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Mini Review

Nanocellulose: A potential and versatile 'Biomaterial' for futuristic research

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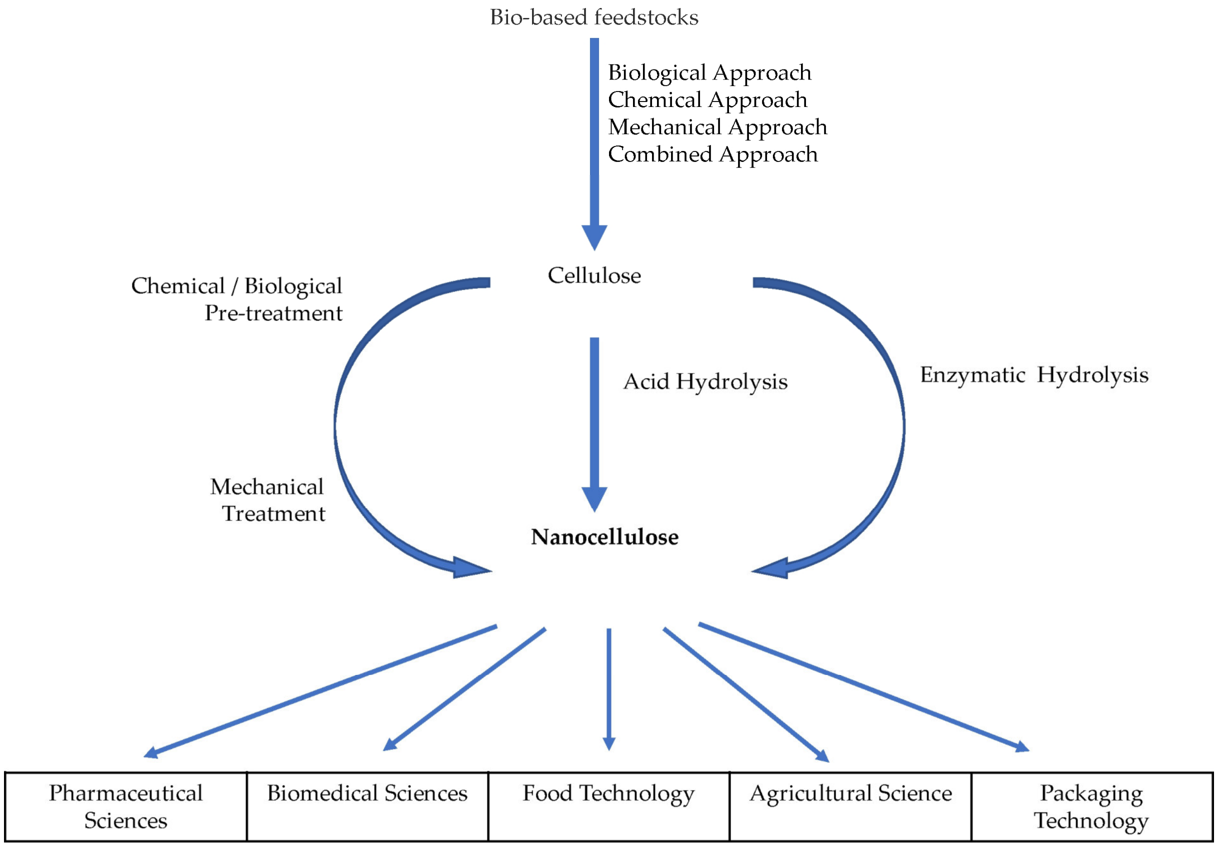
Graphical Abstract



Abstract

Nanocelluloses are unique biomaterials with combined potential characteristics of cellulose with added features of nanomaterials. Cellulose is one of the most abundantly available natural biopolymers with a wide range of applications in the Pharmaceutical, Biomedical and Agricultural fields. Cellulose from natural sources can be modified by acid hydrolysis or by enzymatic treatment to develop nanostructured cellulose. Based on the condition and method of processing cellulose, nanostructured forms of cellulose can be categorised as nanocrystals and nanofibers. Nanostructured cellulose has created much interest among formulation scientists due to its renewability, biocompatibility, recyclability, least toxicity, better mechanical properties and tunable surface characteristics. Though various methods have been discovered for developing nanocellulose, it still possesses formidable challenges in extraction and modification.

Keywords: nanofibers; nanocrystals; bacterial nanocellulose; featured biomaterial.

Introduction

Over the last few decades, natural polymers have received much attention from pharmaceutical scientists due to their biocompatibility, inertness, ready availability, and cost of production. Applications of natural polymers such as starch, cellulose, and collagen as key materials in drug delivery systems have gained prominence due to their versatility and wider applications [1-3]. Cellulose is one of the most abundantly available natural biopolymers having a wide range of pharmaceutical applications. Cellulose can be used in its native form or as physiochemically modified composites [4]. Over the past few years, a nanostructured form of cellulose has created much interest among formulation scientists due to its renewability, biocompatibility, recyclability, least risk of toxicity, better mechanical properties, and tunable surface properties [5-7]. based on the condition and method of processing of cellulose, a nanostructured form of cellulose (Nanocellulose) can be categorized as nanocrystals and nanofibers. Cellulose in nanocrystalline form is small, rigid. In contrast, nanofibers are long and flexible [8]. Development of Nanocellulose from Cellulose involved two steps: pre-treatment of feedstock to obtain pure cellulose and transformation of cellulose to nanocellulose [7].

Nanocellulose can be prepared by liberating crystalline regions of the semicrystalline cellulosic fibers by hydrolysis with mineral acids. It includes the removal of polysaccharides bound at the fibril surface, followed by cleavage and destruction of the more readily accessible amorphous regions to liberate rodlike crystalline cellulose sections. It will be subjected to various pre-treatments to remove debris other than cellulose, such as hemicelluloses, lignin, fat, wax, and pectins surrounding the cellulosic structure. Other methods include Alkali pre-treatment, which involves removing a certain amount of lignin, wax, and oils covering the external surface of the fiber cell wall. Lignin will be structurally destroyed and helps separate lignin and carbohydrates by using sodium hydroxide in a 17-18% concentration. Another method involves the use of TEMPO, which is chemically 2,2,6,6-tetramethylpiperidinyl-1-oxide. Another method utilizes Enzymatic pre-treatment of cellulose, which will not be degraded by a single enzyme but needs two enzymes called as Cellulase-A and Cellulase-B, C, and D type of Cellulases, which are also referred to as endoglucanases Cellobiohydrolases which attack highly crystalline cellulose. In contrast, endoglucanases need a structurally distorted to bring in the degradation of cellulose. The nano cellulose can also be prepared using modified grinders of specially designed disks that can fibrillate cellulose fibers. Cryocrushing is another popular method of preparing nanofibers where fibers will undergo crushing in the presence of liquid nitrogen with a high rate of shearing forces. Hepworth and Bruce developed a mechanical method of preparing highly refined fine nanofibrils measuring 50-1000 nm in diameter. A mechanical method of preparing nanofibers is Refining, and High-pressure Homogenization consists of forcing a dilute fiber suspension through a rotor and a stator using a disk refiner. The mechanical treatment method gives irreversible changes, thereby improving bonding potential due to its morphological modification and size. Ultrasound technology uses ultrasonic waves from 20 KHz to 10 MHz generated by a transducer, transforming mechanical and electrical energy into acoustic energy. These high-energy ultrasonication waves can produce very strong mechanical oscillating power due to cavitation. This physical phenomenon includes the formation, expansion, and implosion of microscopic gas bubbles when the molecules in a liquid absorb ultrasonic energy. Within the cavitation bubble and the immediate surrounding area experience violent shock waves are produced that soar the temperatures up to 5000 °C and pressure of more than 500 atm at the implosion site [7].

Nano cellulose can also be derived from various bacterial sources Bacterial cellulose (BC). Bacterial nanocellulose are of high purity and very crystalline nature [8]. Bacterial nanocellulose (BNC) is derived from the Gram-negative bacteria Acetobacter xylinum (Glucanacetobacterxylinus). Archromobacter, Acetobacter, Alcaligenes, Sarcina, Pseudomonas, and Rhizobium are microbial sources capable of producing nanocellulose. Some other natural sources for nano cellulose include Maize cob, cotton, wheat bran, banana leaves, sugar beet, wood, potato tuber, and mulberry husks are potential plant sources for nanocellulose extraction [9].

The nanocellulose is the safest, most versatile biomaterial with multiple applications, including constructing tissue replacements, tissue regeneration, tissue repair, substitute implants, biosensing, drug delivery, hemodialysis membranes, and absorbable hemostats. The nano cellulose can also be used as a "Pickering Agent" that stabilizes emulsions in place of common surfactants; these tend to get adsorbed onto the emulsion droplets lowering the interfacial tension and also coating individual particles and preventing flocculation and coalescence [7].

Due to its versatility, nano cellulose is readily used in flexible electronic components due to its mechanical flexibility, lightweight, and durability. The flexible substrates of nanocellulose are a critical component for these applications and ultimately decide the device's performance. Apart from this, nanocellulose is used in the manufacture of a wide variety of electronic components like Various electronics with nanoocellulose-based transistors, solar cells, touchscreens, organic light emitting diodes (OLEDs), and self-powered human-interactive transparent flexible systems. They find their application in what is said as skin electronics are flexible, stretchable, and even self-healing electronics that can adhere seamlessly to human skin, and have been proposed for many promising applications in medical diagnostics, autonomous artificial intelligence (e.g., robots), and biomimetic prosthetics. Photodetectors are critical elements in monitoring or sensing various environmental conditions. However, preparing non-toxic, transparent, and biodegradable photodetectors is questionable for medical and environmental monitoring applications—the rapid advancement in research. Park *et al.*, in their research, made a significant breakthrough by using nano cellulose-based films as substrates which are cheap and eco-friendly disposable sensor systems with stable and dependable electric performance when subjected to mechanical bending tests. Nanocellulose-based thin film transistors (TFTs) used in displays have drawn significant scientific interest. These are generally fabricated in two stages physical vapor deposition (PVD) and thermal annealing. PVD helps in the deposition of various active materials onto the substrates, and the thermal annealing operating at a temperature of 300ºC markedly enhances the device's performance. In recent years, nano cellulose film has proved itself as a novel, biodegradable, and cheap ionomer membrane for both polymer electrolyte fuel cells and direct methanol fuel cells with excellent gas barrier properties and good mechanical properties, biodegradability, low cost, and acidic oxygen functional groups. Nanocellulose- based film is a novel green substrate for solar cells due to its tunable physical and chemical performance and low cost. Nanocellulose hence can be regarded as a substance with multiple applications, and yet another application is the development of the "Nanogenerator". It can convert mechanical energy into electricity, which is ideal for compact electronic devices and is regarded as an alternative powerhouse. Two types of nanogenerators are available based on the mode of electricity generation: Triboelectric nanogenerators (TENGs) and Piezoelectric nanogenerators (PENGs) [10].

Cellulose nanocrystals can be employed as a filler material in polymer matrices to enhance their strength. Conventional polymers show poor strength, which renders them a poor choice for most structural applications, hence requiring the support of fillers to reinforce them. Incorporating cellulose nanocrystals at lower concentrations showed enhanced nano-size thermal and physical properties and their ability to absorb stress from the matrix. Nanocellulose also finds its application in bioimaging, wound healing, scaffolds for tissue engineering, and controlled drug delivery [11].

Nanocellulose can also be used for bone regeneration (Bone graft), commonly seen in elderly individuals where significant bone loss occurs due to infections, trauma, and tumors. Hence an ideal bone graft should -initiate the differentiation and growth of the cellular components of the bone, that is, osteoblasts; it must help in bone growth in the required areas, and it must integrate with the new bone growth with that of the surrounding bone. It should initiate the deposition of calcium phosphate crystals, considered the most important components of bone; it must actively contribute to forming blood vessels that nourish novel osteogenic cells. Acyclovir, a potent antiviral drug, can control the replication of herpes simplex, which causes diseases such as herpes labialis and herpes Zoster. In order to impart a desired therapeutic effect, acyclovir is administered by oral route with larger and multiple doses, which results in severe side effects. In order to curtail this menace, acyclovir was delivered as a hydrogel made up of nanocellulose and beta cyclo dextrin, and acrylic acid, which is a combination of excellent biocompatibility, biodegradability, and low immunogenicity and its ability to swell. Nanocellulose in NFC aerogel has been loaded with the hydrophilic drug bendamustine, a nitrogen mustard compound that is an alkylating antineoplastic agent. Bendamustine is a drug of choice in treating chronic lymphocytic leukemia, multiple myeloma, and non-Hodgkin's lymphoma. NFC (nanofabricated cellulose) is preferred because of its flexibility, elasticity, low toxicity, ability to swell in water, and ability to carry hydrophilic compounds. Nanocellulose, due to its strong mechanical properties, is used in dentistry as a filler in many dental materials and composites. Glass ionomer cement (GIC) is readily used in restorative dentistry, and timely modification of its properties offers good flexibility in clinical applications. Even if international bodies recommend GIC cement as the most versatile restorative material, much scientific research is improving its wear resistance and compressive and diametric tensile strength. New GIC formulations are being developed to make use of NFC as an effective reinforcing agent in restorative dentistry [12].

The nano cellulose membranes are synthesized using different methods, both physical and chemical modification. Different grades of nano cellulose like CNF, CNC, or BNC could be turned into membranes or incorporated in fabricating other types of membranes as additives. We can incorporate different groups like Carboxyl, carboxylate, amino, thiol, silanol groups, also nanoparticles to impart surface charges and improve reactivity for effective interactions with the pollutants in water. The efficiency of nanocellulose membranes was fortified with other organic or inorganic additives, producing additive effects which could not be exhibited by nanocellulose alone. Nanocellulose membranes exhibit high porosity, improved hydrophilicity/improved hydrophobicity, good mechanical strength, outstanding chemical resistance, and antifouling properties, which are the benchmarks for their commercial applications in the future. The inorganic nanoparticle-loaded nano cellulose membranes could serve as a thrust area of research that could be investigated for additional improved functionality. The literature review states that the flux and separation efficiency of fabricated membranes could be improved by incorporating a small quantity of nano cellulose which showed improved efficiency. Hence, we can confidently state that "Nanocellulose," even in moderate concentration, will be the material of choice in the membrane industry in the future. The versatile nanocellulose, which can also be regarded as a sustainable material, is being used in the experimental stage in the separation of carbon dioxide, isolation and extraction of DNA, surgical dressings, and development of batteries for a wide variety of applications will make it a much sought after polymeric material which exhibits a broad spectrum of applications [13].

Nanocelluloses are unique biomaterials that combine the potential characteristics of Cellulose with features of nanomaterials [14]. Due to its eco-friendly and economy with a wide range of applicability, nano cellulose is placed as the next-generation material for pharmaceutical and biomedical industries [15,16]. Although having potential applications in pharmaceuticals and biomaterials, an in-depth toxicological evaluation of nanocellulose has to be conducted. In addition to clinical trials and IVIVC, the life cycle of nanocellulose needs to be assessed [17-18]. Biomass processing from natural origin to obtain nanocellulose may also lead to nano-scale impurities. Hence, harsh techniques such as acid hydrolysis need to replace by eco-friendly extraction techniques like enzymatic hydrolysis [16,18].

Conclusion

In conclusion, nanocellulose is a potential biomaterial with a huge spectrum of applications in biomedical engineering and pharmaceutical sciences. Various methods have been developed for the synthesis of nanocellulose. However, researchers and polymer scientists still need to solve cellulose extraction and various modifications. By assessing risk factors and adopting eco-friendly processing techniques, nanocellulose can be developed as a highly flexible material to overcome various challenges in the pharmaceutical and biomedical research field.

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