated antimicrobial peptides into polyelectrolyte multilayer films built by the alternated deposition of polycation (chitosan) and polyanion (alginic acid sodium salt) over cotton gauzes, for preparing an antimicrobial wound-dressing. X-ray microanalysis confirmed the penetration of antimicrobial peptides within the films. Antimicrobial assays showed that all the applied antimicrobial

peptides exhibited higher antimicrobial effect (in the range of 4 log~6 log reduction) for both *Staphylococcus aureus* (Gram-positive bacterium) and *Klebsiella pneumonia* (Gram-negative bacterium) comparing with the control, while possessing non-cytotoxicity to human dermal fibroblasts.

4.3 Textile industry

Textiles are favourable materials for microbial growth under desirable temperature and moisture, which opens new windows for the application of antimicrobial agents onto the textile-used cellulose. The market for antimicrobial textiles has grown dramatically over the past few decades. Among various materials and approaches which have been developed, surface modification of cotton cellulose turns to be the leading trend in textile field to enhance antimicrobial activity and crease resistance.

Bhuiyan et al^[47] studied the use of chitosan for the surface modification of cotton cellulose to overcome its inherent drawbacks, such as low dyes exhaustion, crease formation on wear, and structural degradation upon microbial attack. Different concentrations of chitosan solutions were prepared for the treatment of cotton samples and their physical/antimicrobial properties were investigated. An improvement on the abrasion resistance and crease recovery property of treated fabric samples was observed, while accompanying with a slight deterioration of strength, elongation and handle characteristics. Moreover, experimental results showed that cotton cellulose treated with chitosan exhibited enhanced antimicrobial activities against both *Staphylococcus aureus* and *Escherichia coli*.

The antimicrobial potential of silver nanoparticles prepared by variable synthetic methods has been found useful in a large range of products. Its excellent performance in the inhibition of bacterial growth and less inclination makes it extremely suitable for the textile industry. In a recent study, Ag:ZnO/chitosan nano-substrates were developed using a modified sol-gel method with 3-glycidyloxypropyltrimethoxysilane and tetraethoxysilane as functionalization agents, and

were further applied on cotton cellulose and cotton/polyester (50%/50%, w/w) textiles through “pad-dry-cure” technique^[48]. The antimicrobial activity of Ag:ZnO/chitosan nano-substrates was investigated in comparison to that of the pure chitosan, by using paper disc method. The results showed that Ag-doped ZnO nanoparticles prepared from zinc acetate solution and embedded in chitosan matrix had better antimicrobial performance against both *Escherichia coli* and *Staphylococcus aureus*, comparing with Ag/CS and ZnO/CS coatings. For all samples, a significant reduction of up to 50%~95% of the microbials viability was observed. The blended textile of cotton/polyester (50%/50%, w/w) exhibited the most advanced performance.

Agricultural residue-based cellulose significantly contributes to the control of environmental pollution, therefore various materials have been put in practice for textile fabrication. Jang et al^[49] prepared a novel type of mulberry cellulosic fiber based composite loading of TiO₂ nanorods via a combination of sol-gel electrospinning and facile dip-coating approaches. SEM images showed that TiO₂ nanorods homogeneously distributed into the fibers matrix. The functionalized cellulose textile exhibited improved antimicrobial activity and excellent anti-yellowing properties due to the enhanced UV scattering of TiO₂ nanorods, which is suitable for textile use.

5 Nanocellulose

The currently-used nanobinders/fillers in antimicrobial composites including metal oxide, nanoclay, nanosilica, carbon nanotube, soy-protein and/or nanofibrils. The impact of these nanoparticles on human health highly depends on their chemical composition, surface morphology and physical properties. For example, metal nanoparticles might exert negative impact on cell viability and carbon-based nanomaterials may act as cytotoxic agents. Similarly, there is a high probability that silica-based nanoparticles could increase oxidative stress. However, nanocellulose, as a typical biopolymeric material, can be considered as the most

promising nanobinder/filler since it possesses ideal compatibility with cells and tissues^[50].

5.1 Nanocellulose as biobinder for functional composites

Nanocellulose as a unique type of biobased nanobinder, can be prepared by mechanical, chemical, enzymatic treatment or their combinations^[51-52]. Shown in Fig.5 is the TEM image of rod-like nanocellulose reported previously^[53], with width of 3~10 nm and length of 50~165 nm. These nano-sized cellulose particles are well-dispersed due to the negative charges deriving from the introduced sulfate groups on their surface. Nanocellulose and its derivatives after chemical modification have been widely used due to their high length-diameter aspect ratio as well as excellent mechanical strength^[54-55]. The distinctive rheological properties of nanocellulose can turn it into the gel-like form spontaneously upon contacting the aqueous medium. In addition, nanocellulose generated from biomass, and their use would exhibit a substantial environmental benefit compared with other non-biobased nanobinders. These favorable attributes suggest that it can be potentially used as functional substrate for a wide range of composites. For instance, nanocellulose has been successfully compounded with a photochromic agent, spiropyrans (SP), for the preparation of UV responsive composite^[56]. Shown in Fig.6 are the prepared functional composites with

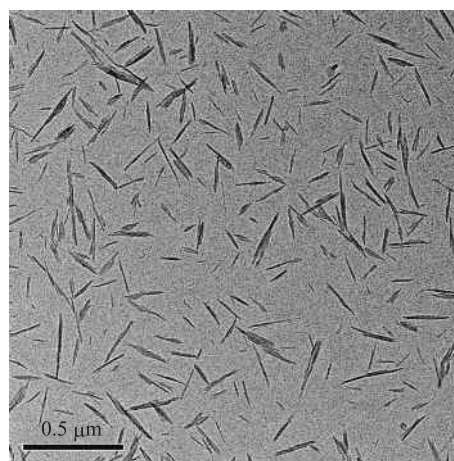


Fig.5 TEM image of nanocellulose^[53]
(Reprinted with permission from *Cellulose*)

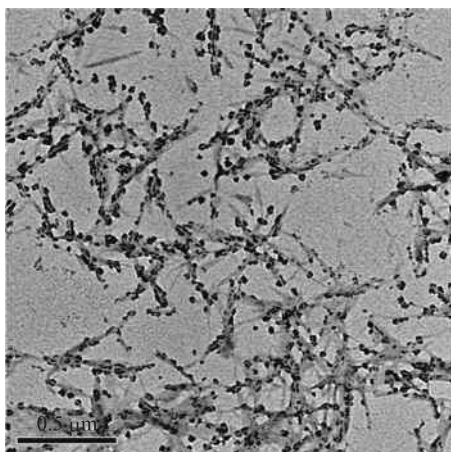


Fig.6 Nanocellulose-SO compounds^[56]
(Reprinted with permission from *Carbohydrate Polymers*)

SO particles carried by nanocellulose rods. The well dispersed SO on the nanocellulose surface indicate the good affinity between these two materials, and a uniform inter-structure can be thus generated.

The acetone-dissolved SO and CNC-dispersed SO compounds were exposed to UV irradiation and the changes of light absorption coefficient (in blue, red and green range) upon different UV exposure time were shown in Fig.7. It can be seen that both CNC-dispersed SO and acetone-dissolved SO had a rapid color increase initially, followed by a plateau. The response rate and equilibrium color of CNC-dispersed SO compounds were faster and higher than acetone-dissolved SO. The results also showed that as soon as the UV irradiation terminated, the color started to fade away and the de-coloration efficiency of the CNC-dispersed SO compounds was higher than acetone-dissolved SO as well. This indicates that CNC can be potentially used

as a color stabilizer upon the compounding with a secondary material.

5.2 Nanocellulose-based antimicrobial composites

Nanocellulose was also widely used as biobinder for the preparation of antimicrobial composites due to its high dispersibility and stability. Liu et al^[57] synthesized silver nanoparticles by reducing AgNO_3 with sodium borohydride in the nanocellulose aqueous medium. The beeswax was then added into the nanocellulose/Ag composites to prepare nanocellulose/Ag/beeswax antimicrobial compounds for paper coating purpose. The immobilization of silver nanoparticles into the nanocellulose/Ag/beeswax compounds was confirmed by the UV-vis spectra, which exhibited a typical absorption band of silver nanoparticles at 410 nm for the antimicrobial compounds (Fig.8(A)). SEM images indicated that a layer of nanocellulose/Ag/beeswax film was coated on the surface of paper (coating amount of 21.53 g/m^2) (Fig.8(C,D)), imparting it with enhanced antibacterial activity against *Escherichia coli* (ATCC 11229). Moreover, a contact angle of coated paper of 113.06° indicated an evident improvement on its water resistance (Fig.8(B)).

In the last decade, a new fiber pretreatment has been proposed to make cellulose fibrillation into MFC, a scale size of nanocellulose^[58]. In this context, different surface-cationized MFCs were prepared by optimizing the pretreatment parameters of cellulose before fibrillation. All MFCs were characterized by conductometric titration to calculate the degree of substitution. Field emission gun scanning electron

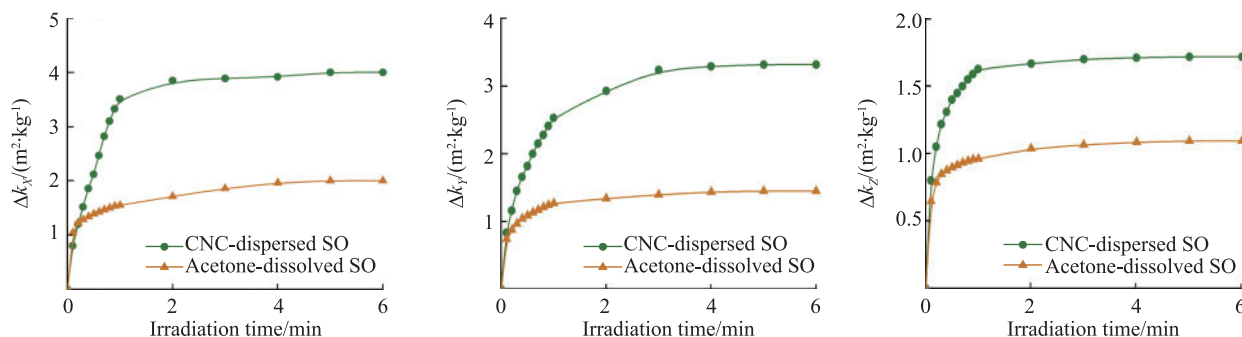


Fig.7 Photochromic activity of acetone-dissolved SO and CNC-dissolved SO^[56]
(Reprinted with permission from *Carbohydrate Polymers*)

microscopy (FEG-SEM), atomic force microscopy (AFM) and optical microscopy were used to assess the effect of pretreatment on the morphology of ensuing MFCs. Antibacterial activities of neat and cationized MFC samples were investigated against Gram-positive bacteria (*Bacillus subtilis*, *Staphylococcus aureus*) and Gram-negative bacteria (*Escherichia coli*). The cationized MFC at substitution degree greater than 0.18 displayed promising results on antimicrobial activity, while with no leaching of quaternary ammonium into the environment. This work proved the potential of cationized MFC with specific substitution degree for loading active antimicrobials, and being used in the fields of food/medical packaging or cosmetic.

Furthermore, a typical type of nanocellulose-based hand sanitizer has been recently commercialized in China which claimed to be 100% alcohol-free (product link: <http://www.hxcellulose.com>). Shown in Fig.9 is the structural schematic which illustrates the homogenously loaded antimicrobial agents on the surface of the nanocellulose rods^[59]. A similar principle which was reported by Sun et al^[56] and Liu et al^[60] in their previous works, can be applied here as accounting for the increased sterilization rate and gel stability. Apart from the above features, the aqueous product can also protect the skin from excessive dehydration. The thin layer of cellulose-film may further moisture hand skin and lock the nutritional oil from loss. The desirable noncytotoxicity as well as the excellent body affinity made the product the most popular hand sanitizer among different ages, especially for female users and young children.

Due to the inherent advantages of cellulose

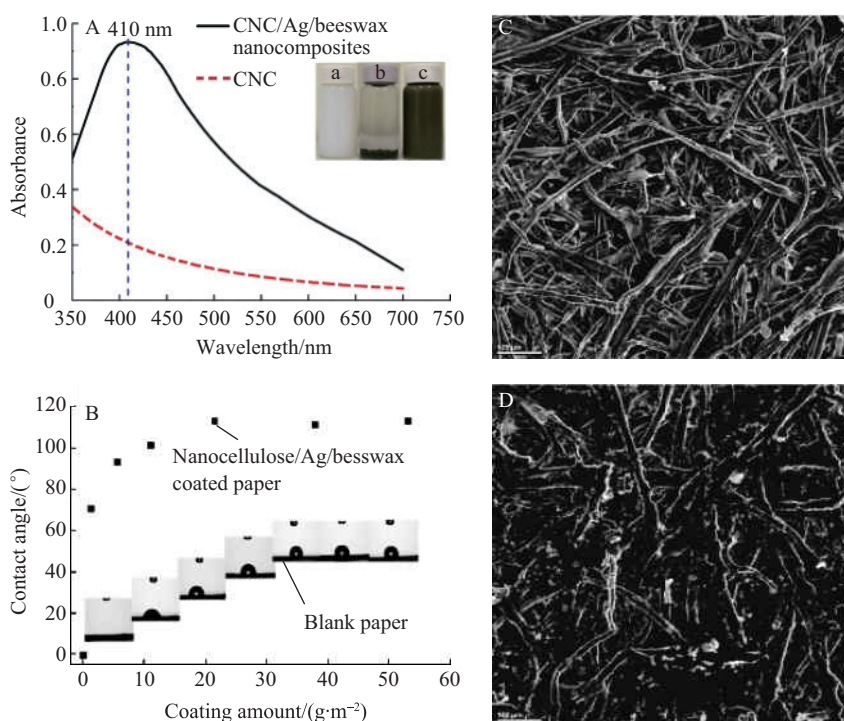


Fig.8 Characterization of the antimicrobial paper coated with nanocellulose/Ag/beeswax compounds. (A) UV-vis absorption spectra of the nanocellulose and nanocellulose/Ag/beeswax compounds (insert pictures of the nanocellulose (a), silver nanoparticles (b), and nanocellulose/Ag/beeswax composites (c)); (B) contact angle of blank paper and paper coated with different amounts of nanocellulose/Ag/beeswax composites; (C) SEM images of the blank paper; (D) nanocellulose/Ag/beeswax coated paper with coating amount of 21.53 g/m²^[57]
(Reprinted with permission from *Carbohydrate Polymers*)



Fig.9 Release behavior of the CNC-based hand sanitizer materials, the development of cellulose-based functional composite products for different applications will move forward, which is partially driven by the demand from consumers for green and healthy living.

6 Summary

Tremendous developments of technologies on antimicrobial composites have led to many applications in different industrial sectors. Cellulose-based antimicrobial materials play an important role in these developments, thanks to their unique properties. In particular, nanocellulose, as a leading-edge and emerging green functional material, is of great importance due to its high charge density and excellent rheological properties. Moreover, the abundant surface hydroxyl groups of nanocellulose can be modified to meet various needs; other attributes include the unique nano-structure and desired aspect ratio. All of them render nanocellulose as an excellent candidate for the preparation of antimicrobial composite products. The use of these nano natural materials has great potential in the food, medical and textile industries.

Acknowledgments

The authors would like to acknowledge the financial support provided by National Natural Science Foundation of China (31501440), Hebei Provincial Scientific and Technological Cooperation & Development Foundation between Province and University of 2018, Tianjin Science and Technology Commissioner Program (16JCTPJC45300), Tianjin International Training Program for Excellent Postdoctoral Fellows of 2015, and China Postdoctoral Science Foundation (2015M571268).

References

- [1] Mao H Q, Gong Y Y, Liu Y L, et al. Progress in nanocellulose preparation and application[J]. Paper and Biomaterials, 2017, 2(4): 65-76.
- [2] Ma X Z, Zhang Y J, Huang J. Surface chemical modification of cellulose nanocrystals and its application in biomaterials[J]. Paper and Biomaterials, 2017, 2(4): 34-56.
- [3] Sankar P K, Ramakrishnan R, Rosemary M. Biological evaluation of nanosilver incorporated cellulose pulp for hygiene products[J]. Materials Science and Engineering: C, 2016, 61: 631-637.
- [4] Dong C, Ye Y, Qian L, et al. Antibacterial modification of cellulose fibers by grafting β -cyclodextrin and inclusion with ciprofloxacin[J]. Cellulose, 2014, 21(3): 1921-1932.
- [5] Ying L, Ren X, Liang J. Antibacterial modification of cellulosic materials[J]. BioResources, 2015, 10(1): 1964-1985.
- [6] Salmieri S, Islam F, Khan R A, et al. Antimicrobial nanocomposite films made of poly(lactic acid)-cellulose nanocrystals (PLA-CNC) in food applications: part A—effect of nisin release on the inactivation of *Listeria monocytogenes* in ham[J]. Cellulose, 2014, 21(3): 1837-1850.
- [7] Amber R, Adnan M, Tariq A, et al. Antibacterial activity of selected medicinal plants of northwest Pakistan traditionally used against mastitis in livestock[J]. Saudi Journal of Biological Sciences, 2018, 25(1): 154-161.
- [8] Yang F. Antibacterial Agent and Its Application in Antibacterial Paper[J]. China Pulp & Paper, 2006, 25(8): 51-55.
- [9] Motta G J, Milne C T, Corbett L Q. Impact of antimicrobial gauze on bacterial colonies in wounds that require packing[J]. Ostomy Wound Management, 2004, 50(8): 48-62.
- [10] Hoseinnejad M, Jafari S M, Katouzian I. Inorganic and metal nanoparticles and their antimicrobial activity in food packaging applications[J]. Critical Reviews in Microbiology, 2018, 44(2): 161-181.
- [11] Dizaj S M, Lotfipour F, Barzegar-Jalali M, et al. Antimicrobial activity of the metals and metal oxide nanoparticles[J]. Materials Science and Engineering: C, 2014, 44: 278-284.
- [12] Seyedpour S F, Rahimpour A, Najafpour G. Facile *in-situ* assembly of silver-based MOFs to surface functionalization of TFC membrane: a novel approach toward long-lasting biofouling mitigation[J]. Journal of Membrane Science, 2019, 573: 257-269.
- [13] Saraswathi M S S A, Rana D, Alwarappan S, et al. Polydopamine layered poly(ether imide) ultrafiltration membranes tailored with silver nanoparticles designed for better permeability, selectivity and antifouling[J]. Journal of Industrial and Engineering Chemistry, 2019, 76: 141-149.
- [14] Thakoersing V S, Gooris G S, Mulder A, et al. Unraveling barrier properties of three different in-house human skin equivalents[J]. Tissue Engineering Part C: Methods, 2011, 18(1): 1-11.
- [15] Patil M P, Kim G-D. Eco-friendly approach for nanoparticles synthesis and mechanism behind antibacterial activity of silver and anticancer activity of gold nanoparticles[J]. Applied Microbiology and Biotechnology, 2017, 101(1): 79-92.
- [16] Koduru J R, Kailasa S K, Bhamore J R, et al. Phytochemical-assisted synthetic approaches for silver nanoparticles antimicrobial applications: a review[J]. Advances in colloid and interface science, 2018, 256: 326-

- 339.
- [17] Kim K-J, Sung W S, Suh B K, et al. Antifungal activity and mode of action of silver nano-particles on *Candida albicans*[J]. *Biometals*, 2009, 22(2): 235-242.
 - [18] Feßler A T, Li J, Kadlec K, et al. *Staphylococcus aureus*[M]. The Netherlands: Elsevier, 2018: 57-85.
 - [19] Fortunati E, Mazzaglia A, Balestra G M. Sustainable control strategies for plant protection and food packaging sectors by natural substances and novel nanotechnological approaches[J]. *Journal of the Science of Food and Agriculture*, 2019, 99(3): 986-1000.
 - [20] Fan X, Ngo H, Wu C. Natural and Bio-based Antimicrobials: A Review, in *Natural and Bio-Based Antimicrobials for Food Applications*[M]. USA: ACS Publications, 2018: 1-24.
 - [21] Onaizi S A, Leong S S. Tethering antimicrobial peptides: current status and potential challenges[J]. *Biotechnology Advances*, 2011, 29(1): 67-74.
 - [22] Kaplan J B. Biofilm dispersal: mechanisms, clinical implications, and potential therapeutic uses[J]. *Journal of Dental Research*, 2010, 89(3): 205-218.
 - [23] Stempel N, Strehmel J, Overhage J. Potential application of antimicrobial peptides in the treatment of bacterial biofilm infections[J]. *Current Pharmaceutical Design*, 2015, 21(1): 67-84.
 - [24] Gomes A, Mano J, Queiroz J, et al. Incorporation of antimicrobial peptides on functionalized cotton gauzes for medical applications[J]. *Carbohydrate Polymers*, 2015, 127: 451-461.
 - [25] Andersson D I, Hughes D, Kubicek-Sutherland J Z. Mechanisms and consequences of bacterial resistance to antimicrobial peptides[J]. *Drug Resistance Updates*, 2016, 26: 43-57.
 - [26] Li H, Peng L. Antimicrobial and antioxidant surface modification of cellulose fibers using layer-by-layer deposition of chitosan and lignosulfonates[J]. *Carbohydrate Polymers*, 2015, 124: 35-42.
 - [27] Pisoschi A M, Pop A, Cimpeanu C, et al. Nanoencapsulation techniques for compounds and products with antioxidant and antimicrobial activity—a critical view[J]. *European Journal of Medicinal Chemistry*, 2018, 157: 1326-1345.
 - [28] Ottenhall A, Seppänen T, Ek M. Water-stable cellulose fiber foam with antimicrobial properties for bio based low-density materials[J]. *Cellulose*, 2018, 25(4): 2599-2613.
 - [29] Vasile B S, Oprea O, Voicu G, et al. Synthesis and characterization of a novel controlled release zinc oxide/gentamicin-chitosan composite with potential applications in wounds care[J]. *International Journal of Pharmaceutics*, 2014, 463(2): 161-169.
 - [30] Gaikwad K K, Singh S, Lee Y S. Antimicrobial and improved barrier properties of natural phenolic compound-coated polymeric films for active packaging applications[J]. *Journal of Coatings Technology and Research*, 2019, 16(1): 147-157.
 - [31] Gaikwad K K, Singh S, Lee Y S. A pyrogallol-coated modified LDPE film as an oxygen scavenging film for active packaging materials[J]. *Progress in Organic Coatings*, 2017, 111: 186-195.
 - [32] Han Y, Wang L. Sodium alginate/carboxymethyl cellulose films containing pyrogallol acid: physical and antibacterial properties[J]. *Journal of the Science of Food and Agriculture*, 2017, 97(4): 1295-1301.
 - [33] Sun B, Zhang M, Ni Y. Use of sulfated cellulose nanocrystals towards stability enhancement of gelatin-encapsulated tea polyphenols[J]. *Cellulose*, 2018, 25(9): 5157-5173.
 - [34] Ren K. Synthesis of some biobased surfactants, and their functionalities as emulsifiers and antimicrobial agents[D]. Iowa: Iowa State University, 2018.
 - [35] Ngo H, Fan X, Moreau R. Poly-phenolic branched-chain fatty acids as potential bio-based, odorless, liquid antimicrobial agents[J]. *INFORM*, 2018, 29(3): 20-22.
 - [36] Zhang X, Ou-yang S, Wang J, et al. Construction of antibacterial surface via layer-by-layer method[J]. *Current Pharmaceutical Design*, 2018, 24(8): 926-935.
 - [37] Xu Y, Li S, Yue X, et al. Review of silver nanoparticles (AgNPs)-cellulose antibacterial composites[J]. *BioResources*, 2017, 13(1): 2150-2170.
 - [38] Ahmad I, Kamal T, Khan S B, et al. An efficient and easily retrievable dip catalyst based on silver nanoparticles/chitosan-coated cellulose filter paper[J]. *Cellulose*, 2016, 23(6): 3577-3588.
 - [39] Hebeish A, Hashem M, El-Hady M A, et al. Development of CMC hydrogels loaded with silver nano-particles for medical applications[J]. *Carbohydrate Polymers*, 2013, 92(1): 407-413.
 - [40] Livazovic S, Li Z, Behzad A R, et al. Cellulose multilayer membranes manufacture with ionic liquid[J]. *Journal of Membrane Science*, 2015, 490: 282-293.
 - [41] Chook S W, Chia C H, Zakaria S, et al. Effective immobilization of silver nanoparticles on a regenerated cellulose-chitosan composite membrane and its antibacterial activity[J]. *New Journal of Chemistry*, 2017, 41(12): 5061-5065.
 - [42] Benavente J, Garcia M, Urbano N, et al. Inclusion of silver nanoparticles for improving regenerated cellulose membrane performance and reduction of biofouling[J]. *International Journal of Biological Macromolecules*, 2017, 103: 758-763.
 - [43] Shen Z, Cai N, Xue Y, et al. Engineering Sustainable Antimicrobial Release in Silica-Cellulose Membrane

- with CaCO₃-aided Processing for Wound Dressing Application[J]. *Polymers*, 2019, 11(5): 808.
- [44] Makaremi M, Pasbakhsh P, Cavallaro G, et al. Effect of morphology and size of halloysite nanotubes on functional pectin bionanocomposites for food packaging applications[J]. *ACS Applied Materials & Interfaces*, 2017, 9(20): 17476-17488.
- [45] Rollini M, Mascheroni E, Capretti G, et al. Propolis and chitosan as antimicrobial and polyphenols retainer for the development of paper based active packaging materials[J]. *Food Packaging and Shelf Life*, 2017, 14: 75-82.
- [46] El-Naggar M E, Shaarawy S, Shafie A E, et al. Development of antimicrobial medical cotton fabrics using synthesized nanoemulsion of reactive cyclodextrin hosted coconut oil inclusion complex[J]. *Fibers and Polymers*, 2017, 18(8): 1486-1495.
- [47] Bhuiyan M R, Hossain M, Zakaria M, et al. Chitosan coated cotton fiber: physical and antimicrobial properties for apparel use[J]. *Journal of Polymers and the Environment*, 2017, 25(2): 334-342.
- [48] Buşilă M, Muşat V, Textor T, et al. Synthesis and characterization of antimicrobial textile finishing based on Ag: ZnO nanoparticles/chitosan biocomposites[J]. *RSC Advances*, 2015, 5(28): 21562-21571.
- [49] Jang Y-S, Amna T, Hassan M S, et al. Nanotitania/mulberry fibers as novel textile with anti-yellowing and intrinsic antimicrobial properties[J]. *Ceramics International*, 2015, 41(5): 6274-6280.
- [50] De France K J. Structured Cellulose Nanocrystal Composite Hydrogels for Biomedical Applications[D]. Canada: McMaster University, 2019.
- [51] Duan C, Meng J, Wang X, et al. Synthesis of novel cellulose-based antibacterial composites of Ag nanoparticles@ metal-organic frameworks@ carboxymethylated fibers[J]. *Carbohydrate Polymers*, 2018, 193: 82-88.
- [52] Liu K, Nasrallah J, Chen L, et al. A facile template approach to preparing stable NFC/Ag/polyaniline nanocomposites for imparting multifunctionality to paper[J]. *Carbohydrate Polymers*, 2018, 194: 97-102.
- [53] Sun B, Wang W, Zhang M, et al. Biomass-based edible film with enhanced mass barrier capacity and gas permeable selectivity[J]. *Cellulose*, 2018, 25(10): 5919-5937.
- [54] Sun B, Hou Q, Liu Z, et al. Stability and efficiency improvement of ASA in internal sizing of cellulosic paper by using cationically modified cellulose nanocrystals[J]. *Cellulose*, 2014, 21(4): 2879-2887.
- [55] Sun B, Hou Q, Liu Z, et al. Sodium periodate oxidation of cellulose nanocrystal and its application as a paper wet strength additive[J]. *Cellulose*, 2015, 22(2): 1135-1146.
- [56] Sun B, Hou Q, He Z, et al. Cellulose nanocrystals (CNC) as carriers for a spirooxazine dye and its effect on photochromic efficiency[J]. *Carbohydrate Polymers*, 2014, 111: 419-424.
- [57] Liu K, Liang H, Nasrallah J, et al. Preparation of the CNC/Ag/beeswax composites for enhancing antibacterial and water resistance properties of paper[J]. *Carbohydrate Polymers*, 2016, 142: 183-188.
- [58] Saini S, Falco Ç Y, Belgacem M N, et al. Surface cationized cellulose nanofibrils for the production of contact active antimicrobial surfaces[J]. *Carbohydrate Polymers*, 2016, 135: 239-247.
- [59] Sun B, Zhang M, He Z, et al. Towards greener and more sustainable cellulose-based hand sanitizer products[J]. *Journal of Bioresources and Bioproducts*, 2017, 2(2): 56-60.
- [60] Liu K, Chen L, Huang L, et al. Enhancing antibacterium and strength of cellulosic paper by coating triclosan-loaded nanofibrillated cellulose (NFC)[J]. *Carbohydrate Polymers*, 2015, 117: 996-1001. PBM