

Cellulose Nanomaterials and its Applications: Mini Review

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Abstract

Cellulose nanomaterials have emerged as a groundbreaking and versatile class of materials with profound applications in both the biomedical and packaging sectors. This mini-review concentrates on the specific applications of cellulose nanomaterials in the biomedical and packaging fields. Cellulose nanomaterials, established for their innovative and multifunctional characteristics, are particularly emphasized for their applications in the biomedical sector, where they are utilized for their exceptional biocompatibility and low toxicity. These applications span from advanced drug delivery systems, enhancing therapeutic efficacy through controlled release, to scaffolds in tissue engineering that promote cell proliferation and differentiation. In the context of sustainable packaging, these nanomaterials contribute significantly to improving mechanical strength and barrier functionality, aligning with the growing demand for environmentally friendly packaging solutions. This review focuses on the latest research and development advancements in the utilization of cellulose nanomaterials, highlighting their bespoke applications that address the unique needs of these sectors. By focusing on these specific areas, the review underlines the tailored impact and prospective advancements of cellulose nanomaterials, reinforcing their vital role in advancing biomedical innovations and sustainable packaging technologies.

Keywords: Cellulose Nanomaterials; Drug Delivery; Tissue Engineering; Wound Healing; Sustainable Packaging

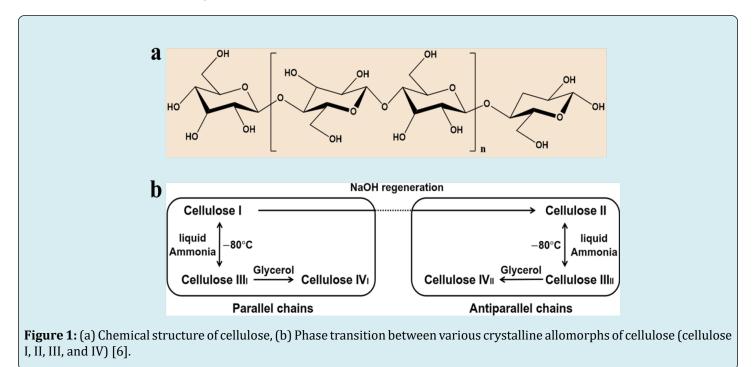
Abbreviations: CNCs: Cellulose Nanocrystals; CNFs Cellulose Nanofibrils; TEM: Transmission Electron Microscopy.

Introduction

Cellulose, the most abundant renewable polymer on Earth, is projected to have an annual production of 75 billion tons. This versatile, amphiphilic polysaccharide boasts exceptional physicochemical properties, making it highly suitable for a broad range of applications. Its low cost, plentiful availability, rich surface chemistry, biodegradability, biocompatibility, and eco-friendliness distinguish it as a sustainable alternative to materials derived from fossil fuels [1-5]. For millennia, cellulose has played a crucial role in various industries, especially in paper and textiles, and continues to be a staple globally. Its molecular structure comprises linear β -D-glucopyranose units linked by β -1,4 glycosidic bonds. The abundance of intra- and intermolecular hydrogen bonds grants cellulose various structural forms.



In its crystalline state, cellulose fibers are tightly packed due to an organized hydrogen bonding network, making them strong, water-insoluble, and resistant to many organic solvents. This organization provides cellulose with its high stiffness and mechanical strength, whereas the less ordered amorphous regions offer flexibility. Cellulose exhibits different polymorphic forms—cellulose I, II, III, IV, etc. based on molecular orientation and interactions, which can change through thermal and chemical treatments [6]. These polymorphs exhibit a crystallinity index ranging from 40-70%, influenced by the cellulose source and extraction method (Figure 1). The crystalline areas are robust against mechanical, chemical, and enzymatic actions, while the amorphous regions are more reactive. Cellulose is sourced from natural plants like wood, cotton, and hemp, or through microbial means from bacteria, algae, or fungi, with woodbased cellulose being the most common. The properties of cellulose are determined by its origin, age, pretreatment methods, and processing conditions. The preparation of lignocellulosic cellulose involves removing non-cellulosic substances, delignification, and bleaching, which are significant cost factors in cellulose production. These processes break down the tough lignocellulosic structure, enhancing its utility. Unlike plant-derived cellulose, bacterial cellulose doesn't require pretreatment as it lacks lignin, hemicellulose, and extractives.



In recent years, there has been a significant surge in interest in the field of nanotechnology as it pertains to cellulosic materials. Cellulose nanomaterials have gained significant attention in recent years due to their exceptional properties and wide range of applications in various fields. Derived from renewable sources such as wood and plants, cellulose nanomaterials have emerged as a promising alternative to traditional materials derived from fossil fuels. Cellulose nanomaterials are characterized by their nanoscale dimensions, high aspect ratio, and exceptional mechanical properties. These materials possess remarkable strength, stiffness, and flexibility, making them suitable for a wide range of applications. Additionally, cellulose nanomaterials are biodegradable, non-toxic, and have low environmental impact, making them more sustainable than many other materials currently in use. In terms of their structure, cellulose nanomaterials are composed of cellulose chains

that are organized into a crystalline form. These chains can be further broken down into cellulose nanocrystals (CNCs) or cellulose nanofibrils (CNFs), depending on the method of extraction. CNCs are rod-like particles with diameters in the nanometer range, while CNFs are long, flexible fibers with diameters ranging from tens to hundreds of nanometers. The unique properties of cellulose nanomaterials make them suitable for a wide range of applications. In the field of materials science, they can be used as reinforcing agents in composites, enhancing the mechanical properties of the resulting materials. Cellulose nanomaterials have also shown potential in the development of flexible and transparent films, which could be used in electronic devices and packaging materials. In the biomedical field, cellulose nanomaterials have been explored for drug delivery systems, tissue engineering scaffolds, and wound healing applications [7]. Their biocompatibility, biodegradability, and ability

to be functionalized with various molecules make them attractive for these applications [7-9]. Moreover, cellulose nanomaterials have demonstrated their potential in the field of energy storage and conversion. They can be used in the development of supercapacitors, batteries, and fuel cells, owing to their high surface area, good electrical conductivity, and ability to store and release energy efficiently [10]. Figure 2a illustrates the molecular structure of cellulose, depicting the repeating cellobiose units connected by β -1,4-glycosidic bonds, and identifies the crystalline and amorphous regions within cellulose fibers, highlighting the intra- and intermolecular hydrogen bonding that contributes to the polymer's rigidity and fibrous nature. Figure 2b presents cellulose nanocrystals (CNCs), which are highly ordered structures typically extracted from larger cellulose sources through acid hydrolysis. The transmission electron microscopy (TEM) image shows distinct, rod-like entities that are characteristic of CNCs. These structures are known for their high strength and stiffness due to the crystalline nature of cellulose, which

is evident from their sharp edges and clear boundaries. Figure 2c displays cellulose nanofibers (CNFs), which are a network of entangled fibrils with a high aspect ratio. The TEM image reveals a web-like structure consisting of long, intertwined fibers. CNFs are produced through mechanical or enzymatic treatments that partially disintegrate cellulose fibers while preserving their fibrous nature. Their network structure provides a large surface area and is conducive to applications requiring robust mechanical properties and high flexibility. Figure 2d depicts TEMPO-oxidized cellulose, a form of nanocellulose that has been chemically modified using the TEMPO (2,2,6,6-tetramethylpiperidine-1-oxyl) oxidation process. This treatment introduces carboxyl groups on the cellulose chain, rendering the fibers negatively charged and thus more hydrophilic and dispersible in water. The TEM image shows a more diffuse and finer network compared to CNFs, indicating the effect of TEMPO oxidation in breaking down the fibers into finer structures.

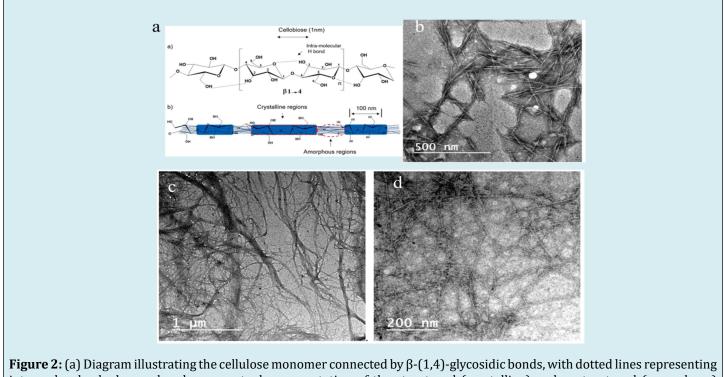


Figure 2: (a) Diagram illustrating the cellulose monomer connected by β-(1,4)-glycosidic bonds, with dotted lines representing intramolecular hydrogen bonds; conceptual representation of the structured (crystalline) and unstructured (amorphous) areas within cellulose nanofibrils [11]. (b) TEM of cellulose nanocrystals [9], (c) TEM of cellulose nanofibers and (d) TEM of TEMPO oxidized cellulose nanofibers [12].

Properties of Cellulose Nanomaterials

Cellulose nanomaterials such as CNCs CNFs, are observed for their exceptional properties, largely attributable to their nanoscale dimensions and the intrinsic characteristics of cellulose [13-18]. These materials exhibit remarkable mechanical strength and stiffness, rivaling some metals and synthetic fibers, thanks to the crystalline structure of cellulose, which confers high tensile strength and modulus. Their surface is rich in hydroxyl groups, enabling extensive chemical modification to tailor their properties for specific applications, ranging from drug delivery to materials science. In terms of thermal behavior, cellulose nanomaterials demonstrate considerable stability, which is crucial for their application in areas requiring high-temperature processing. Optically, the ordered structure of CNCs, in particular, allows for unique light diffraction properties, while the transparency of CNFs is beneficial for applications in optically clear composites. Furthermore, the dense hydrogen bonding network within these materials imparts excellent barrier properties, making them ideal for packaging applications to protect against gases, aromas, and oils. Their biocompatibility and biodegradability are perhaps among their most attractive attributes, aligning with an increasing demand for environmentally friendly and sustainable materials, especially in the biomedical field. Additionally, the rheological properties of cellulose nanomaterials can be exploited to modify the viscosity and gelation behavior of various substances, which is critical in industries such as food, cosmetics, and pharmaceuticals. Overall, the multifaceted properties of cellulose nanomaterials underscore their versatility and potential in a wide array of applications, driving continued research and innovation in this dynamic field [19-22].

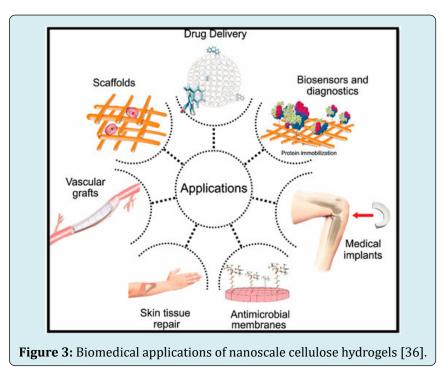
Applications of Cellulose Nanomaterials

Food Packaging Applications

Cellulose nanomaterials have found significant applications in the packaging industry, capitalizing on their unique properties to address some of the critical challenges faced by this sector. The demand for sustainable, strong, and effective packaging materials has led to the exploration and incorporation of cellulose nanomaterials as either additives or coatings in packaging solutions [23,24]. One of the primary applications of cellulose nanomaterials in packaging is the enhancement of mechanical strength. When added to paper, plastic, or biopolymer matrices, these nanomaterials are distributed within the matrix, creating a reinforcing effect that improves the tensile strength and toughness of the packaging material [25,26]. This increased strength is particularly beneficial in reducing the damage rates during transportation and handling, thereby extending the lifecycle of the packaging and the safety of the contents. Another critical attribute of cellulose nanomaterials is their ability to enhance barrier properties in packaging materials. They can significantly reduce the permeability of the material to gases like oxygen, carbon dioxide, and water vapor, as well as to oils and other substances [27]. This is crucial for preserving the freshness and extending the shelf life of food products, as well as protecting sensitive electronics or pharmaceuticals from moisture and other environmental factors. The nanoscale dimensions of cellulose particles allow them to form a tight, impermeable network when integrated into packaging films, which acts as a barrier against external agents. With increasing environmental concerns and the push for sustainable development, the biodegradability of packaging materials has become a paramount factor [28,29]. Cellulose nanomaterials are derived from renewable resources and are inherently biodegradable, making them an eco-friendly alternative to conventional petroleumbased packaging. When used in packaging materials, they contribute to the creation of products that can be composted or degraded naturally, reducing waste and the carbon footprint of the packaging industry. Water Coating packaging materials with cellulose nanomaterials can significantly improve their water resistance. This is especially important for paper-based packaging, which is prone to water damage. The cellulose nanomaterial coatings create a barrier on the surface of the packaging, preventing water penetration and protecting the contents. This water resistance can be crucial for extending the range of applications for paper-based packaging, making it suitable for more humid environments or for containing moist or liquid products. The use of cellulose nanomaterials in the packaging industry offers a multifaceted approach to enhancing packaging performance. By improving the mechanical strength, barrier properties, and water resistance, while also ensuring biodegradability, cellulose nanomaterials contribute to the development of advanced, sustainable packaging solutions. As research progresses and the scalability of cellulose nanomaterial production improves, their role in the packaging industry is set to expand, offering new opportunities for innovative and environmentally responsible packaging designs [30,31].

Biomedical Applications

Cellulose nanomaterials have garnered significant attention in the field of biomedicine, where their unique properties offer numerous applications, particularly in drug delivery systems, wound healing, and tissue engineering [32]. The biocompatibility and low cytotoxicity of these materials make them ideal candidates for various medical applications, where they can interact beneficially with biological systems without inducing adverse reactions [33]. In the realm of drug delivery, cellulose nanomaterials are particularly valued for their ability to be engineered with controlled release profiles. Due to their high surface area and reactive surface chemistry, these nanomaterials can be loaded with therapeutic agents, either through physical adsorption or chemical conjugation. The release of drugs can be finely tuned by modifying the properties of the cellulose nanomaterials, such as their degree of crystallinity, particle size, or the chemistry of the surface modifications. This controlled release is crucial for maintaining therapeutic drug levels in the body, minimizing side effects, and improving patient compliance [34]. For wound healing, cellulose nanomaterials offer a promising avenue due to their ability to form biocompatible and biodegradable films or gels that can conform to wound sites (Figure 3) [35].



These materials can provide a protective barrier against infection, maintain a moist environment to facilitate healing, and support the growth and migration of skin cells. Additionally, cellulose nanomaterials can be functionalized with antimicrobial agents or growth factors to further promote healing and tissue regeneration. Their natural origin and ability to degrade into non-toxic products align well with the requirements for materials to be used in wound dressings. In tissue engineering, cellulose nanomaterials can be utilized to create scaffolds that support the growth and differentiation of cells, aiding the formation of functional tissue. The nanofibrous structure of these materials closely mimics the extracellular matrix of tissues, providing an ideal environment for cell attachment and proliferation [6]. The mechanical properties of the scaffolds can be tailored to match those of the target tissue, ensuring structural support while also promoting cellular activities. Furthermore, the porosity and degradation rate of the scaffolds can be controlled, which are critical factors for nutrient transport and the gradual transfer of mechanical load to the developing tissue. The applications of cellulose nanomaterials in biomedicine are vast and varied, offering innovative solutions to longstanding challenges in drug delivery, wound healing, and tissue engineering. Their natural origin, coupled with their impressive array of tunable physical and chemical properties, positions them as a valuable resource in the ongoing development of advanced biomedical technologies. As research continues to evolve, the potential for cellulose nanomaterials in the medical field is expected to expand, further underscoring their significance in advancing healthcare and therapeutic strategies.

Various Other Uses of Cellulose Nanofibers

The other uses of cellulose nanofibers span a remarkable array of applications, reflecting their versatility and potential in cutting-edge technology and innovation. In the field of energy, they are pivotal in the development of storage devices [37], where their unique properties enhance the efficiency and durability of batteries and super capacitors [10]. Their flexibility and conductivity make them ideal for flexible electronics, enabling the creation of wearable devices and foldable screens that require materials that can withstand bending and twisting. In transportation, cellulose nanofibers contribute to the advancement of conductive films, essential for touchscreens and other interactive technologies. Their lightweight yet strong nature offers significant benefits in aerospace and automotive industries, where reducing weight without compromising strength is crucial [38]. Moreover, cellulose nanofibers are integral to advanced composites, enhancing the strength, durability, and functionality of materials used across various sectors, including construction, sports equipment, and protective gear. Their role in energy applications extends to solar cells and fuel cells, where they contribute to the efficiency and effectiveness of these renewable energy technologies [32,39]. Table 1 presents a summary of cellulose nanofiber applications in various nanocomposite materials, outlining the types of materials, their production processes, forms, and specific uses, complemented by reference numbers for in-depth exploration.

Materials	Fabrication	Form	Applications	Ref.
BC-CTS	Submerging bacterial cellulose in chitosan and subsequently undergoing lyophilization.	Membrane	Wound dressing	[40]
Cellulose nanofibers	Filtration technique	Membrane		[41]
CNF	Autoclaving with sodium hydroxide followed by oxidation mediated by TEMPO.	Gels		[42]
BACNF/QCR	Exchange of cations followed by lyophilization.	Sponge		[43]
Cellulose Nanofibrils/ Polyvinyl Alcohol/Sodium Alginate Hydrogels	T-CNFs combined with Alg and PVA formed a stable mineralized hydrogel.	Hydrogel		[7]
T-CNF-graft-SPH	SPH was bonded to T-CNF through carboxyl group amidation	Bio-composites	Bone regeneration	[44]
CNC/polyacrylamide composite	The expansion process increases the helical pitch in the chiral nematic structure.Top of Form	Composite		
Nanocellulose/TiO ₂	Nano-cellulose from microcrystalline cellulose was used to create mesoporous TiO ₂ .	Nanocomposites	Catalytic activity	[45]
Nanocellulose/Pd NPs	-	Nanocomposites		[46]
Surface functionalized BC/Au NPs	AOBC was created with a simple two- step method, preserving the original structure of bacterial cellulose.	-		[47]
Nanocellulose aerogels/ methyl aluminoxane	NC aerogels, created by freeze- drying CNF and impregnating with methylaluminoxane.	Aerogels	Catalytic activity Fuel cell Electrical materials Solar cell	[48]
Nanocellulose/ZnO	-	Nanocomposites		[46]
BC/Pt NPs	Platinum (Pt) nanoparticle deposition on bacterial cellulose membranes (BC) for fuel cell use.	Membrane		[49]
TOCNs/carbon nanotube	Ultrastrong, transparent, conductive nanocomposites were made by combining CNTs with TOCNs, featuring sodium carboxyl groups on their surfaces.	Composites		[50]
CMFS/tin-doped indium oxide thin layer	Flexible, conductive nanopaper aerogels were made using CNT and cellulose nanofiber dispersions.	Aerogels		[51]
Nanocellulose/Au NPs	-	Composites	Biosensors	[46]
CNC _s /Ag NPs	Ag nanoparticles were produced using carboxylated cellulose nanocrystals and NaBH4 reduction.		Electrical materials	[52]
PDDA–CNC _s /Au NPs	Au nanohybrids were synthesized on PDDA-CNC supports through self-assembly between negative Au precursors and PDDA-CNC's positive charges.	Nanohybrids	Solar cell	[53]

Table 1: Outline of some uses of cellulose nanofiber in different polymer-based nanocomposites.

Challenges and Future Perspectives

Cellulose nanomaterials offer a wealth of potential across various fields, yet their journey from the laboratory to widespread industrial application is fraught with challenges. Scaling up production to meet industrial demands remains a significant hurdle, as processes that are effective on a small scale often encounter efficiency, consistency, and quality control issues when expanded. The cost of manufacturing these nanomaterials also poses a challenge; for cellulose nanomaterials to become a viable alternative to conventional materials, their production costs must be competitive. This necessitates innovations to reduce expenses related to raw materials, energy consumption, and specialized equipment. Moreover, the lack of standardized manufacturing protocols complicates the assurance of uniformity in the nanomaterials' properties, which is crucial for their application across diverse industries. Despite these challenges, the future looks promising for cellulose nanomaterials, with ongoing research aimed at overcoming these obstacles. Technological advancements are expected to enhance production processes, making them more efficient and cost-effective, while also allowing for the customization of nanomaterials for specific applications. As the field matures, we anticipate broader integration of cellulose nanomaterials into various sectors, driven by their sustainable and versatile nature, which aligns with the global push towards greener and more sustainable industrial practices.

Conclusion

This review has highlighted the significant advancements and potential applications of cellulose nanomaterials in key areas such as biomedical engineering and sustainable packaging. These materials, derived from the most abundant renewable polymer on Earth, offer exceptional properties that are being harnessed to drive innovations and provide solutions to critical challenges in various industries. Their biocompatibility, mechanical strength, and environmental sustainability position them as ideal candidates for a range of applications, from enhancing drug delivery mechanisms to revolutionizing packaging materials. The future of cellulose nanomaterials is bright and promising. There are, however, challenges along the way, particularly in terms of scalability, cost reduction, and standardization of material properties. Researchers and technologists are pivotal in overcoming these obstacles, which facilitates the transfer of cellulose nanomaterials from research labs to industry.

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