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Editorial

Nanocellulose-based Materials for Biomedical Applications

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EDITORIAL

Cellulose is the most abundant terrestrial polymeric material in nature composed of β-D-glucopyranose units linked by β-(1-4) glycosidic bonds. Due to its characteristics of broad availability, biodegradability, biocompatibility, and renewability, cellulose can be used as sustainable materials for biomedical and industrial applications such as packaging, hygiene, paper, films, membranes, tissue engineering, hydrogels, and aerogels. Currently, the study of nanoscale celluloses attracts much attention because nanoscale celluloses combine several unique properties including large surface area, attractive strength and stiffness properties, hydrogen-bonding capacity and eco-friendliness [1]. Depending on the preparation procedure nanocelluloses can be classified into four main categories: cellulose nanocrystals (CNC), nanocellulose balls, cellulose nanofibrils (CNF), and bacterial nanocellulose (BNC) [2-4].

The primary parameters of different nanocelluloses were listed in Table 1. As shown, the main procedure for CNC production is based on acid hydrolysis. Acid treatments can remove the amorphous region of purified cellulose fibers leaving behind crystalline cellulose that is resistant to the acid attack. This process yields rigid and rod-like cellulose crystals with approximate dimensions of 100-200 nm in length and 5-60 nm in width [2]. Nanocellulose balls have been prepared by using a combination of cellulose swelling reactions followed by acid hydrolysis and yielding spherical-like structures [5]. CNF is prepared by delamination of cellulose pulps through mechanical treatments such as using high-shear homogenizers or micro fluidizers [6]. CNF is more flexible and longer than CNC with lengths of 100 nm to several micrometers and widths of approximately 5-60 nm [7]. The energy costs of CNF have been a serious commercialization challenge that is being addressed using either an enzymatic and/or chemical pretreatment to help reduce fibrillation energy requirements. BNC can be made from several carbon sources (e.g. glucose) by a biotechnological assembly process via select microorganisms, mainly the genus *Gluconacetobacter*. BNC has opened a number of new application fields due to its unique nano fiber architecture, such as homogeneous three-dimensional network and web-like network [4].

Nanocellulose-based materials have shown a great potential in medical and pharmaceutical applications due to their biodegradability, biocompatibility, low-cytotoxicity, porosity, and desirable mechanical properties [8]. A promising field of research is to use the 'solubility' properties of CNC as a drug delivery platform. Dash and Ragauskas utilized the surface hydroxyl groups of CNC to oxidized C2 and C3 glucose units and then graft gamma aminobutyric acid to the aldehyde units as a linking arm [9] and since this publication, several other routes have been explored [10]. Nanocellulose scan mimic an extracellular matrix (ECM) and promote tissue growth which can act as cell carriers with suitable mechanical support and have the ability to generate tissues and organs possessing biological structures and functions [11]. In addition, nanocellulose hydrogels [12] and aerogels have been developed for a variety of biomedical applications such as vascular grafts, artificial skin, blood vessels, and implantable scaffolds [13].

The fabrication procedures of nanocellulose aerogels presented in Figure 1 can be used to prepare porous nanocellulose-based materials which have the potential for wound dressing and scaffolds [14]. In recent studies, the application of nanocellulose-based materials in the biomedical fields, such as tissue engineering, has gained tremendous attention due to the aforementioned advantages. The fabrication of nanocellulose/hydroxyapatite composites through various methods has successfully generated a porous scaffold with 4.91MPa of compressive strength, 650% water sorption ability, and similar nature bone hydroxyapatite ratio [15]. The strong mechanical properties, high water sorption, and osteogenesis capability indicated this porous scaffold has the potential to be used as bone substitutes. The blending of nanocellulose and cellulose acetate propionate followed by casting led to a 200 μm film with twofold improvement in tensile stress at body temperature which could be used in the vascular engineering of small diameter grafts [16]. TEMPO generated CNF has been used as scaffold in a cell culture study which contributed less than 5% cell death without cell toxicity after 72 h incubation of cells. Moreover, up to 447 times of water could be absorbed and retained in this 3D TEMPO-CNF scaffolds, revealing the nanocellulose scaffolds have the ability to maintain a moist environment and suggesting it can act as a non-toxic and biocompatible wound healing scaffold [17]. Similarly, cross-linked nanocellulose/collagen composite aerogelsas a wound dressing material have also showed good biocompatibility,

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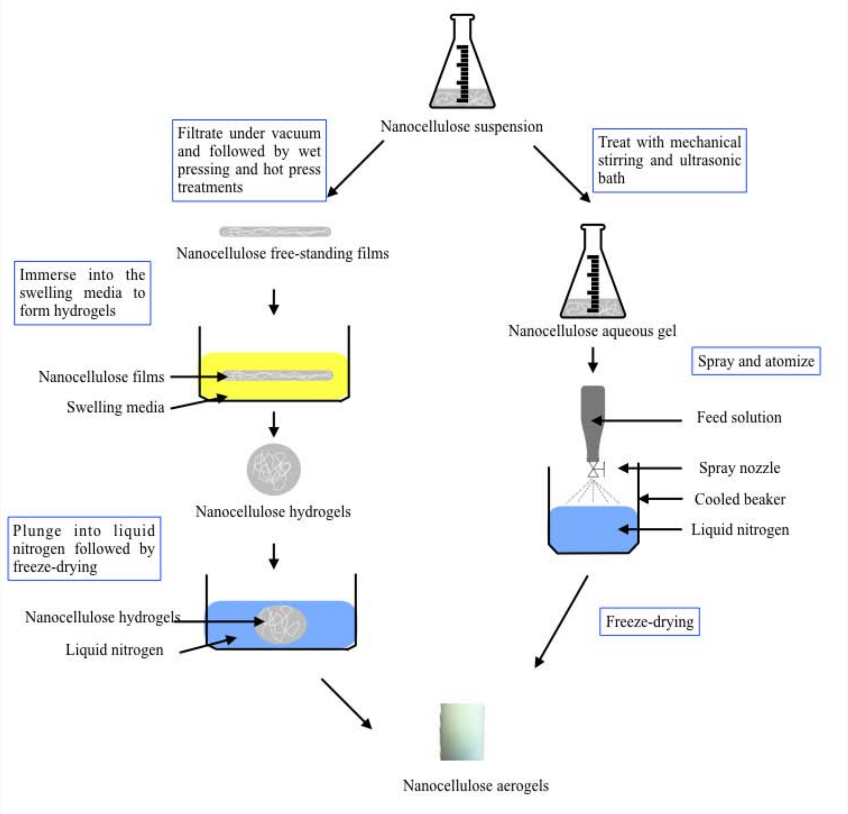

Figure 1 Fabrication procedures for nanocellulose aerogels.

Table 1: Classification of nanocellulose.

Type of nanocellulose	Synonyms	Typical Sources	Approx. Dimensions
Cellulose nanocrystals (CNCs)	Nanocrystalline celluloses, cellulose nanowhiskers	Wood, plant cell walls, bacteria, and etc.	5-50 nm in width; 100-200 nm in length
Cellulose nanofibrils (CNFs)	Microfibrillated celluloses, nanofibrillated celluloses	Wood pulp, kraft pulp, soybean stock, wheat straw, and etc.	5-60 nm in width; 100 nm to several micrometers in length
Nanocellulose balls	-	Cotton Wood pulp	50-300 nm in diameter
Bacterial nanocelluloses (BNCs)	Bacterial cellulose, biocelluloses	Low-molecular-weight sugars	20-100 nm in width with different types of nanofiber architecture

high level of cell activity and proliferation, up to 4000% water sorption and 90% to 95% porosity range [11]. Porosities of nanocellulose scaffolds are highly dependent on temperature and pH of swelling environment (e.g. 99.7% porosity at 50 °C, pH7 vs. 93.5% porosity at 25 °C, pH3) [14]. The ability to control porosity using directional freezing and lyophilization opens a new methodology to generate porous nanocellosics structures [18,19]. Furthermore, the porous structure of nanocellulose hydrogels/aerogels could influence gases diffusion, nutrients transportation, and metabolic waste education in cell culture, which plays an important role in biomedical applications.

In summary, nanocellulose-based materials are now recognized as unique materials that can be used to prepare unique composites, films, foams, and gels that exhibit unique properties as an alternative to petroleum-based materials with environmentally friendly and renewable characteristics. The studies in mechanical performances, biocompatibility, and biodegradability showed that nanocellulose-based materials have a variety of promising applications in biomedical fields. These recent studies have illustrated several innovative and promising nanocellulose-based materials in biomedical applications, and although studies of long-term biocompatibility between nanocellulose and biological needs to be explored, the results to-date point to a promising future.

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