

Nanocellulose in polymer composites and biomedical applications

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ABSTRACT: Nanocellulose materials are nano-sized cellulose fibrils or crystals produced by bacteria or derived from plants. These materials exhibit exceptional strength characteristics, light weight, transparency, and excellent biocompatibility. Compared with some other nanomaterials, nanocellulose is renewable and less expensive to produce, and a wide range of applications for nanocellulose has been envisioned. The areas most extensively studied include polymer composites and biomedical applications. Cellulose nanofibrils and nanocrystals have been used to reinforce both thermoplastic and thermoset polymers. Given the hydrophilic nature of these materials, the interfacial properties with most polymers are often poor; thus, various surface modification procedures have been adopted to improve the interaction between polymer matrix and cellulose nanofibrils or nanocrystals. The applications of nanocellulose as a biomaterial also have been explored, including wound dressing, tissue repair, and medical implants. Nanocellulose materials for wound healing and periodontal tissue recovery have become commercially available, demonstrating the great potential of nanocellulose as a new generation of biomaterials.

Application: Continuing research on the effect of nanocellulose on mechanical properties of polymer composites, as well as its surface modification and biomedical applications, will lead to new opportunities for mills.

Cellulose, the most abundant polymer on earth, is a biodegradable material with low cost, low density, and excellent mechanical properties. It has been widely used in many industries, including papermaking and textiles [1]. Recently, cellulose-based nanomaterials (nanocellulose) have attracted enormous attention from both academic and industry researchers, because of extraordinary mechanical strength, transparency, and proven biocompatibility [2].

The nanocellulose family consists of bacterial nanocellulose, plant-derived cellulose nanofibrils (CNF), and cellulose nanocrystals (CNC). Bacterial nanocellulose is produced by *Acetobacter xylinum* (*Gluconacetobacter xylinus*) bacteria using a fermentation process. The fibers are often characterized by an average diameter of 50 nm. The length can be engineered over scales ranging from nanometers to micrometers. Compared with plant-derived nanocellulose, bacterial nanocellulose presents greater purity, degree of polymerization, crystallinity, water content, and mechanical stability [3]. Unfortunately, procedures for bacteria removal may limit industrial scale production. On the other hand, large-scale production of plant-derived nanocellulose has already been realized. Cellulose nanofibrils are isolated from wood-based fibers using high-pressure homogenizers and grinders. Pretreatments of the fibers (e.g., enzymatic, mechanical treatment, [2,2,6,6-tetramethylpiperidin-1-yl]oxy {TEMPO}-mediated oxidation) have been performed to reduce the energy consumption of this process [4-6]. The cellulose nanofibrils have a diameter of 5-20 nm and length ranging from nanometers to several micrometers. In contrast, CNC are

rod-like nanoparticles with a length of 200-500 nm, formed by acid hydrolysis of native cellulose fibers using sulfuric acid (H_2SO_4) or hydrochloric acid (HCl). The size of the CNC can be tuned by varying the hydrolysis conditions [7]. Compared to HCl hydrolysis, H_2SO_4 hydrolysis needs lower temperature, lower acid-to-cellulose ratio, and less process time and thus is adopted more often in the preparation of CNC. Of note, chemical treatments in the preparation of CNF and CNC result in carboxylic acid and sulfate groups on the fiber or particle surface in contrast to 100% hydroxyl groups for bacterial nanocellulose [3].

To date, the use of nanocellulose materials in a wide range of applications has been explored. One of the most extensively studied areas is polymer composites [8]. Cellulose nanofibrils and nanocrystals have been used to reinforce both thermoplastic and thermoset polymers. Unfortunately, the dispersion of nanocellulose and interfacial interactions with most polymers are often poor due to incompatibility with polymer matrices. Various surface modification procedures have thus been adopted to improve the interaction between polymer matrix and cellulose nanofibrils or nanocrystals [9-13]. In addition, nanocellulose materials have been used in biomedical applications, including wound dressing, tissue repair, and medical implants because of their proven biocompatibility and unique rheological properties [3,14-17]. This review highlights the key reports on the polymer-nanocellulose composites and the influence of surface functionality on their mechanical properties, along with the biomedical applications of nanocellulose.

POLYMERIC NANOCELLULOSE COMPOSITE

Nanocellulose composites from different types of celluloses and different types of polymers were studied by researchers, and variable composite properties (e.g., thermal, mechanical, and optical properties) were reported based on these studies. It was also shown that the preparation methods have a significant impact on the final properties of these composites [18]; some of these studies were summarized here.

Both thermosets (such as epoxy and polyurethane [PU]), and thermoplastics (such as polypropylene [PP], poly(propylene carbonate) [PPC], poly(vinyl alcohol) [PVA], poly(ethylene oxide) [PEO], polylactic acid [PLA], and poly(ethylene [PE]) were employed as a matrix material [19–23], while mainly three types of cellulose nanomaterials were used as a reinforcing agent. In particular, CNF, CNC or cellulose nanowhiskers, and microfibrillated cellulose (MFC) were used. To classify them, their usual diameters and aspect ratios were reported as 2–10 nm; 2–20 nm; 10–40 nm; and >1000 nm, 10–100 nm, and 100–150 nm, respectively [8,24–26].

Thermosets

Marcovich et al. [20] studied the reinforcing effect of CNC and microcrystals on polyurethanes. They prepared a stable suspension of CNC in a polar organic solvent (dimethylformamide [DMF]) and mixed with a PU formulation (polyol and prepolymer). A reaction occurred between the hydroxyl groups on the surface of CNC and the prepolymer (i.e., isocyanate) causing an increase in glass transition temperature (T_g). Because of this strong interaction between the filler and the matrix, crosslinking density of the matrix increased. They observed a more than two-fold increase in modulus with 5 wt% filler loading; however, a decrease in yield strength was observed with the inclusion of CNC.

Another CNC-thermoset composite study was reported by Xu et al. [27]. They mixed aqueous suspension of CNC with waterborne epoxy and amine to prepare composite films. Despite the aggregation of some CNC particles, they observed that T_g and mechanical properties of the composites increased compared with neat epoxy. At 15% loading, about a 60% increase in modulus was obtained and, unlike the PU study mentioned previously, a 50% increase in tensile strength was observed.

Thermoplastics

Another study using CNC and PU was carried out by Saralegi et al. [28]; however, they used thermoplastic PU in their study. Transparent PU film composites were prepared via solvent casting method. Polyurethane was dissolved in DMF and CNCs at different ratios were added. While the increase in CNC content resulted in increased modulus, tensile strength decreased.

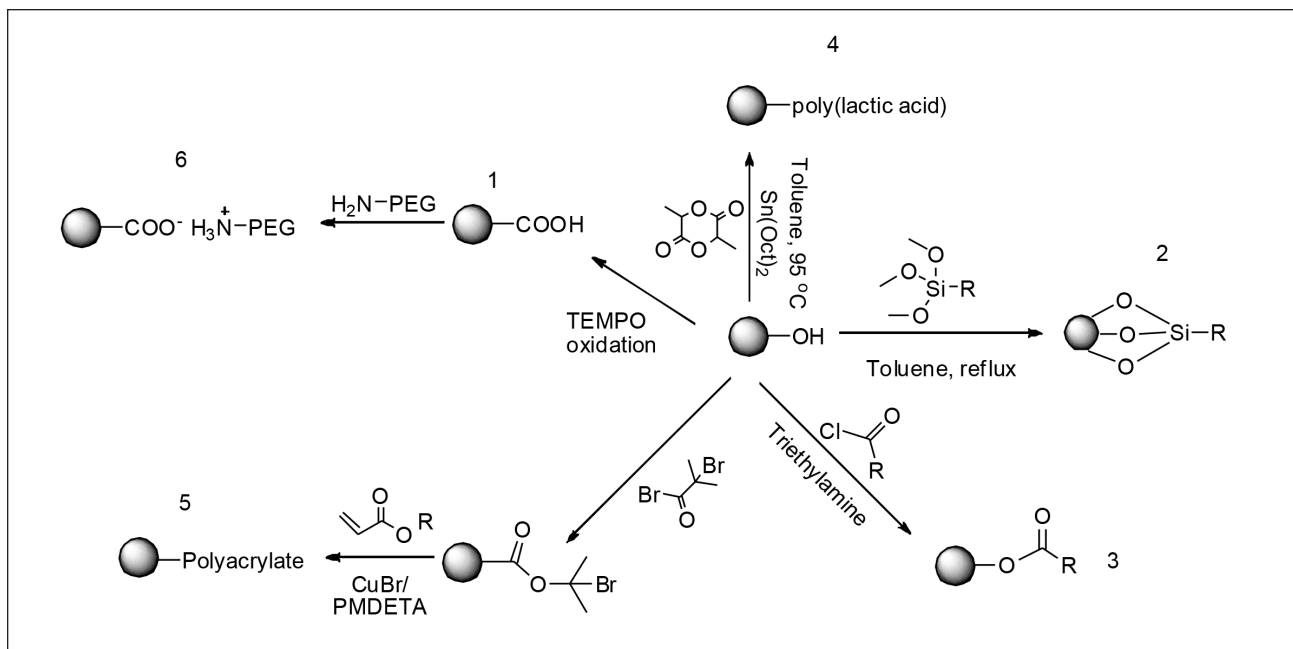
Because nanocellulose particles are easily dispersed in water due to their highly hydrophilic nature, poly(vinyl alcohol) (PVA), which is a water-soluble polymer, has been employed in many studies as a nanocellulose composite matrix.

Liu et al. [29] prepared PVA-CNF composite films by mixing an aqueous PVA solution and CNF suspension. By 60 wt% CNF loading, tensile strength increased about 87%, while modulus increased around six-fold. They have also observed an increase in strain below 5 wt% loading, indicating an increase in toughness. Cellulose nanofibers also improved thermal stability and T_g of the composite material. Moderate transparency and ultraviolet light absorption of the films showed a good potential for future optical applications.

Likewise, Lu et al. [30] studied PVA as a matrix material while using MFC with a diameter range of 10–100 nm with a web-like structure as a reinforcing agent. Similarly, they mixed an aqueous solution of PVA with MFC suspensions at different ratios (1–15 wt%), and produced samples via film casting. They concluded that the crystallization behavior of PVA was not affected by MFCs, and T_g and melting temperature (T_m) remained the same. They observed a 76% increase in strength and a 40% increase in modulus at 10 wt% MFC loading compared with the neat PVA samples. Both strength and modulus values remained the same when MFC loading was increased from 10 wt% to 15 wt%. The authors explained this with possible aggregation of the nano-sized fibers above 10% loading. The reinforcement they obtained from MFC with good dispersion seems low compared with CNC and CNF. To elaborate, CNCs are basically free of chain folding and have a crystalline structure with minimal defects, thus having dramatically high tensile strength and modulus. However, how much of the filler strength can be passed on to the composite strongly depends on the interfacial adhesion and the aspect ratio of the reinforcing material. Microfibrillated cellulose can be preferred to obtain a good reinforcement, provided that polymer molecules can penetrate the cellulose structure [31]. However, CNC and CNF were reported to possibly form an interconnected network inside the polymer matrix (above percolation threshold) via hydrogen bonding because of their small diameters, resulting in a more dramatic reinforcement effect than MFC [8,32].

There are still differences between CNC and CNF in terms of crystallinity and aspect ratio, which would also lead to different composite properties. Xu et al. [33] compared the morphological, crystallinity, and dispersion differences between the PEO composites of CNC and CNF. At the same nanocellulose concentrations, CNF-PEO composites showed higher tensile strength and modulus values compared with CNC-PEO composites because of their higher aspect ratio and fiber entanglement; they also showed lower failure strain values due to fiber agglomerations.

Bulota et al. [18] prepared composite films by mixing an MFC suspension with an aqueous PVA solutions at different concentrations and mixing times to show the effect of preparation method, and to address the variations in the reported results in the literature. Based on their findings, the mechanical performance of the composite films depends on the concentration of the MFC-PVA mixture, rather than the concentration of the polymer solution. When it is too dilute (i.e., too



1. Surface modification of nanocellulose via (1) carboxylation [37]; (2) silylation [39]; (3) esterification [42]; (4) polymer grafting by ring opening polymerization [49]; (5) atom transfer radical polymerization [52]; and (6) ionic interaction [9]. TEMPO (2,2,6,6-tetramethylpiperidine-1-oxyl); PMDETA (N,N,NETAtetrapentamethyldiethylenetriamine).

much water), MFC can move freely and tends to agglomerate more, causing a decrease in mechanical properties. Also, longer mixing times adversely affected the mechanical performance of the composites. Furthermore, the impact of the testing environment (i.e., relative humidity) was shown to be significant on tensile test results due to the moisture sensitivity of cellulose fibers; higher relative humidity resulted in lower modulus and strength measurements.

In addition to traditional MFC, CNC, or CNF, electrospun cellulose nanofibrous mat has been used as filler for PVA composites. Tang and Liu [23] prepared their mat using cellulose acetate and obtained composite films with 50% higher strength and 600% higher modulus at 40 wt% nanocellulose loading. Furthermore, they achieved 75% visible light transmittance, showing a potential for future optical applications.

Despite the promising results with water-soluble polymers, the compatibility of nanocellulose with hydrophobic polymers is of greater interest given that most polymer materials are not soluble in water. Bahar et al. [22] prepared composite films using CNC and PP. They added maleic anhydride-grafted PP into the composite as a coupling agent. They observed good film transparency, although there were slight CNC agglomerations. They reported 70%-80% strength increase and 50% crystallinity increase at 15 wt% CNC loading.

Hu et al. [19] studied the effect of the addition of CNC into PPC and observed a ten-fold increase in yield strength and a seven-fold increase in modulus with addition of only 0.1 wt% of CNC. Although the yield strength of the composite is only 19 MPa even after a ten-fold increase, the results look quite

promising and are much higher than the results reported for PPC composites prepared with other reinforcing agents, such as graphene oxide, montmorillonite, and glass fiber.

In nanocellulose composites, dispersion is one of the key parameters that significantly affects the reinforcement efficiency, as it is in all nanocomposites. Dispersing the hydrophilic nanocellulose inside a polymer matrix that is hydrophobic is even harder. As a result, different methods were tried or developed to prepare nanocellulose composite. To illustrate a few, Noorani et al. [34] developed a solvent exchange process, in which they were able to transfer an aqueous CNC dispersion into an organic solvent successfully to prepare a CNC-polysulfone membrane film. Nakagaito et al. [35] prepared a MFC-PLA film without using an organic solvent, but water. They first prepared a suspension of MFC-PLA mixture in a blender and then dewatered the mixture on a mesh screen following a process similar to a papermaking process. In another study, Dong et al. [36] used electrospinning to facilitate better dispersion of CNC in a poly(methyl methacrylate) (PMMA) polymer matrix.

SURFACE MODIFICATION

Although CNF and CNC have shown great potential as mechanical reinforcing fillers, their poor dispersibility in non-polar organic solvent and poor interfacial-attractive interaction with polymer matrix become the hurdle to reaching their theoretical predictions [9]. As a result, surface modification of native CNF and CNC has attracted much attention recently to improve their compatibility with polymers. **Figure 1** depicts surface modification approaches.

Carboxylation

TEMPO (2,2,6,6-tetramethylpiperidine-1-oxyl) oxidation is one of the common approaches to impart carboxylic acid groups on the surfaces of CNF and CNC [37]. It is often performed in alkaline media with sodium hypochlorite (NaOCl) and sodium bromide (NaBr) as primary oxidant and co-oxidant, respectively. The addition of NaBr generates the more reactive hypobromite (OBr⁻) molecule, which has been shown to accelerate the reaction [38]. TEMPO-oxidized CNC has been employed as a filler to crosslink alginate sponges via a freeze-thaw cycle process [10]. The divalent calcium ions (Ca²⁺) allow for ionic crosslinking within the polymer network, resulting in enhanced mechanical properties. For compressive strain of 30%, 50%, and 70%, the compressive strength increased by factors of 2.78, 2.80, and 2.94, respectively, in comparison with composites with unmodified nanocrystals [10].

Silylation

Silylation of the surface hydroxyl groups has proven effective at improving the compatibility of nanocellulose with non-polar organic solvents [39,40]. The hydrocarbon chains by the covalently bounded silanes also restrain fiber swelling. It has been reported that partially silylated CNC (i.e., degree of substitution of 0.6-1) becomes readily dispersible in solvents with low polarity (e.g., tetrahydrofuran). Of note, degree of substitution >1 results in disintegration of the CNC [41].

Esterification

Esterification of the hydroxyl groups on the nanocellulose surface can be achieved by the reaction with anhydride, fatty acids, esters, and acid chloride [42-46]. De Menezes et al. [43] reported the functionalization of surface hydroxyl groups on CNC using organic acid chlorides with variable aliphatic chain length. It was noted that the crystallinity of the particles was not altered by the chain grafting. Both modified and native nanocrystals were extruded with low-density PE to study the effect of surface functionalization. Dispersion of CNC improves with the aliphatic chain lengths. When long chains were grafted onto the crystal surface, significant increase in elongation at break was observed [43]. The authors claim it is because the grafted long chains act as long tails protruding into the matrix, creating a continuous phase between the nanocrystal and polymer.

Polymer grafting

Grafting of polymer chains onto the CNF or CNC surface has become one of the most active areas in the development of polymer-cellulose nanocomposites to fully realize the demonstrated advantage of long aliphatic chain modification [47]. Polymer chains can be covalently bound to the cellulose surface by either “grafting from” or “grafting on” approaches. Entanglement and co-crystallization occur between the grafted polymer and the matrix when the molecular weight of the graft polymer is sufficiently high [48]. These grafted polymer

chains also act as compatibilizer to improve the interfacial adhesion properties [49]. To date, maleated polypropylene (MaPP) [50], PU [12], polyethyleneglycol (PEG) [9,51], polyacrylates [52], and PLA [49] have been successfully anchored onto the surfaces of CNF and CNC. Ljungberg et al. [50] reported the preparation of atactic polypropylene (aPP) composites doped with MaPP-grafted CNC. The MaPP was grafted onto the CNC by the ring opening reaction of maleic anhydride to the surface hydroxyl groups. Unfortunately, the resulting nanocrystals showed poor dispersion in toluene, the solvent used for film casting, and thus failed to enhance the mechanical property of the PP-cellulose nanocomposite films compared with controls [50].

Cao et al. [12] reported the preparation of waterborne polyurethane (WPU)-CNC composites with in situ grafting of WPU prepolymer onto the nanocrystals. The WPU chains were anchored onto the nanocrystal surface by the reaction of isocyanate on the prepolymers with the hydroxyl groups on the nanocrystals. These grafted-WPU chains formed a crystalline structure on the nanocrystal surface and induced the crystallization of the WPU matrix, resulting in a co-continuous phase. As such, great dispersion and strong interfacial adhesion between the nanocrystals and the WPU matrix were guaranteed. The tensile strength of these composite films increased with nanocrystal content. At 10 wt%, the tensile strength increased from 4.4 to 9.7 MPa compared with WPU films. However, this enhanced mechanical property was a result of both the surface modification and CNC. Because unmodified nanocrystals were not used as control, it is not clear what extent of the strengthening effect was attributed to the surface modification [12].

Polyethylene glycols have been grafted onto the surfaces of CNF and CNC by either ionic absorption [9] or covalent bonding [51]. For the ionic absorption, CNF were treated by TEMPO oxidation to yield carboxylic acid groups, which were used for the ionic bonding of primary amine-functionalized PEG chains [9]. The resulting PEG-grafted CNF were mixed with poly(L-lactic acid) (PLLA) in chloroform, followed by solvent removal and compression molding to yield PLLA-nanocellulose composites. The Young's modulus, tensile strength, and work of fracture of the nanocomposites containing 1 wt% CNF increased by 40%, 26%, and 52%, respectively, compared with neat PLLA film. However, no data were presented regarding films with unmodified CNF. As such, it is not conclusive that the improvement in mechanical properties is completely attributed to the surface modification. In another study reported by Lin et al. [51], PEG was covalently attached to the surface of CNC by the condensation of carboxylic acid on TEMPO-oxidized nanocrystals and primary amine-functionalized PEG (i.e., molecular weight of 5,000). High molecular weight PEG was then anchored onto the resulting nanocrystals through entanglement and physical absorption. These modified nanocrystals were collected by lyophilization and mixed with polystyrene in a twin-screw compounder. Due to

the protection of coated PEG chains, these nanocrystals allowed for extrusion at high temperature (200°C) without degradation of the nanocrystals. The extruded nanocomposites with modified nanocrystals exhibited a 200% increase in storage modulus at 389 K (i.e., $T_g + 10^\circ\text{C}$).

In addition to the “grafting on” technique shown previously, polymers (e.g., polyacrylates, PLLA) can also be grafted from the CNF surface [49,52]. Lacerda et al. [52] demonstrated the grafting of polyacrylates on the CNF surface via atom transfer radical polymerization (ATRP). An initiator was anchored onto the surface first, followed by the growth of PMMA, poly(*n*-butyl acrylate) (PBA), or poly(MMA-co-BA) brushes from the nanofibrils surface by ATRP. However, the application of these fibers for nanocomposites has not yet been investigated [52]. In addition, the growth of poly(L-lactide) on the surface of CNC has been studied [49]. Ring opening of L-lactide to the hydroxyl groups on the nanocrystal surface was performed in toluene with tin(II) ethylhexanoate as the catalyst. The PLLA composite with modified or native nanocrystals was prepared by melt-blending in an extruder. It was noted that the PLLA coating was necessary to avoid the degradation of CNC during extrusion. Despite the improved thermal stability, limited reinforcing effect was observed below T_g because of a plasticization effect of the grafted PLLA chains. Above the T_g , the stiffness was improved for the composites containing PLLA-grafted nanocrystals [49]. Although these studies have shown promising results, significant enhancement in composite strength has not been realized, necessitating further studies on the surface modification of CNF and CNC and its impact on the mechanical properties of polymer-cellulose nanocomposites.

BIOMEDICAL APPLICATIONS

Bacterial nanocellulose has been used in a variety of biomedical applications because of its biocompatibility, excellent mechanical properties, and tunable degradability [15,17,53-55]. Bacterial nanocellulose implants demonstrated no signs of inflammation and great tissue and blood compatibility in vivo [1,15,56-59]. The rheological resemblance of nanocellulose hydrogel to soft tissue allows for the development of bio-mimicking scaffolds [15]. In addition, native nanocellulose exhibited limited degradation in vivo due to the lack of cellulase in the human body [60]. This non-degradability results in both durability and long-term chemical stability, which proved to be beneficial for a wide range of biomedical applications [60-64]. Of note, biodegradable nanocellulose derivative 2,3-dialdehyde cellulose can also be prepared for applications where biodegradability is desirable [55,65]. In the following section, we review the application of nanocellulose for wound healing, dental repair, tissue engineering, and cardiovascular implants.

Wound healing

Nanocellulose hydrogels are optimal materials for wound healing because they provide a moist environment to a wound



2. A never-dried bacterial cellulose membrane for wound healing shows conformability to body contours, maintains a moist environment, and significantly reduces pain [68]. (Reprinted with permission of the American Chemical Society, © 2007).

and absorb exudates during the healing process [66]. Heleinus et al. [54] implanted bacterial nanocellulose subcutaneously into rats, which did not elicit any chronic inflammatory responses. Bacterial nanocellulose dressings also proved to accelerate the healing of large-area full-thickness wounds in rats [17]. Histology results revealed extensive tissue regeneration and lower inflammatory reaction in the nanocellulose-treated group in contrast to the control group [17]. Recently, nanocellulose wound dressings have become commercially available (e.g., Biofill®, Bioprocess®, and XCell®) [67]. Unfortunately, despite the proven healing effect, nanocellulose is not able to prevent wound infections, which often leads to persistent inflammation and non-healing wounds [68]. Over the past few years, scientists have been working on the incorporation of silver nanoparticles into nanocellulose scaffolds to impart antimicrobial efficacy [16,69,70]. Silver nanoparticles can be either formed in situ by the reduction of silver nitrate [16,69] or loaded by flowing a silver nanoparticle suspension through the nanocellulose matrix [70]. These silver-containing nanocellulose materials exhibited enhanced antimicrobial efficacy compared with native nanocellulose. **Figure 2** shows an example of a cellulose membrane for wound healing.

Periodontal tissue repair

Bacterial nanocellulose has already been successfully employed in dentistry as implants for periodontal tissue recovery (e.g., Gengiflex®, Gore-Tex®) [71]. Gengiflex® consists of a bacterial nanocellulose inner layer and an alkali-cellulose outer layer while Gore-Tex® is a composite of bacterial nanocellulose, polytetrafluoroethylene, nylon, and PU [72]. Complete restoration of an osseous defect around an implant with a Gengiflex® therapy was reported. Compared to conventional surgical techniques, the advantage of

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Gengiflex® therapy include reestablishment of aesthetics and function of the mouth as well as fewer surgical steps [72]. The comparison of Gengiflex® and Gore-Tex® for periodontal tissue repair in vivo revealed that both membranes promoted comparable bone formation with Gore-Tex® resulting in significantly less inflammation [71].

Cartilage repair

Nanocellulose hydrogels have been widely studied for tissue engineering, including cartilage, bone, and nervous tissue repair [60,64,73-77]. Mechanical properties of bacterial nanocellulose hydrogels can be controlled by varying the fiber concentration. The hydrogel reaches comparable mechanical properties to cartilage at 14% cellulose content [60]. Pretzel et al. [64] have developed a long-term in vitro model with mature, adult bovine cartilage that is suitable for the evaluation of cartilage regeneration by nanocellulose. They also synthesized bacterial nanocellulose hydrogels with large pores as scaffolds for cartilage repair [14]. Three-dimensional laser perforation was performed to yield the porous structure for chondrocytes ingrowth. These hydrogels were found to support chondrocytes migration, differentiation, matrix production, and phenotypic stabilization in vitro [14].

Bone regeneration

A nanocellulose membrane has been employed for guided bone regeneration in bone defects. It acts as a barrier membrane to occlude fibroblastic cells and fibrous connective tissues. Promoted bone formation at the site was observed [74]. Furthermore, Fang et al. [76] reported the preparation of bacterial nanocellulose-hydroxyapatite composites for bone regeneration. These scaffolds demonstrated promoted human bone marrow adhesion, proliferation, and differentiation in vitro. Other in vitro studies also revealed the excellent biocompatibility of bacterial nanocellulose-hydroxyapatite composites, indicating the great potential for in vivo applications [77]. In an in vivo evaluation reported by Saska et al. [78], composites were prepared such that hydroxyapatite nanocrystals presented low crystallinity similar to physiological bone. The resulting composites accelerated new bone formation at the defect sites and no inflammatory reaction was induced after 4 weeks of implantation, indicating great biocompatibility to the bone tissue [78].

Nervous tissue reconstruction

Nervous tissue reconstruction remains a challenge to today's medicine due to poor recovery of damaged peripheral nerves [79]. Kowalska-Ludwicka et al. [73] reported the use of bacterial nanocellulose tubes for peripheral nerve regeneration in rat model. Nanocellulose tubes effectively prevent the overgrowth of connective tissue and the formation of neuromas, allowing for neurotropic factor accumulation and thus facilitating nerve regeneration. Biocompatibility of these materials was suggested by minimal tissue response and susceptibility to vascularization [73].

Cardiovascular implants

Atherosclerotic vascular diseases, such as coronary artery disease and peripheral vascular disease, are the largest cause of mortality in the western societies [3]. Surgical treatment suggested replacement of diseased blood vessels with synthetic plastic such as Dacron and expanded polytetrafluoroethylene (PTFE) [80]. Despite the widespread clinical application, small-diameter grafts (i.e., <6 mm) of both materials rapidly failed due to occlusion after 6 months of implantation [81]. Due to its nonthrombogenic property, bacterial nanocellulose tubes such as BASYC® represent an innovative solution for small-diameter grafts. BASYC® tubes with diameter <6 mm were used as grafts in a pig model to replace the carotid arteries. After 3 months, these tubes were removed for analysis. Seven grafts remained unclogged while one was blocked. This result demonstrated great potential of nanocellulose materials as cardiovascular bypass implants [58,82].

NANOCELLULOSE TECHNOLOGY MARKET

The commercial development of nanocellulose over the past few years has grown dramatically as evidenced by its use in a wide range of industries, including pharmaceuticals, food, cosmetics, paint, and paper. Some nanocellulose products have become commercially available as food or cosmetics thickener, artificial blood vessels, and wound dressing. According to the report by FP Innovations [83], nanocellulose-based polymer composites and antimicrobial dressings will be released to the market in the near future. The total market value in North America alone was estimated to be \$250 million by 2020.

CONCLUSIONS

Considerable evidence implicates the great potential of nanocellulose for biomedical applications, including wound healing and tissue repair. The excellent biocompatibility of bacterial nanocellulose has been proven in animal models and clinical trials. Despite the demonstrated application of plant-derived CNF for tissue engineering, its biocompatibility needs further assessment. In addition to their biomedical application, commercially available CNF and CNC have been used as reinforcing fillers for polymer composites. Surface modification has been proposed to improve the dispersion of nanocellulose within polymer matrix and the mechanical property of the resulting composites. Unfortunately, previously reported modifications have resulted in limited enhancement, especially the tensile strength of the composites. As such, future studies are necessary to shed a light on the interaction between nanocellulose and polymers and to develop unique surface chemistry to reach its theoretical prediction as a reinforcing filler. **TJ**

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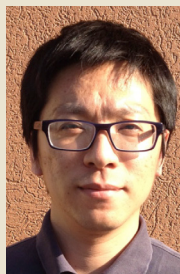
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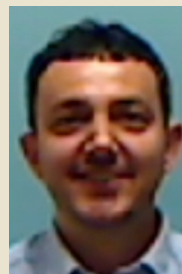
Nanocellulose is an emerging research area with a promising future. This paper is complementary to Ozcan's previous research projects on composites. We found that water uptake of cellulosic materials is a challenging issue that has been addressed using surface modification.

Research on nanocellulose is continuing. When the applications arise from nanocellulose research, it will lead to totally new areas for mills. The next step is to investigate further possibilities for high volume applications of nanocellulose.

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